Cryptosporidiosis

Cryptosporidiosis is the infection in humans and animals with *Cryptosporidium* spp., which are protozoan, obligate intracellular parasites. These were first discovered in mice in 1912 and first linked with disease in man in 1976. A single species was first thought to cause disease in man but molecular diagnostic tools have enabled several different species to be identified. \[1\] *Cryptosporidium hominis* is found only in humans and this, together with *Cryptosporidium parvum* (which also infects cattle), are amongst the most common species found in man. \[2\]

It has emerged as an important cause of diarrhoeal illness worldwide, particularly in young children and immunocompromised patients. The clinical problems associated with *Cryptosporidium* spp. are being recognised more widely and the parasite was included in the World Health Organization’s 2004 list of diseases that “exhibit a considerable and increasing global burden and impair the ability of those infected to achieve their full potential, both developmentally and socio-economically.” \[3\]

Pathophysiology \[4\]

Cryptosporidial oocysts when ingested are immediately infectious at quite low doses (10 to 30 oocysts are required to produce human disease). Oocysts attach to cells of the small bowel and invade the cells of the intestine. They become intracellular but extracytoplasmic and are resistant to treatment. The life cycle is completed in the host and large numbers of oocysts are then excreted with the potential to spread the infection. The oocysts are resistant to quite harsh environmental conditions and can resist chlorine levels used in water treatment.

*Cryptosporidium* spp. cause diarrhoea in a number of different ways, including malabsorption. Essentially, all are part of the host response to infection. In normal subjects the infection is confined to the small intestine but in the immunocompromised (for example, AIDS and congenital immunodeficiency) it may spread to the biliary tree.

Epidemiology

- The seroprevalence of antibodies to *Cryptosporidium* spp. is about 25-35% in developed countries and 60% in regions with poor hygiene. Seropositivity indicates past exposure to infection but not necessarily current active infection. \[5\]
- Just under 3,000 cases in England and Wales were reported to the Health Protection Agency in 2011, down from approximately 4,000 in 2008. \[6\]
- Before the advent of highly active retroviral treatment, 10-15% of AIDS patients developed cryptosporidiosis but the incidence has fallen, as have other opportunistic infections with better treatments. \[5\]
- Asymptomatic carriage of the organism is possible and a study of young children in daycare nurseries found 3 out of 230 (1.3%), without any symptoms, were carrying the parasite. \[7\]
- The high prevalence of AIDS in developing countries is associated with a high prevalence of cryptosporidiosis. One study found that 39-60% of HIV-seropositive patients infected with cryptosporidiosis had chronic diarrhoea. \[8\]
- Children with acute leukaemia seem also to be at risk from cryptosporidiosis, particularly those on chemotherapy. \[9\]
- Interestingly, epidemic peaks in incidence have been identified in spring and autumn coinciding with high precipitation. \[10\]
- Studies demonstrated seasonal variations in samples from sea water, river water and underground reservoirs. \[11\]
Risk factors
The risk factors for acquisition of cryptosporidiosis are determined by the modes of transmission. Transmission is:

- Direct from livestock (common).[12] Beware of risk from:
  - Farms or petting zoos (especially in young ruminants).
  - Contact with animal dung (for example, during outdoor recreation).

- From personal contact with infected individuals (who may or may not have symptoms). Beware particularly of the risk within playgroups, nurseries and day centres.

- Waterborne. Note that new standards relating to monitoring of water supply were introduced in 2000 in the UK. This has lowered but not completely eradicated the risk from waterborne infection in the UK.[13] Beware of risk from:
  - Contaminated water supply.
  - Contamination of swimming pools and other water-based recreational sites.
  - Travel to less developed countries.

- Foodborne (unprocessed foods, notably raw milk, meat, shellfish, fresh fruit and vegetables).[14]

- From infected patients in hospital.

Presentation
- The incubation period is dose-dependent and typically 5-10 days. However, it can be less and also up to 28 days.
- Can be asymptomatic in developing countries; rarely so in developed countries.
- The fever is characteristically low-grade and a fever over 39°C should alert to other infections.
- In healthy subjects it presents with:[15]
  - Mild fever (59% of consulting patients).
  - General malaise progressing rapidly to further symptoms.
  - Sudden onset of watery diarrhoea - often green and offensive, sometimes with blood (98% of patients).
  - Abdominal cramps (95%).
  - Nausea and anorexia (65%).
  - Symptoms which are prolonged and last on average for two weeks but can persist for up to one month.
  - Relapse of symptoms, indicating persistent infection - occurs in over a third of cases.
  - Other more protracted symptoms following infection - for example, headaches, dizzy spells, fatigue, and joint pains have been reported, more commonly with *C. hominis*.[16]
  - Illness can be severe enough to necessitate admission to hospital (14% of patients in one study).[3]

Immunocompromised patients
Those patients most at risk are those with:[17]

- T-cell immune deficiency (including those with haematological malignancies - especially children).
- Patients with HIV infection and CD4 counts lower than 200 cells/mm$^3$ (and in particular those with counts below 50 cells/mm$^3$).
- Patients with primary T-cell deficiencies (for example, severe combined immunodeficiency).

Immunocompromised patients:

- Commonly experience more chronic symptoms.
- Have more widespread infection within the gastrointestinal tract, which may involve the pancreatic duct and gallbladder.
- Can experience more profuse diarrhoea with almost cholera-like intensity, accompanied by dehydration, malabsorption and collapse.[18]
- Experience more complications. With biliary complications, right upper quadrant pain and vomiting may be prominent.[18]

Differential diagnosis
This includes the range of other forms of gastroenteritis including:

- *Campylobacter enteritis*
- *Escherichia coli* O157
- *Salmonellosis*
- *Shigellosis*
- *Giardiasis*
- *Viral gastroenteritis*
- *Amoebiasis*

Investigations
- Request stool microscopy for oocysts. However, routine requests may not include microscopy for *Cryptosporidium* spp. It is important to specify this request where infection is suspected. Special tests and staining can be used, including immunofluorescent assays, enzyme-linked immunosorbent assay (ELISA) and the most sensitive polymerase chain reaction (PCR) assays.[2]
- Stool culture.
- U&E; LFTs may be necessary in more protracted infection.
- Other tests of immune function may be required in the immunocompromised (eg, CD4 counts, etc).

Management

Immunocompetent patients
In healthy individuals, the disease is self-limiting and requires no treatment other than routine rehydration measures.

Immunocompromised patients
In malnourished or immunocompromised patients, drug management can be more complicated and should be referred for specialist advice. The aim of treatment is symptomatic improvement and clearance of the infection. Complete clearance of the parasite is unlikely without correction of the immunodeficiency.

- Treatment of the immunodeficiency:
  - In patients with HIV, highly active antiretroviral therapy (HAART) is the treatment of choice. These are given in combination after the antiparasitic drugs, to assist absorption of subsequent antiretroviral drugs.\(^{[19, 20]}\)
  - Protease inhibitors can produce dramatic improvements in clinical response. As well as improving the CD4 cell level and restoring a degree of immunity, they increase oocyst shedding, resulting in a sustained therapeutic effect after follow-up.\(^{[21]}\)
  - In other patients, improving immunity can also lead to improvement. For example, reduction of immunosuppression in transplant patients has been associated with parasite clearance and resolution of complications.

- Specific treatment:
  - Nitazoxanide is not licensed in the UK but is available on a named patient basis. It shortens duration and reduces mortality in malnourished children.\(^{[22]}\)
  - Nitazoxanide is well tolerated with a good safety profile.\(^{[22]}\)
  - Nitazoxanide, paromomycin and azithromycin are only partially effective and results with cryptosporidiosis in AIDS patients remain disappointing.\(^{[22]}\)
  - All the drugs currently available in the UK are of unproven benefit and unlicensed for treatment of cryptosporidiosis. Trials are small and evidence is conflicting. Drugs include the aminoglycoside paromomycin and macrolides such as azithromycin and clarithromycin.\(^{[23]}\)
Complications

These are more common in immunocompromised patients - for example:

- Pancreato-biliary infection leading to pancreatitis, cholecystitis (acalculous), sclerosing cholangitis and (rarely) subsequent biliary cirrhosis. Papillary stenosis has also been reported.[18]
- Tracheo-bronchial and sinus involvement (rare).
- Pneumatosis cystoides intestinalis (cysts containing gas occur in the gut wall) occurs rarely in cryptosporidiosis with advanced HIV infection. Cysts can rupture causing pneumoretroperitoneum and pneumomediastinum.

Acalculus cholecystitis may need treating with cholecystectomy. Lactose intolerance may develop and dietary advice will be needed. Complications are unusual in the immune-competent person.

Prognosis

In healthy patients the condition is self-limiting and a full recovery is normal. With complications or in immunocompromised patients the prognosis will be determined by the nature of the complication and by the underlying condition.

Prolonged diarrhoea of more than a month and biliary disease carry a poor prognosis in AIDS.[18]

Prevention

Specific preventative advice for patients diagnosed with cryptosporidiosis[24]

- Expect diarrhoea to last longer than most other causes of gastroenteritis, with possible relapses.
- Observe strict personal hygiene measures (careful hand washing and no towel sharing).
- Avoid swimming pools for two weeks after cessation of diarrhoea.
- Avoid nursery attendance, food-handling occupations and care of vulnerable adults for 48 hours after cessation of diarrhoea.

General preventative measures

These include:

- Boiling water to kill oocysts:
  - When contamination of water supply is notified.[18]
  - When T-cell function is compromised. Special filtration or boiling of water for high-risk patients is recommended.[25] The Department of Health in England advises that those with compromised T-cell function should boil all drinking water (including bottled water) to reduce the risk of infection.[26]
  - Boiling or filtration of water is also recommended in countries with high rates of contamination and/or transmission.[27]
  - In particular, avoid newborn animals, including pets, especially in the immunocompromised.
  - Healthcare workers and childcare workers should prevent faecal-oral spread with wearing of gloves and with hand washing.
Further reading & references


3. Diagnostic tests for Cryptosporidium; Public Health Wales


5. Cryptosporidium; WHO Drinking Water Quality, World Health Organization, 2006

6. Laboratory reports of Cryptosporidium sp, 2000-2012; Health Protection Agency (archived content)


15. Alexander C; Update on Clinical Parasitology Developments, Scottish Parasite Diagnostic and Reference Laboratory, 2012.


23. Ramamurthy T; Cryptosporidium Factsheets; Health Protection Agency (archived content)


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