MEDDOCS Open Access Publisher

ISSN: 2637-4501

Annals of Gastroenterology and the Digestive System

Open Access | Review

Giardia, 338 years after its discovery: The challenge ahead

Angel A Escobedo[1]*; Emelina Diaz[2]; Caridad Almanza[2]; Pedro Almirall[3]; Luis E Morera[3]; Jhossmar Auza-Santivanez[4]; Susana Terry[5]

[1]Institute of Gastroenterology, Calle 25 No. 503 esquina I, Plaza, La Habana, CP 10400, Cuba

[2]Central Clinic "Cira García", Cuba

[3]Municipal Centre of Hygiene, Epidemiology and Microbiology "Plaza"Cuba

[4]Academic Clinical and Surgical Hospital "Dr. Miguel Enriquez", Cuba

[5]Centre for Health Promotion and Prevention of Sexually Transmitted Infections. Cuba

***Corresponding Author(s): Angel A Escobedo**

Department of Epidemiology, Institute of Gastroenterology, Calle 25 No. 503 esquina I, Plaza. Havana City, 10400, Cuba

Email: escobedo@infomed.sld.cu

Received: Jan 15, 2020

Accepted: Mar 30, 2020

Published Online: Mar 31, 2020

Journal: Annals of Gastroenterology and the Digestive System

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Abstract

Antony van Leeuwenhoek, the Dutch tradesman who first identified Giardia in 1681, has become a legend in Parasitology. Last November 4th marked the 338th anniversary of the submission of his letter, addressed to Sir Robert Hook, the then Secretary of the Royal Society of London, in which he described his observations in his own faecal sample:

"[…] I have looseness, at intervals of 2, 3 or 4 times a day. But this summer this befell me very often, and especially when I partook of hot smoked beef, that was a bit fat, or ham, which food I´m very fond of; indeed, it persisted once for three days running, and whatever food I took, I kept in my body not much above 4 hours… My excrement being so thin, I was at divers times persuaded to examined it; and each time I kept in mind what food I had eaten, and what food I had drunk, and what found afterwards" […] "All the particles aforesaid lay in a clear transparent medium, wherein I have sometimes also seen animalcules a-moving very prettily; some of them a bit bigger, others a bit less, than a blood-globule, but all of one and the same make. Their bodies were somewhat longer than broad, and their belly, was flattish, furnished with sundry little paws, where with they made such a stir in the clear medium and among the globules, that you might even fancy you saw a wood-louse running up against a wall; and albeit they made a quick motion with their paws, yet for all that they made but slow progress" [1].

These observations were not only the first credited description of a protozoan, but also the first description of its clinical manifestations, even when van Leeuwenhoek did not associated any organism with his disease symptoms. Despite initial observations were followed by a long silence, during these 338 years, mainly the last 75 years, there have been many other key discoveries and notable developments in the history of Giardia, including the observations of Rendtorff on transmission [2] and the inclusion of 5-nitroimidazole (5-NIs) compounds into the antigiardial arsenal [3,4].

Cite this article: Escobedo AA, Diaz E, Almanza C, Almirall P, Morera LE, et al. Giardia, 338 years after its discovery: The challenge ahead. Ann Gastroenterol Dig Syst. 2020; 3(1): 1014.

Years have been passing by and Giardia infection still remains one of the most prevalent intestinal parasitic infections (IPIs) world-wide. Many people harbor this pathogen, and many of them lack symptoms; in this sense there is a curious paradox that one of the reasons for Giardia infection's effective "invisibility" may be its ubiquity in some populations. But, how could something so common be important?

The protozoan

Giardia is a genus of intestinal flagellates that infects a wide range of vertebrate hosts. The genus currently comprises 6 species, namely Giardia agilis in amphibians, Giardia microti and Giardia muris in rodents, Giardia ardeae and Giardia psittaci in birds, and Giardia duodenalis (synonymous. G. intestinalis, G. lamblia) in humans, although it is also found in other mammals, including pets and livestock [5]. During the last decades, the development of molecular techniques have been used to distinguish and characterize the epidemiology of human giardiasis. G. duodenalis from human and various animals are morphologically similar; however, distinct host-adapted genotypes have been demonstrated within this species complex whose members yet can be assigned to at least 8 distinct assemblages (A to H) based on genetic analyses [6].

The disease

Human giardiasis, the disease Giardia causes, is a clinically significant and treatable condition. It may be treated using a single dose of an inexpensive drug such as tinidazole or secnidazole, or multiple doses with metronidazole, albendazole, furazolidone or nitazoxanide [7]. However, if poorly diagnosed and ineffectively treated, may lead to some consequences and a significant public heath burden. This protozoan has been estimated to cause annually 184 million clinical cases [8] and an associated 171,100 (115,777–257,315) disability-adjusted life years [9]

In addition to causing diarrhoea, abdominal pain, flatulence, nausea, vomiting and other classical gastrointestinal manifestations, in some people, this flagellated protozoan has been linked with a broad range of clinical features (also extra-intestinal), including post-infectious- irritable bowel syndrome, chronic fatigue and, in young children, failure to thrive [6,10,11]. All these features suggest a need for increased control efforts.

Evidence for a possible correlation between genotypes and clinical manifestations is accumulating; however, larger studies are needed to validate these observations.

Sanitation, human behavior and Giardia infection

The infectious form of Giardia, the cyst, is highly resistant and infectious immediately upon being excreted in feces; it has also the ability to survive for weeks to several months in cold water. In addition, the infectious dose is as low as 10 cysts. In this sense it is easily to understand that transmission of this protozoan is usually by the faecal-oral route either indirectly, through contaminated drinking water or food products, particularly in areas with a high prevalence of the infection, and directly, via person-to-person spread; i.e., among men having sex with men (MSM) and among day care centres attendees, who -the latter- may acquire Giardia in their own immediate environment [12].

In industrialized countries, the lower prevalence of Giardia infection -in comparison with developing countries - has been attributed to continued improved water, sanitary and living conditions, with reduced exposure to infection. However, it may be also observed; i.e., annually, in the United States, an estimated 1.2 million cases occur [13]; outbreaks result from waterborne, foodborne, person-to-person, and animal contact transmission [14] and hospitalizations resulting from giardiasis cost approximately $34 million [15]. In fact, giardiasis in resource-rich countries has been considered as a re-emerging disease [16]. Risk factors associated with this sporadic infection include contact with ill persons, travel abroad, drinking untreated water [17], and swallowing water while swimming in pools, eating lettuce, and recreational fresh water contact had positive and independent associations with Giardia infection in a case-control study carried out in residents who had not recently traveled outside the from United Kingdom [18]. Outbreaks in daycare centres are also common, and can result in spread to the community [19].

The situation for resource poor nations is completely different; however, according to some estimates, as much as 33 % of the population has a record of giardiasis [20]. In Asia, Africa, and Latin America, about 200 million people have symptomatic giardiasis, with some 500,000 new cases reported each year [21]. At-risk populations of this infection (mainly in early childhood) are unlikely to have safe water and improved sanitation for many decades. Although 'point of use' water treatment provides protection when used properly, this has been difficult to sustain on a large scale, and drinking pure water does not negate the risk from contaminated water which may also be consumed [22].

Data unequivocally show that Giardia is especially frequent in disadvantaged poor populations in both the developing and industrialized world [23,24]; however, the true global burden of giardiasis is not known, owing at least in part to the lack of simple, inexpensive sensitive diagnostic tools, under appreciation of the frequency of disease in industrialized countries, and difficulties quantifying the impact of an infection that causes an acute illness with long term sequelae [25].

Diagnosis and treatment

The diagnosis of giardiasis begins with the recognition by the practitioner [26], under appreciation of the frequency of disease and difficulties quantifying the impact of an infection that causes an acute illness with long term sequelae [27]. Concerning laboratory diagnosis, although nucleic acid amplification testing [for instance, polymerase chain reaction] is available in research settings and some in reference laboratories, globally the mostly used diagnostic test for Giardia is the microscopic examination of faecal smear, either by direct wet mount or concentration techniques. These two latter even when are not technically difficult, are dependent upon the number and way of collection- of faecal specimens, and on the experience and diligence of the microscopist.

Otherwise, concerning pharmacological management, although Rendtorff´s classical study found that giardiasis was a self-limiting condition in most of the human volunteers [2], patients with giardiasis should receive a course of antigiardial drugs to clear the infection and to shorten the course of the illness, if clinically significant. In most instances, a single dose of an inexpensive antimicrobial agent is enough. The 5-nitroimidazole compounds are the commonest drugs used against giardiasis; however, there is often poor patient compliance, toxicity issues and adverse effects on the normal gut microflora. Additionally,

treatment failures are increasingly reported in patients despite having received successive courses of treatment that have been documented to result in a cure for most people [28]. In that cases, longer treatment schedules or combination of two drugs with different mechanisms of action have been suggested [29]. In addition, it seems that quinacrine, an old drug against this protozoan infection, may experience a new youth, alone or in combination, in the fight against treatment failures [30]. Other drugs like mebendazole and chloroquine may also be employed [31].

Steps to prevention and control

Nowadays, the focus of giardiasis prevention and control perhaps should be less on response to outbreaks or individual patients -which certainly have a significant economic impact-, than on prevention and control ongoing transmission. Vaccines, the cornerstone of public health and one of the most cost-effective means of preventing several infectious diseases, are not available for human giardiasis.

Continued research on the epidemiology, ecology, sociology, anthropology, pathogenesis, diagnosis, treatment and prevention of giardiasis can most optimally be pursued in the endemic regions which, unfortunately, also suffer from a lack of research capacity, funding support, and institutional infrastructure. Much needs to be done to promote and strengthen giardiasis research in these regions if true progress is to be made. It is necessary that scientific communities from both, the industrialized and developing world, share knowledge and experiences, and jointly face this parasitic disease. As a starting point, a successful translation from basic knowledge into effective giardiasis control interventions will ultimately depend on the active collaboration and communication between researchers from the aforementioned disciplines. Also, interdisciplinary investigations should be encouraged as collaborative efforts between human and veterinary health professionals.

Unfortunately, within the world of IPIs and its researchers, Giardia has never been the subject of a focused diagnosis and control programme such as the ones undertaken for soil-transmitted helminths. Giardia is mainly harbored among people having limited financial resources and access to care. This infection may, in some cases, persist for years or people become chronically re-infected, and those affected have no recourse but to live with their symptoms. It is likely that many of these people have had persistent infection for so long that they do not report their clinical manifestations because most of their signs and/or symptoms have become the norm. It might be assumed that a high proportion of those infected received either no treatment, inappropriate treatment or incomplete treatment. The result is that this treatable IPI continues its spread within the community even though its transmission could be prevented or reduced with attention to water quality, food hygiene, and a few cents worth of generic drugs previously mentioned, when these measures fail.

In considering a public health response to giardiasis might be implemented, important questions must be addressed and responses will differ according to socioeconomic issue and endemicity in different countries. Should people be screened for Giardia infection? If so, who would be screened and at what intervals? How many faecal samples should be examined? What diagnostic method should be used? Which would be the definition of an episode of Giardia infection and its endpoint, according to the settings (endemic or non-endemic)? Which would be the optimal drug for treatment? Which of the single dose schedules would be routinely used to ensure patient compliance? What should be done to understand the epidemiology of low prevalence transmission and persistence of giardiasis in communities? Which is the main mode of transmission involved? What control measures work better according the different settings (travellers to endemic areas, MSM, children in child care settings, etc.)? Could they be integrated into other control programmes? While the answers to these questions are beyond the scope of this article, it is worth noting that the essential tools for the control of Giardia infections are already available. A range of diagnostic tests, including faecal saline and/or Lugol wet mount microscopy, rapid antigen testing, and nucleic acid amplification and detection, provide alternatives that could be used in a variety of settings. Oral drugs offer inexpensive, effective, and generally well-tolerated treatment options that are widely available [7].

Conclusions

Giardia is still a formidable adversary in our society, causing substantial morbidity in poor countries, and might be of substantial health relevance in rich countries even in settings where it is not commonly considered as a health problem [25].

Cooperation of international health organisms; and the implementation, by the governments, is necessary for programs of sanitary education and environmental sanitation. A community involvement in giardiasis prevention efforts is needed and could benefit-and/or be a port of entry of- the prevention of other infections with similar modes of transmission. In this sense it is necessary to avoid the divorce between communities at high risk for giardiasis and public health officials. The dialogue that is needed must be horizontal and bidirectional, with public health needing to understand the perceptions, concerns, norms of those communities, at least, as much as it needs to inform about giardiasis and other public health issues [33,34]. We hope that the inclusion of Giardia into the neglected tropical diseases initiative by WHO, may catalyze further research and actions to tackle this protozoan and the disease it causes. Also, other initiatives including the regular celebration of the International Giardia and Cryptosporidium Conference, from which its most recent edition (the 7th) took place in France, in April 2019, joined any parties together: Doctors, researchers, veterinaries, academics, representatives of the pharmaceutical and water industry, public health officials and others who recognize the seriousness of the problem, may have had an additional impact.

While specific options for control of Giardia infection in various settings has been explored elsewhere [35], a first step is to change the way the disease is viewed by the various layers of the health sector and the community [25,26]. Only through a better understanding of the inherent (and fascinating) complexities in Giardia infection and transmission will more effective control tools emerge. Maybe, our primary challenge today is not a lack of knowledge but a failure to scale up what we already know works. No one doubts the extension of the challenge facing. On the contrary, it should inspire hope and the notion that action is possible. Effective action will not only ameliorate a major problem but will also demonstrate that different groups around the world can work together difficult issues with a similar goal. However, we cannot make real steps in the control of this protozoan infection until we finish our ambivalence concerning the significance and health consequences of this important old traveler fellow, a relevance that van Leeuwenhoek -its own discoverer- did not probably realize.

References

1. Dobell C. The discovery of the intestinal protozoa of man. Proc R Soc Med. 1920; 13: 1-15.
2. Rendtorff RC. The experimental transmission of human intestinal parasites. II. Giardia lamblia cysts given in capsules. Am J Hyg. 1954; 59: 209-220.
3. Mandoul R, Dargelos R, Millan J. Destruction des protozoaires intestinaux de la souris par un dérivé nitré de l'imidazole. Bull Soc Pathol Exot Filiales. 1961; 54: 12-16.
4. Schneider J. Traitement de la giardiase (lambliase) par le metronidazole. Bull Soc Pathol Exot Filiales. 1961; 54: 84-95.
5. Thompson RCA. The zoonotic significance and molecular epidemiology of Giardia and giardiasis. Vet Parasitol. 2004; 126: 15-35.
6. Escobedo AA, Almirall P, Robertson LJ, Mørch K, Franco RM, et al. Giardiasis: The ever present threat of a neglected disease. Infect Disord Drug Targets. 2010; 10: 329-348.
7. Escobedo AA, Cimerman S. Giardiasis: A pharmacotherapy review. Expert Opinion Pharmacother. 2007; 8: 1885-1902.
8. Pires SM, Fischer-Walker CL, Lanata CF, Devleesschauwer B, Hall AJ, et al. Aetiology-specific estimates of the global and regional incidence and mortality of diarrhoeal diseases commonly transmitted through food. PloS one. 2015; 10: e0142927.
9. Kirk MD, Pires SM, Black RE, et al. World health organization estimates of the global and regional disease burden of 22 foodborne bacterial, protozoal, and viral diseases, 2010: a data synthesis. PLoS Med. 2015; 12: e1001921.
10. Escobedo AA, Almirall P, Cimerman S, Rodríguez-Morales AJ. Sequelae of giardiasis: An emerging public-health concern. International J Infect Dis. 2016; 49: 202-203.
11. Litleskare S, Rortveit G, Eide GE, Hanevik K, Langeland N, et al. Prevalence of Irritable Bowel Syndrome and Chronic Fatigue 10 Years After Giardia Infection. Clin Gastroenterol Hepatol. 2018; 16: 1064-1072.e4.
12. Escobedo AA, Almirall P, Robertson LJ, et al. Giardiasis: The ever present threat of a neglected disease. Infect Disord Drug Targets. 2010; 10: 329-348.
13. Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States-major pathogens. Emerg Infect Dis. 2011; 17: 7-15.
14. Adam EA, Yoder JS, Gould LH, Hlavsa MC, Gargano JW. Giardiasis outbreaks in the United States, 1971–2011. Epidemiology & Infection. 2016; 144: 2790-2801.
15. Collier SA, Stockman LJ, Hicks LA. Direct healthcare costs of selected diseases primarily or partially transmitted by water. Epidemiol Infect. 2012; 140: 2003-2013.
16. Thompson RC. Giardiasis as a re-emerging infectious disease and its zoonotic potential. Int J Parasitol. 2000; 30: 1259-1267.
17. Snel SJ, Baker MG, Kamalesh V, French N, Learmonth J. A tale of two parasites: The comparative epidemiology of cryptosporidiosis and giardiasis. Epidemiol Infect. 2009; 137: 1641-1650.
18. Stuart JM, Orr HJ, Warburton FG, Jeyakanth S, Pugh C,et al. Risk factors for sporadic giardiasis: a case-control study in southwestern England. Emerging infectious diseases. 2003; 9: 229-233.
19. Katz DE, Heisey-Grove D, Beach M, Dicker RC, Matyas BT. Prolonged outbreak of giardiasis with two modes of transmission. Epidemiol Infect. 2006; 134: 935-941.
20. Centers for Disease Control and Prevention. Parasites-Giardia. 2015.
21. World Health Organization. The World Health Report 1996. Fighting Disease Fostering Development. World Health Organization: Geneva, Switzerland; 1996.
22. Enger KS, Nelson KL, Rose JB, Eisenberg JN. The joint effects of efficacy and compliance: a study of household water treatment effectiveness against childhood diarrhea. Water Res. 2013; 47: 1181–1190.
23. Yoder JS, Gargano JW, Wallace RM, Beach MJ; Centers for Disease Control and Prevention (CDC). Giardiasis surveillance--United States, 2009-2010. MMWR Surveill Summ. 2012; 61: 13-23.
24. Barry MA, Weatherhead JE, Hotez PJ, Woc-Colburn L. Childhood parasitic infections endemic to the United States. Pediatr Clin North Am. 2013; 60: 471-485.
25. Escobedo AA, Almirall P, Hanevik K, Cimerman S, Rodríguez-Morales AJ, et al. Giardiasis: a diagnosis that should be considered regardless of the setting. Epidemiology & Infection. 2018; 146: 1216-1218.
26. Escobedo AA, Almirall P, Rodríguez-Morales AJ, Cimerman S, Salazar Y, et al. Why are patients with giardiasis not treated earlier? Two sides of the same coin. Clin Infect Dis. 2018; 67: 480.
27. Escobedo AA, Almirall P, Hanevik K, Cimerman S, Rodríguez-Morales AJ, et al. Giardiasis: A diagnosis that should be considered regardless of the setting. Epidemiology & Infection. 2018; 146: 1216-1218.
28. Nabarro LE, Lever RA, Armstrong M, Chiodini PL. Increased incidence of nitroimidazole-refractory giardiasis at the Hospital for Tropical Diseases, London: 2008-2013. Clin Microbiol Infect. 2015; 21: 791-796.
29. Escobedo AA, Lalle M, Hrastnik NI, Rodríguez-Morales AJ, Castro-Sánchez E, et al. Combination therapy in the management of giardiasis: what laboratory and clinical studies tell us so far. Acta Tropica 2016; 162: 196-205.
30. Escobedo AA, Almirall P, Rodríguez-Morales AJ, Duquesne-Rivero E, Suarez-Mella R, et al. Could the fight against treatment failures in giardiasis lead to a second childhood for quinacrine? J Infect Dis. 2017; 216: 1180-1181.
31. Escobedo AA, Almirall P, González-Fraile E, Ballesteros J. Efficacy of mebendazole in paediatric patients with giardiasis: A systematic review and meta-analysis. Acta Trop. 2018; 188: 50-57.
32. Escobedo AA, Almirall P, Cimerman S, Lalle M, Pacheco F, et al. Chloroquine: An Old Drug with New Perspective Against Giardiasis. Recent Pat Antiinfect Drug Discov. 2015; 10: 134-141.
33. Escobedo AA, Almirall P, Alfonso M, Ávila I, Cimerman S, et al. Caregiver perspectives for the prevention, diagnosis and treatment of childhood giardiasis in Havana City, Cuba. A qualitative study. Acta Tropica. 2011; 11: 99-106.
34. Almirall P, Escobedo AA, Salazar Y, Alfonso M, Ávila I, et al. Parental perceptions of giardiasis. A study in an outpatient paediatric hospital setting in Havana, Cuba. ISRN Preventive Medicine. 2013.
35. Bartlett AV, Englender SJ, Jarvis BA, Ludwig L, Carlson JF, Topping JP. Controlled trial of Giardia lamblia: Control strategies in day care centers. Am J Public Health. 1991; 81: 1001-1006.