

PROLONGED DIARRHEAL DISEASE CAUSED BY *CYCLOSPORA CAYETANENSIS*

SINCE JUNE, reports of an epidemic of diarrheal disease affecting the eastern United States and Canada have assailed the public. While details of the investigations have not yet been published, according to the most recent accounts, most of these many clusters were apparently caused by consumption of strawberries raspberries contaminated with a little-known protozoan parasite, *Cyclospora cayetanensis*. This article reviews basic information about this parasite and the disease it can cause.

HISTORY

C. cayetanensis was only definitively identified as a coccidian in 1993.^{1,2} As our readers will recall, other "well-known" coccidia include both human parasites (*Cryptosporidium parvum*, *Isospora belli*, *Toxoplasma gondii*) and important veterinary pathogens (e.g., *Eimeria* spp.).

Reports of what now are recognized as *Cyclospora* infections* date back to at least 1979, when Ashford described an organism seen in the stools of three patients in Papua New Guinea.⁴ Later on, sporadic cases, small outbreaks, and eventually endemic foci of diarrheal disease were reported from Nepal, Peru, London, Chicago and elsewhere.^{1, 5-10} Until its taxonomic affinities were settled, this pathogen was variously described as a cyanobacterium (blue-green alga), coccidian-like, "big Crypto" (a reference to its similarity to *Cr. parvum*), and CLB (cyanobacterium-like body).

CLINICAL MANIFESTATIONS

Clinically, cyclosporiasis cannot be reliably distinguished from cryptosporidiosis or giardiasis. Symptomatic infections are characterized by frequent, non-bloody diarrhea accompanied by anorexia, mal-

aise, weight loss, fatigue, and abdominal cramps. For many patients the chief complaint is the lack of energy, rather than the diarrhea. Nausea, vomiting, myalgias, and low-grade fever may also be present. Though symptoms may be intermittent, they are often doggedly persistent, lasting an *average* of 45 days in one series.¹¹ Asymptomatic and mild infections are probably common.

While infections are self-limited if you don't mind waiting, TMP/SMX has been shown to be an effective treatment in placebo-controlled trials.¹²

Cyclosporiasis may be more protracted and/or severe among immunodeficient patients, e.g., persons with AIDS.^{13,14} Response to treatment is gratifyingly prompt, however.

DIAGNOSIS

Identification of the parasite requires careful microscopic examination of stool, either in wet mounts or in stained preparations. Oocysts stain light pink to deep red with the modified acid-fast stain often used to detect *Cryptosporidium*. At 8-10 μm in diameter, *C. cayetanensis* oocysts are larger than those of *Cr. parvum* (4-6 μm) but are otherwise somewhat similar in appearance, necessitating careful measurement.

Unlike *Cryptosporidium*, *Giardia*, and *Isospora*, *C. cayetanensis* oocysts autofluoresce strongly when illuminated by UV light (365 nm),¹⁵ making this a useful method to screen fresh or formalin-fixed stool (assuming you have this filter for your microscope).

Oocysts in fresh stool can also be incubated at room temperature (20-30°C) in 2.5% potassium dichromate. Sporulation (development of two sporocysts, each containing two sporozoites) should be detectable within 5-10 days.¹

The suspicious clinician should request specific examination for *C. cayetanensis*. Microbiologists at the Public Health Lab are available for consultation about specimen handling and identification (503/229-5885).

EPIDEMIOLOGY

Many questions about the natural history of this parasite are unanswered. To date, no carriers other than infected humans have been identified. Aside from *Cryptosporidium* spp., most coccidia are very host-specific, and it is possible that humans are the only hosts. Unlike all other common pathogens that cause diarrheal disease, *Cyclospora* oocysts require a period of development outside the human host before they become infectious.[†] Depending on temperature and other factors, oocysts take at least five to ten days to sporulate. Thus, there is little or no potential for direct person-to-person spread, e.g., via fecal contact in a day-care center.

The incubation period is probably variable, ranging between 1 and 10-14 days. Data from the recent outbreaks should help pin this down.

In Nepal, where the incidence is seasonal (May-August), cases in the expatriate community were four times more likely to have consumed untreated surface water than controls ($p=0.012$). Only 28% of cases reported this exposure in the week before onset, however,¹⁶ and this association could be confounded by other exposures.

An outbreak amongst housestaff at a Chicago hospital^{10, 17} was traced to consumption of water. Although the water tank feeding the physicians' dormitory was not well sealed, no obvious mechanism for human fecal contamination was identified. *C. cayetanensis* oocysts were found in a water tank that supplied a military barracks in Nepal where an outbreak occurred; the water was chlorinated, suggesting that (like *Cryptosporidium*) this organism may be resistant to disinfectants.¹⁸

Sporadic cases have been attributed (with more or less credence) to sewage exposure,¹⁹ "foreign travel,"^{8, 13} and swimming.¹³

[†] Hookworms can cause GI symptoms, but most people would not consider them in this category.

* Ed. note: No consensus has yet been achieved for the common name of this infection. "Cyclosporiasis" or "cyclosporiasis" would seem to be leading contenders, were derivative names for *Giardia* and *Toxoplasma* infections any guide. At least one source³ floated the somewhat more euphonious "cyclosporidiosis," but on reflection this seems unjustifiable. Most authors to date have avoided this issue. Comments from interested readers—particularly those with a classical background—are welcome.

CURRENT OUTBREAKS

In May and June, over 800 lab-confirmed cases were reported in the eastern United States and Ontario, Canada, primarily associated with at least 42 apparent "point-source" outbreaks (e.g., a luncheon). A number of sporadic cases were also reported.²⁰

Raspberries were served at all of the events under investigation for which complete information is available.²⁰ Case-control studies by health departments in Florida, New Jersey, and New York indicated an association between eating raspberries and *Cyclospora* infection. Findings from the first 21 completed tracebacks indicated that Guatemalan raspberries either definitely were or could have been served at each of these events.²⁰ How Guatemalan raspberries (allegedly from different sources and distributors) could have become widely contaminated with a (human?) fecal parasite is not yet crystal clear.

Unfortunately, preliminary conclusions from several investigations implicating strawberries as the culprit were widely publicized. Strawberry sales plummeted. Subsequently, it was learned that informants had forgotten raspberries when reconstructing relevant menus, effectively confounding the investigations. Oh well....

Media accounts notwithstanding, it is important to understand that this is not a "berry parasite" per se, and one outbreak, however large, does not define where this bug comes from. Lettuce, strawberries, carrots, water...: the list of potential vehicles is long. As with shigellosis, hepatitis A, and many other enteric diseases, the problem is coprophagy.

SURVEILLANCE ISSUES

Public health officials often struggle with the issue of when to "go public" with information about health risks. This dilemma is particularly acute when risks may be ongoing (e.g., when implicated products remain on the market). In most investigations, many leads are developed, investigated, and discarded before a cause is determined (assuming one is). Premature disclosure of "suspects" not only can have a devastating effect on "innocent" people and businesses, but may compromise the epidemiologist's ability to collect unbiased information. On the other hand, delays may mean more people getting sick—sometimes with serious, even fatal consequences.

No cyclosporiasis cases have been reported in Oregon since 1992 (a traveler to Bali and Thailand), but we invite physicians and laboratorians to report possible cases to local health departments. To conduct outbreak investigations and other studies, we depend on and greatly appreciate the cooperation of health care professionals and the public, be it providing medical records, taking the time to talk with epidemiologists, or filling out our famous questionnaires.

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