The gastrointestinal tract is the largest organ of immune surveillance in the body, home to two-thirds of the total lymphocyte population.\(^1\) Intestinal lymphocytes manifest a variety of responses which depend upon their CD phenotype, histologic location and communication with other effector cells. Stimulation of intestinal immune response networks by lumen-dwelling microbes may produce a variety of systemic responses that are independent of gastrointestinal symptoms.\(^2\) Immunologic hypersensitivity to \textit{Giardia lamblia} has been shown to provoke asthma\(^3\)\(^4\), urticaria\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\), arthritis (reference 11 + 12 + 13 + 14; 15) and uveitis\(^16\). Hypersensitivity reactions may occur in the absence of digestive complaints (refs 6, 10, 15). In none of these cases was the mechanism of hypersensitivity known; eosinophilia was a feature in only two cases (refs 10, 11)). A high frequency of pre-existing atopic disease occurs in patients with chronic giardiasis\(^17\)\(^18\) and may be a factor in susceptibility to infection.

Immunologic mechanisms other than hypersensitivity reactions may also be associated with chronic giardiasis. In humans, chronic giardiasis has been associated with deficiency of secretary IgA\(^19\) and with impaired macrophage cytotoxicity\(^20\), characteristics that may predispose to systemic illness. Athymic mice chronically infected with \textit{Giardia muris} do not develop mucosal damage\(^21\). Gillon \textit{et al.} have proposed that the release of enteropathic lymphokines by intraepithelial T cells is the cause of the intestinal injury in chronic giardiasis\(^22\). In humans, the severity of malabsorption observed with chronic giardiasis is more closely related to the presence of intraepithelial lymphocytes and the antibody titer to \textit{Giardia} cyst antigen than to the estimated parasite burden\(^23\). A normal
immunologic response to the parasite may be necessary to avoid chronic infection but also creates much of the tissue damage associated with chronic giardiasis.

Giadia may provoke systemic illness by non-immunologic mechanisms. *G. lamblia* can cause intestinal protein loss without producing diarrhea\(^24\). Specific micronutrient deficiencies have also been described in chronic giardiasis. Low levels of carotene and folate\(^25\) and abnormal vitamin A, folic acid and vitamin B12 absorption (ref 24) occurs in a large minority of patients with chronic symptoms. Nutritional deficiency associated with chronic giardiasis may add to the burden of illness. Bacterial overgrowth of the small bowel has been described in giardiasis and may contribute to malabsorption (ref 24 +\(^26\)). Colonization of the jejunum with *Candida albicans* was reported in 30% of patients with giardiasis and was absent in controls\(^27\). A role for intestinal candidosis in provoking systemic illness has been debated for a quarter century (review in ref # 2\(^2\)). Some strains of *G. lamblia* contain double-stranded RNA viruses\(^28\). The role of *Giardia* as a vector for viral infection requires further study.

Galland et. Al. conducted a two-year retrospective study of 218 patients who presented to our medical clinic with a chief complaint of chronic fatigue (ref 18). *G. lamblia* infection was identified in 61 patients. The symptoms of patients with and without giardiasis, are shown in Table 1. All patients with giardiasis and 86% of patients without giardiasis complained of digestive symptoms, but these were generally mild. The most interesting difference between the two groups lies in the positive association between giardiasis and
symptoms such as myalgia, muscle weakness, flu-like feelings, sweats and adenopathy. In fact, 61% of fatigued patients with giardiasis had been diagnosed elsewhere as suffering from chronic fatigue immune dysfunction syndrome (CFIDS), compared to only 19% of fatigued patients without giardiasis. Cure of giardiasis resulted in clearing of fatigue and related 'viral' symptoms (myalgia, sweats, flu-like feelings) in 70% of cases, some palliation of fatigue in 18%, and was of no benefit in 12%. The association between intestinal protozoa and chronic fatigue in patients without prominent digestive complaints may not be limited to giardiasis. In an, unpublished presentation, Galland reported that 80% of patients with a diagnosis of CFIDS who were infected with the protozoan *Blastocystis hominis* showed significant improvement of fatigue associated with treatment that cleared the protozoa from stool specimens.29

Chronic infestation with *Entamoeba histolytica*, another common protozoan parasite, has been associated with autoimmue phenomena, including the appearance of antibodies to colonic epithelial cells30 and the development of ulcerative colitis after cure of amebic colitis31. Extra-intestinal autoimmune reactions to intestinal amebiasis include a case of antiphospholipid antibody syndrome with deep vein thrombosis and pulmonary embolism32 and development of symmetrical polyarthritis very similar to rheumatoid arthritis (RA)33 34 35. Singh et al.36 measured amoebic antibody levels in 41 Indian patients with a primary diagnosis of RA, 35 age- and sex-matched healthy volunteers, 162 hospital inpatients and 26 patients with other arthritides. Amoebic antibodies were elevated in 39% of RA patients and 0-11% of the various control groups. Only two patients with RA had experienced recent diarrheal disease. These authors suggest that an
excessive and prolonged antibody response to *Entamoeba histolytica* or other enteric organisms may contribute to joint inflammation in RA.

Galland (ref 15) described a patient with rheumatoid-like arthritis and antinuclear antibodies whose arthritis went into rapid and complete remission upon treatment of *G. lamblia* infection with metronidazole. Relapse occurred when the patient acquired *Entamoeba histolytica* during a trip to Egypt; remission occurred slowly following treatment of amoebiasis. Diarrhea, polyarthritis and circulating antinuclear antibodies developed in a United States serviceman heavily infested with *Endolimax nana*, an allegedly non-pathogenic ameba. Metronidazole rapidly reversed all abnormalities. The reported cases of amoebic arthritis may represent a variant of parasitic rheumatism, an inflammatory polyarthropathy produced by circulating antigen-antibody complexes. The presence of autoantibodies, however, is not characteristic of parasitic rheumatism, and suggests other mechanisms of immune dysfunction: either a pre-existing disease is exacerbated by intercurrent amoebic infection or amoebic infection itself provokes autoimmunity, perhaps mediated by the action of immune response genes (ref 23).

Reiter’s Syndrome (arthritis, uveitis and urethritis) has been reported as a complication of infection with two other intestinal protozoa, *Cryptosporidium* and *Cyclospora*. *Cyclospora cayatenensis* has also provoked Guillain-Barre syndrome, a severe autoimmune neuropathy.

*Entamoeba histolytica* contains a soluble lectin which is mitogenic for T lymphocytes. T helper cell activation by this lectin may induce HIV replication *in vivo*. A soluble
Entamoeba histolytica protein, although not mitogenic itself, induced HIV replication in tissue culture of lymphocytes obtained from three out of seven men with chronic HIV infection. Infection with E. histolytica and other parasites may promote the development of AIDS in HIV-infected individuals. Epidemiologic evidence associates pre-existing intestinal protozoan infection with the appearance of Kaposi’s sarcoma among homosexual men in the United States. Although the influence of treating intestinal protozoan infection on the course of HIV infection has not been systematically studied, treatment of intestinal helminth infestation decreases the HIV viral load among African patients with AIDS. Synergism between intestinal parasites and other lymphotrophic retroviruses has been advanced as an explanation for the pathogenesis of Burkitt’s lymphoma and adult T cell leukemia/lymphoma.

Protozoan infection is usually diagnosed by stool examination, however, comparison of stool microscopy with duodenal aspiration has consistently shown that stool may fail to contain identifiable parasites even at the height of acute giardiasis. Collecting multiple specimens over several days increases the sensitivity to 85-90%. Laboratories that specialize in tropical medicine or parasitology are more likely to find organisms in stool specimens than are general or hospital laboratories [reference to be supplied]. Some authors have suggested empirical treatment for intestinal parasites in high risk groups, such as immigrants to the United States from Asia, the Middle east, sub-Saharan Africa, Eastern Europe, Latin America and the Caribbean and have justified this on a cost effective basis, given the safety of current medical therapies. A similar case might be
made for treating chronically ill patients at high risk for parasitic infection because of residence, travel, sexual practices or the context in which illness occurred.

Numerous naturally occurring substances have anti-protozoan activity. The most extensively studied is *Artemisia annua* (sweet Annie or qinghao), a plant that yields the lactone artemisinin (qinghaosu) which is the basis for a new class of anti-malarial compounds widely used in Asia and Africa..55 Artemisinin is thought to owe its anti-protozoan effects to its content of endoperoxides and to kill parasites through oxidation. Its activity, at least in the treatment of Simian malaria, is enhanced by co-administration of cod liver oil and diminished by co-administration of vitamin E (reference to follow). Artemisinin has low toxicity. In addition to its antibiotic activity, it stimulates macrophages, an important component of the immune response to protozoan infestation.56 Artemisinin may induce abortion if given during pregnancy.

The alkaloid berberine can be extracted from the roots of several plant species, notably *Berberis aquifolium* (Oregon grape), *Hydrastis Canadensis* (goldenseal) root, and *Coptis chinensis* (goldthread). Berberine has protostatic and protocial activity against *E. histolytica*, *G. lamblia* and *B. hominis*.57,58,59 It has shown benefit in the treatment of giardiasis in children60
Allium sativum (garlic) and Juglans nigra (black walnut) have a long history of use as antimicrobials. Allicin inhibits growth of *E. histolytica* in culture\(^6\) and may be responsible for the antimicrobial activity of garlic.\(^6\)

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Title

Evaluation of the antiparasitic effect of aqueous garlic (Allium sativum) extract in hymenolepiasis nana and giardiasis.

Source


Abstract

The effect of serial dilutions of crude garlic (Allium sativum)
The intestinal bacterial milieu may be important in the treatment of protozoan infestation, especially for colonic organisms like *E. histolytica*. Pathogenic strains of *Entameba histolytica* are able to evade lysis by both classical and alternative pathways of complement. Intestinal bacteria, *E. coli* in particular, are necessary for complement resistance and for amebic virulence. Mirelman has suggested that ingested bacteria lower the redox potential within the parasite and allow the amebae to escape destruction by oxidative enzymes. He has reported that one can reversibly change the zymodeme patterns of *Entameba histolytica* isolates from non-pathogenic to invasive by culturing...
amebae with the gut flora of patients who have either invasive disease or no symptoms.\textsuperscript{65} Optimal treatment of protozoan infection requires not only the administration of antimicrobial substances, but strategies aimed at enhancing the function of intestinal resistance factors like secretory IgA and phagocyte function and creating a bacterial milieu that is not parasite friendly.

\begin{table}
\centering
\caption{Systemic symptoms of CFS patients}
\begin{tabular}{lcc}
\hline
 & With giardiasis & Without giardiasis \\
 & \%(N = 63) & \%(N = 157) \\
\hline
Depression & 61 & 41 \\
Muscle weakness & 46 & 19 \\
Headache & 41 & 36 \\
Sore throat & 41 & 11 \\
Lymphadenopathy & 36 & 8 \\
Arthralgia & 36 & 27 \\
Myalgia & 34 & 18 \\
\hline
\end{tabular}
\end{table}


29 “Patient-centered diagnosis and treatment for chronic fatigue syndrome”, annual scientific session of the American Academy of Environmental Medicine, Virginia beach, Virginia, October 7, 1994.


61 Mirelman D, Monheit D, Varon S (1987). Inhibition of growth of *Entamoeba histolytica* by allicin, the active principle in garlic extract (allium sativum). Journal of Infectious Diseases. 156, 243-244.


