THE NORTHERN HOSPITAL

GIARDIASIS

Anton van Leeuwenhoek, (1632–1723), c. 1680 oil on canvas, Jan Verkolje, Museum Boerhaave, Leiden.

"Delft December 25th...

...In structure these little animals were fashioned like a bell, and at the round opening they made such a stir, that the particles in the water thereabout were set in motion thereby. . .

...And though I must have seen quite 20 of these little animals on their long tails alongside one another very gently moving, with outstretched bodies and straightened-out tails; yet in an instant, as it were, they pulled their bodies and their tails together, and no sooner had they contracted their bodies and tails, than they began to stick their tails out again very leisurely, and stayed thus some time continuing their gentle motion: which sight I found mightily diverting...."

Anton van Leeuwenhoek, letter to the Royal Society London,
December 25th, 1702.

In 1676, the learned Royal Society of London received a most unusual communication from the Dutch microscopist Anton van Leeuwenhoek of Delft. Van Leeuwenhoek had been sending astonishing reports of his microscopical observations to the Society for over three years, but nothing compared to this latest report. He claimed he had seen microscopic life forms, so tiny they could not be seen by the naked eye. Even more alarming they appeared to be no more than a single "cell", alive with the most energetic and graceful movement, disturbing the tiny particles around them within the drop of water in which they swarmed. These cells seemed to be alive and he called them accordingly his "animalcules". The concept of a "cell" was well understood, as the brilliant Robert Hooke had described these as the basic units of life in his famous "Micrographia", of 1665, a work which had inspired van Leeuwenhoek, and launched him on his lifelong interest in the microscopic world. But to suggest that a cell itself could constitute an entire animal was simply stretching the imagination too far. Just as there would be over a century later when the first reports of the "Platypus" came in from the great southern continent of "Nova Hollandia", there was at first widespread disbelief and derision. To settle the matter the Royal Society sent a team of respected observers to Delft to confirm van Leeuwenhoek's findings. To their astonished surprise, he was able to show them through his superior microscopes the truth of his claims. Robert Hooke himself would later confirm van Leeuwenhoek's findings. In recognition of his extraordinary discovery he was elected a member of the Royal Society. This was the world's first discovery of the previously and totally unexpected existence of microscopic life forms.

Today Anton van Leeuwenhoek is acknowledged as the father of microbiology. He did not "invent" the microscope as is sometime supposed, but he did create vastly superior eye pieces that allowed him to magnify objects over 200 times, compared with previous instruments which could only manage magnifications of 20 - 30 times at most. He had no formal education, no university degrees. He was completely self-taught, the son of a basket maker - who was apprenticed as a Cloth Merchant at the age of 16 years. It was during his apprenticeship he first came into contact with the crude magnifying lenses which the clothiers then used to assess the quality of their cloth. Though he became a successful draper, he never lost his wonder of the power of the magnifying lenses to see the very small. With this wonder he created vastly superior lenses, by teaching himself

glass blowing allowing him to create ever superior lenses. He guarded his secrets of lens making very carefully his whole life. It was with these superior instruments that over the course of the rest of his life he made many great discoveries, including not only the discovery of single cell life forms, but also the discovery of capillaries, which put the final piece of evidence in place for William Harvey's theory on the circulation of the blood. He also discovered, yet smaller life forms than the protozoa which we know today as bacteria. He discovered the muscle fibers of skeletal muscle and spermatozoa, yet another landmark in the history of biology. Towards the end of his long life, on June 12, 1716, he wrote a letter to the Royal Society, explaining his groundbreaking successes, thus:

". . . my work, which I've done for a long time, was not pursued in order to gain the praise I now enjoy, but chiefly from a craving after knowledge, which I notice resides in me more than in most other men. And therewithal, whenever I found out anything remarkable, I have thought it my duty to put down my discovery on paper, so that all ingenious people might be informed thereof...."

His words poignantly echoed those of Sir Isaac Newton, who also explained his great discoveries in terms of an insatiable curiosity about the world - a curiosity that he likened to that of a small child on a beach discovering seashells for the first time...

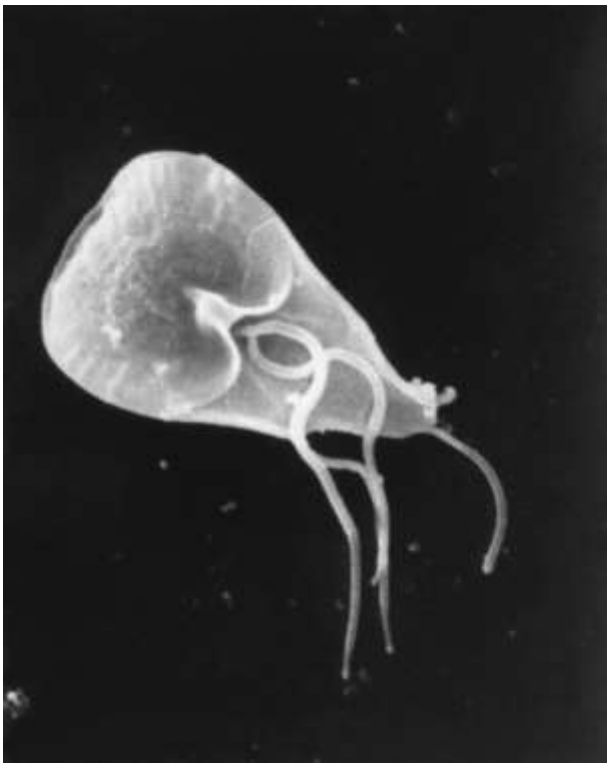
"..I don't know what I may seem to the world, but as to myself, I seem to have been only like a boy playing on the sea-shore and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me".

Unlike most of us, the true scientific geniuses, never lost their child-like wonder of the world around them.

Nearly four centuries after the brilliant work of Anton van Leeuwenhoek, we understand the scheme of life and the world around us to a degree unimaginable (but aimed for) - by the learned Royal Society of London of the Seventeenth century. Yet there is still much to be learnt, and it appears we have barely even scratched the surface of nature's secrets. Albert Einstein suspected that "we still do not know one thousandth of one percent of what nature has revealed to us". Today we loosely know Anton van Leeuwenhoek's "animalcules" as the protozoa. The magisterial Richard Dawkins wrote in his "Ancestors Tale", "The choanoflagellates are the first protozoans to join our pilgrimage...which very tentatively on molecular evidence with worryingly large extrapolations we date at 900 million years....It has long been suspected that either they represent a hangover from a sponge ***ancestor****, or they are the evolutionary descendents of sponges that have degenerated to a single cell or very few cells. Molecular genetic evidence suggests the former...."*

Evolutionary theory gives us the astonishing conclusion, that if we go back far enough through untold eons of geological time, perhaps over 900 million years, we find a protozoan ancestor, the origin of all metazoan life. The direct descendents of this simple life form were discovered by Anton van Leeuwenhoek in 1676. Amoung his tiny "animalcules" are the Giardia lamblia.

GIARDIASIS



Giardia lamblia trophozoite, scanning electron microscope, (CDC)

Introduction

Giardiasis is the result of GIT infection with Giardia lamblia, (also known as *Giardia intestinalis or Giardia duodenalis*).

Clinical manifestations include:

- Asymptomatic GIT shedding.
- Acute / subacute gastroenteritis
- Chronic infection with malabsorption.

History

Giardia is thought to have been originally observed by the famous Dutch microscopist **Anton van Leeuwenhoek** in 1681.

The organism was described scientifically by the Czech physician **Vilem Dusan Lambl** in 1859.

It was also decribed by the French biologist **Alfred Mathieu Giard** in 1895.

In 1915 the species was named Giardia lamblia by the American zoologist Charles Wardell Stiles, in honour of both Lambl and Giard.

Giardia lamblia was the first **protozoan parasite** described, and the organism was thought to be a harmless commensal organism of the intestine.

Its role as a **pathogenic** organism was not recognized until the 1970s, after the appearance of the disease in travelers returning from endemic regions.

Epidemiology

Occurrence is worldwide and endemic in most regions. Is more prevalent in warm climates.

Infection is detected more frequently in children than adults.

Pathology

Organism

- **Giardia lamblia**, (also known as *Giardia intestinalis or Giardia duodenalis*), is a flagellate protozoan.

  Protozoa is an older term essentially referring motile unicellular eukaryotic organisms inhabiting aquatic environments.

  They can be flagellates (motile with flagella), ciliates (motile with cilia), or amoebas (motile by means of pseudopodia).

  The flagellates are the most numerous soil protozoa.

  Giardia lamblia can in the human duodenum and jejunum.

Life Cycle

- **See Appendix 1 below.**

Transmission

- Transmission occurs person to person and animal to person via hand to mouth transfer of cysts from infected faeces or faecally contaminated surfaces.

- Water-borne outbreaks may occur due to faecal contamination of public water supplies or recreational swimming areas.

- It is readily transmitted in institutions such as day care centers among children who are not toilet trained.

- Other risk factors for infection include travel to high risk areas, immunosuppression, male to male sexual intercourse and achlorhydria
- The cysts can survive for months in water in the environment.

Incubation Period

- The incubation period is usually one to three weeks but it can be longer.
- It is on average seven to ten days.

Reservoir

Reservoirs include:

- Human
- Animal
- Contaminated water.

Period of Communicability

- It is communicable for the entire period of cyst excretion.

Susceptibility and Resistance

- Everyone is susceptible to infection.
- Reinfection can occur.

Clinical Features

The spectrum of disease can vary widely and includes:

1. Asymptomatic carriage:
    - The rate of asymptomatic carriage may be high.
2. Acute / subacute symptomatic disease:

    Symptoms usually last one to two weeks but may also last some months.

    - Gastroenteritis:
        - ♥ A small number of persons develop abrupt onset of explosive, watery diarrhea, abdominal cramps, foul flatus, vomiting, fever, and malaise; these symptoms last 3 - 4 days before transition into the more common subacute syndrome.

- ♥ Most patients however experience a more insidious onset of symptoms, which are recurrent or resistant.

- Post *Giardia* lactose intolerance may also occur. [1]

3 Chronic symptomatic infection:

Associated with:

- Malabsorption/ Steatorrhoea
- Non-specific constitutional symptoms; fatigue, anorexia and weight loss.

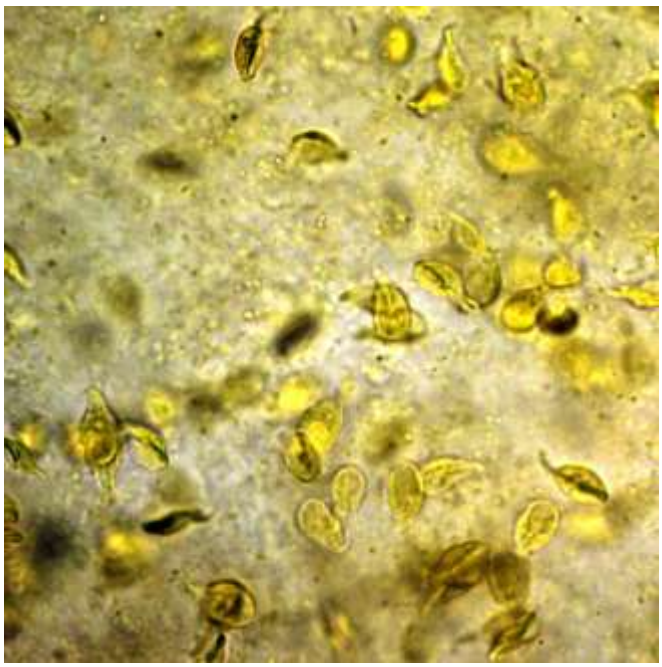
Investigations

These may include:

Bloods:

- FBE
- U&Es/ glucose
- LFTs

Stool for microscopy and culture:



Giardia trophozoites on stool examination

- Stool *microscopy* for cysts or trophozoites can be used for diagnosis of Giardia.

  A single negative test however does not necessarily however preclude infection, **as cyst excretion can be variable.**

  Multiple stool collections (i.e., three stool specimens collected on separate days) increases test sensitivity.

  The organism is identified in 50-70% of patients after a single stool examination and in more than 90% after 3 stool examinations.

  The pathogenic species *Entamoeba histolytica* is identical on microscopy to non-pathogens *Entamoeba dispar* and *Entamoeba moshkovskii*, but it can be differentiated by antigen and PCR testing.

  Fecal leukocytes are **not** typically seen in giardiasis.

Antigen testing:

- Stool antigen enzyme-linked immunosorbent assays are available.

  These tests are best used as a screening test in high-incidence settings such as day care centers or for identification of subjects during an epidemic, but they should not take the place of stool microscopy

PCR testing

- **PCR** testing of stool identifies giardiasis

Serology

- IgM testing can be done, and if elevated suggests acute infection
- IgG is more suggestive of subacute/ chronic/ previous infection.

Endoscopy

- Endoscopy may occasionally be used to obtain a duodenal aspirate or biopsy, especially in the investigation of more chronic cases of GIT upset/ malabsorption.

Management

1. Oral or IV rehydration, as clinically indicated.
2. Asymptomatic patients: [1]
   - The need for treatment of immunocompetent patients with asymptomatic carriage is controversial.

3. Symptomatic patients:

Antibiotics: [1]

Symptomatic cases are treated with

- **Tinidazole:**

  Tinidazole 2 grams (child: 50 mg/kg up to 2 g) orally, as a single dose

Or

- **Metronidazole:**

  Metronidazole 2 grams (child: 30 mg/kg up to 2 g) orally, daily for 3 days

  Or

  Metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 8 hourly for 5 to 7 days

Alternatives include:

- **Nitazoxanide:**

  Nitazoxanide 500 mg (child 1 to 3 years: 100 mg; 4 to 11 years: 200 mg) orally, 12-hourly for 3 days

- **Albendazole:**

4. Pregnancy:

- **For pregnant women, use paromomycin.**

  Systemic absorption is low, but the cure rate is lower than with other agents.

  Paromomycin is a poorly absorbed aminoglycoside.

See the latest Antibiotic Therapeutic Guidelines for full prescribing details of all agents.

5. **Recurrence** of symptoms after therapy:

This may be due to:

- Post-Giardia lactose intolerance
- Re-infection

- Drug resistance.

Notification

- Giardiasis (Group B disease) must be notified in writing within five days of diagnosis.

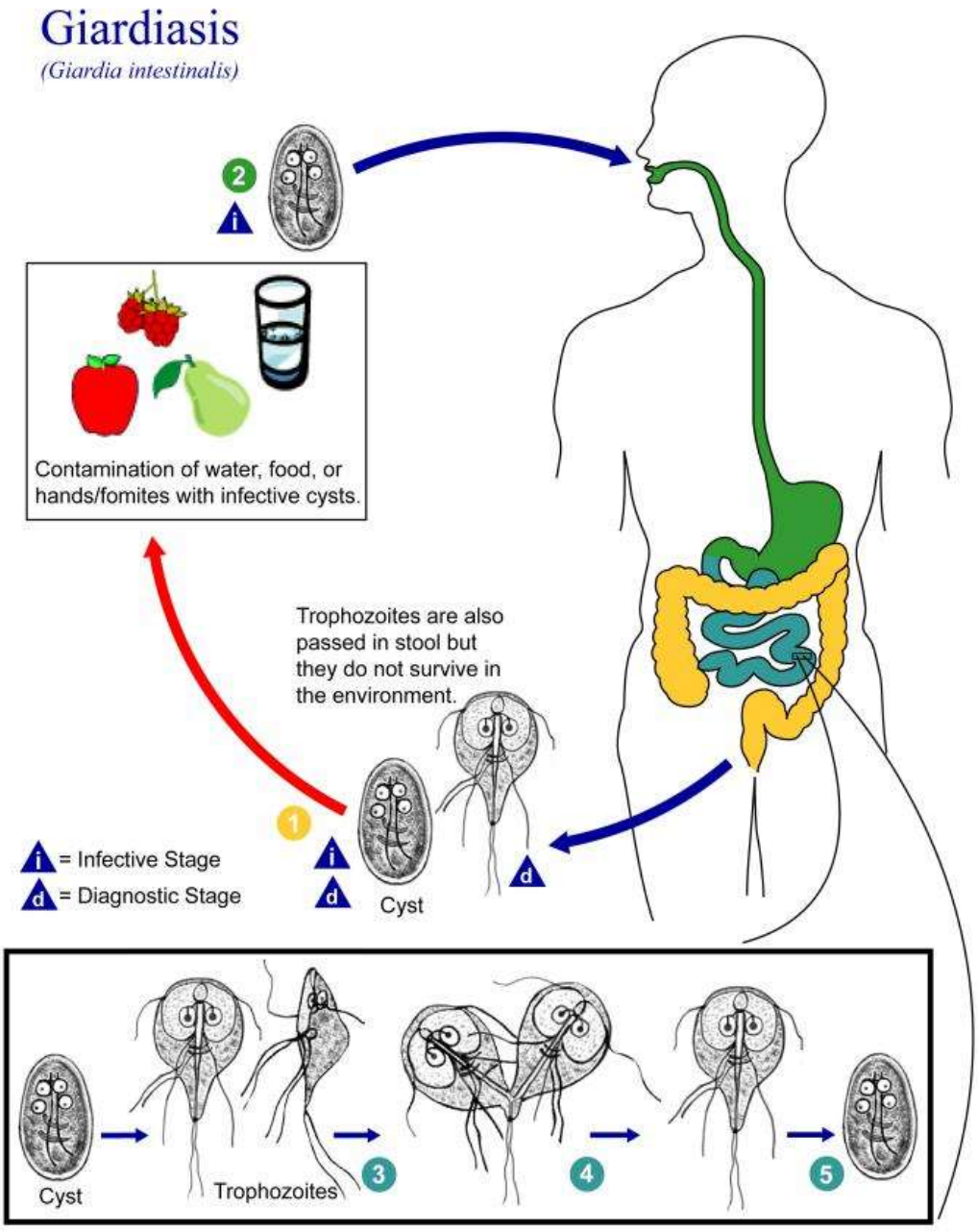
School exclusion

- Exclude cases from child care and school until diarrhoea has ceased or until a medical certificate of recovery is produced.

Appendix 1

Life Cycle

Giardia lamblia exists in two forms, cysts and trophozoites.



Life cycle of giadia lamblia, (From CDC Website)

Cysts are resistant forms and are responsible for transmission of giardiasis. Both cysts and trophozoites can be found in the feces (diagnostic stages)

1. *The cysts are hardy and can survive several months in cold water. Infection occurs by the ingestion of cysts in contaminated water, food, or by the fecal-oral route (hands or fomites)*

2. *In the small intestine, excystation releases trophozoites (each cyst produces two trophozoites)*

3. *Trophozoites multiply by longitudinal binary fission, remaining in the lumen of the proximal small bowel where they can be free or attached to the mucosa by a ventral sucking disk*

4. *Encystation occurs as the parasites transit toward the colon. The cyst is the stage found most commonly in nondiarrheal feces*

5. *Because the cysts are infectious when passed in the stool or shortly afterward, person-to-person transmission is possible. While animals are infected with Giardia, their importance as a reservoir is unclear.*

References

1. eTG - November 2014

   - Antibiotic Therapeutic Guidelines, 15th ed 2014.

2 The Blue Book, Website

3. Hisham Nazer, Giardiasis in eMedicine Website January 3, 2013

Dr J. Hayes

Reviewed August 2015.