Nutritional Implications of Intestinal Parasites

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Intestinal parasites, which comprise a host of biologically diverse organisms ranging from unicellular protozoa to complex roundworms, flatworms, and flukes, can cause interference with the nutritional status of the host by a number of mechanisms. Nutrients can be lost by malabsorption, maldigestion, competition, and endogenous loss. Associated bacterial overgrowth also may play a role in certain parasitoses. Parasites that provoke diarrhea compromise water and electrolyte balance. However, parasites also can impair the host's nutriture with respect to a number of other nutrients, including carbohydrate, protein, fat, vitamin A, ascorbic and folic acid, vitamin B_{12}, iron, zinc, and selenium. Evidence is suggestive, but not conclusive, that subclinical infections with ascaris or giardia will retard the growth of preschool children. The pre-existing nutritional status of the presumptive host also may condition the host-parasite interaction. Poor general nutritional status may make a patient more susceptible to invasion by a given parasite, but specific nutrient deficiencies actually may seem to protect the host from the more fulminant complications of amebiasis. The interaction with nutrition is an important and fundamental consideration in the understanding of intestinal parasitism.

Intestinal parasitism is a worldwide problem, affecting populations not only in rural areas of tropical countries, but also in temperate, industrialized nations. However, neither in its public health nor in its clinical context has gastrointestinal parasitosis been regarded with serious concern by medical authorities in the developed nations. Recently, investigation into the interaction of nutrition and infection has focused attention on intestinal parasites.[1] At the same time, epidemiologic studies have revised our assessment of the prevalence of certain parasites among Westernized populations.[2,3] The result of these investigations has been to refine our knowledge, and, perhaps, to revise conventional views that parasites have an innocuous impact on public health.

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Classification of Intestinal Parasites

The term *parasite* is defined as a plant or animal that lives upon or within another living organism at whose expense it obtains some advantage without compensation.[4] The universe of intestinal parasites encompasses a variety of species with diverse biologic natures. Tiny, single-celled protozoa, for example, are quite distinct from complex roundworms and flukes in their interaction with the host intestine. In the context of the potential nutritional impact of host-parasite interaction in man, the intestinal area that a given species inhabits is of utmost importance. The primary infestation site of gastrointestinal parasites is either the small intestine or the colon. Certain parasites, however, can migrate to other viscera outside of the gastrointestinal tract.

Mechanisms of Nutritional Impairment

Given the diverse biologic nature of different gastrointestinal parasites and their interactions with the host, a series of mechanisms can be responsible—alone or in combination—for acute or long-term deterioration of the host's nutritional status. The various mechanisms are listed in *Table I.*

Malabsorption and maldigestion are the two predominant mechanisms of nutritional impairment. Theoretically, these would be most important for parasites inhabiting the small intestine. However, the colon plays an important role in absorption of water and electrolytes, and recently it has been observed that carbohydrate

Table I

Mechanisms of Nutritional Impairment in Intestinal Parasitoses
Maldigestion of food components
Malabsorption of nutrients
Parasitic competition for nutrients
Gastrointestinal loss of nutrients
Catabolic loss of nutrients
Bacterial overgrowth syndrome (?)

substrates derived from dietary fiber or incompletely absorbed sugar and starch can be metabolized to volatile, low-molecular-weight fatty acids, and can be absorbed quantitatively from the colon.[5,6] Thus, potential for nutritionally important malabsorption exists for all types of gastrointestinal parasites. Parasites may interfere with absorption by massive proliferation over the mucosal absorptive surface as proposed for giardiasis,[7] and they can damage the mucosa or invade mucosal cells. The precipitation of an inflammatory response in the lamina propria also could produce malabsorption, especially that of lipid nutrients. A curious phenomenon is the documented malabsorption of vitamin B_{12} in giardiasis.[8] Vitamin B_{12} is absorbed exclusively in the distal ileum and requires the participation of ionic calcium, gastric intrinsic factor, and trypsin, in addition to an appropriate pH. The mechanism by which parasites impair vitamin B_{12} absorption is not understood.

Parasites also have been implicated in maldigestion. Digestion of oligopeptides and di- and oligosaccharides at the membrane level would be interrupted by blockage of or damage to the enterocyte. The action of intraluminal digestive enzymes of pancreatic origin also is impaired by some species.[9,10] Parasites do not affect intraluminal pH, but a change in pancreatic responsiveness to intestinal hormones also has been suggested to occur in giardiasis.[11] Physical obstruction of the biliary ducts is a frequently reported complication of the migration of ascaris roundworm into the biliary tree.[12] Bacterial overgrowth may partially explain impaired digestive efficiency in the face of certain parasitoses.

Another mechanism by which parasites impair the nutrition of the host is by competing with the host for a nutrient. The most notorious case of this phenomenon is the utilization of dietary and endogenous vitamin B_{12} by the fish tapeworm, *Diphyllobothrium latum*. Layrisse[13] has suggested that ascaris might compete with its host for proteins and calories, but it is doubtful that the biomass of an intestinal ascaris burden could make a substantial inroad into the availability of a person's macronutrients. Five female ascaris worms produce 10^6 eggs daily containing 4.24 mg of nitrogen (26.5 mg of protein).[14] Thus, even massive infestation with roundworms would not impinge on the dietary requirements for protein, even in a young child.

Parasites can provoke gastrointestinal loss of nutrients from the body. Parasites associated with watery diarrhea, eg, giardia, can produce acute and substantial losses of water, electrolytes, zinc, and magnesium. Blood-feeding parasites or parasites that produce ulceration of the mucosal surfaces will deplete the host of iron. Protein-losing enteropathy also is observed in certain parasitoses.

Parasitic infections of the intestine usually are not associated with fever or other systemic manifestations. An exception is amebic colitis, which produces an inflammatory colitis. Similarly, giardia or ascaris can migrate into the biliary tree and initiate cholecystitis/cholangitis. Amebae also can establish extraluminal foci, as in the case of hepatic abscesses. All of these extraluminal complications are accompanied by fever, chills, anorexia, and other systemic manifestations. Catabolic losses of protein-nitrogen have been observed to accompany infectious and inflammatory stress.[15] Energy metabolism is severely disrupted,[16] and a large amount of protein synthesis is diverted into the production of acute-phase reactant proteins.[17] Serum zinc and iron levels drop precipitously to 50% of their prefebrile concentrations.[18] This constellation of catabolic processes can alter the nutritional status of the host in those rare parasitoses that produce systemic effects and fever.

Some parasitic infections, notably giardiasis, are associated with bacterial overgrowth.[19,20] The cause-and-effect relationship is unclear; that is, we do not know whether bacterial contamination predisposes to the establishment of a giardial infection, or whether giardiasis predisposes to bacterial proliferation in the upper gut. The nutritional consequences of bacterial overgrowth are well known. These include fat malabsorption due to bile salt deconjugation, vitamin B_{12} utilization, protein- and fat-losing enteropathies, and malabsorption of carbohydrates and fat-soluble vitamins.[21] Bacterial overgrowth might provide a mechanistic explanation for the steatorrhea and vitamin B_{12} malabsorption observed in numerous patients with giardial enteritis.

Table II

Specific Nutrients Affected by Parasites of the Small Intestine

Water and electrolytes (giardia, coccidia, capillaria, intestinal fluke)
Carbohydrates (giardia, coccidia, hookworm [?], ascaris [?])
Protein (giardia, intestinal fluke, hookworm)
Fat (giardia, coccidia, intestinal fluke, capillaria, strongyloides [?], ascaris [?])
Vitamin A (giardia, ascaris)
Ascorbic acid (ascaris)
Folic acid (hookworm)
Vitamin B_{12} (giardia, fish tapeworm, hookworm)
Iron (strongyloides, hookworm)
Zinc (coccidia*)
Selenium (coccidia*)

*Extrapolation from experimental animal data

Nutritional Impairment by Parasites of the Small Intestine

The specific nutrients that can be affected by parasites infecting the small intestine and the corresponding pathogens involved in each case are listed in *Table II*. Parasitoses capable of producing watery diarrhea, such as giardiasis, coccidiosis, capillariasis, and *Fasciolopsis* infections, will result in loss of fluids and electrolytes. D(-)xylose malabsorption has been reported in giardiasis[22-25] and in human coccidiosis.[26] Some investigators have found impaired xylose absorption in hookworm-

infected patients,[27,28] but not in others.[29] Similarly, controversy exists as to whether or not ascaris does or does not impair monosaccharide uptake.[30,31] Giardia also are known to decrease mucosal disaccharidase activity and to cause maldigestion of lactose and, to a lesser extent, sucrose and maltose.[32-35]

Experience in animals[36] and in man[9,10] suggests that proteolytic enzyme secretion by the pancreas is reduced in giardiasis. Hypoproteinemia is common in *Fasciolopsis buski* infection[37] and in severe hookworm infestation.[38] Steatorrhea is a hallmark of giardiasis,[32,34,39-41] coccidiosis,[26] intestinal fluke infection,[37] and capillariasis.[42] Conflicting data exist regarding the efficiency of fat absorption in strongyloidiasis and ascariasis. Kotcher et al[31] found no impairment in Puerto Rican patients, while Mayoral et al[43] found excessive fecal fat excretion in ascariasis infection, and García et al[44] found excessive fecal fat excretion in strongyloides infection—both in malnourished Colombian patients. A curious feature of both Colombian studies was the resolution of steatorrhea solely with nutritional rehabilitation, and *without specific eradication of the helminths.*

Malabsorption of vitamin A has been conclusively demonstrated to occur in giardiasis[45] and ascariasis.[46,47] The ascorbic acid status of rural U.S. children with ascariasis has been found to be reduced as compared with noninfected controls.[48] Folic acid status was diminished similarly in hookworm-infected vs. hookworm-free patients.[49] Vitamin B_{12} malabsorption is common in fish tapeworm infection, but it also occurs in giardiasis[8] and hookworm infection.[49]

Iron nutriture is affected adversely by blood-feeding parasites. Both the New World hookworm, *Necator americanus*, and the Old World hookworm, *Ancylostoma duodenale*, produce intestinal blood loss. The Old World variety, however, causes greater iron waste. Strongyloidiasis also can produce appreciable losses of blood and iron.[50,51] If the experimental evidence regarding zinc[52] and selenium[53] malabsorption in animals caused by *Coccidioides* organisms can be extrapolated to humans, then this protozoan may interfere with trace mineral nutrition in man.

Despite scattered anecdotal reports, no interference in man with respect to any nutrients has been confirmed in *Gastrodiscoides hominis, Taenia saginata*, or *Taenia solium* infections.

Nutritional Impairment by Parasites of the Large Intestine *(Table III)*

Entamoeba histolytica establishes an infection in the mucosa of the colon. Nonetheless, amebiasis can produce fulminant colitis with substantial loss of water and electrolytes occurring with the associated diarrhea. It can also be assumed that protein is lost from the bowel wall in amebic dysentery. In an unexplained fashion, amebic abscesses seem to result in impaired absorption of vitamin B_{12}.[54] Amebic dysentery involves iron loss as a result of colonic ulceration and bleeding. Similarly, the colonic infestation in the life cycle of *Schistosoma mansoni* has been associated with substantial blood loss.[51,55] Whipworm also is believed to produce bleeding in the colon. No pathologic nutritional state has been demonstrated convincingly in association with *Balantidium coli* and *Enterobius vermicularis* infections.

Table III

Specific Nutrients Affected by Parasites of the Large Intestine

Water and electrolytes (amebae)
Protein (amebae [?])
Vitamin B_{12} (amebae, in abscesses)
Iron (amebae, schistosomes, whipworms)

Growth Effects of Parasitic Infections

In addition to effects on the absorption and metabolism of specific nutrients, growth is an important gauge of the nutritional impact of parasitic infections on the host. It is clear that parasitic infections presenting overt clinical symptoms can produce growth failure in children. Overwhelming infections with the intestinal fluke *Fasciolopsis buski* can lead to stunting of growth in the infected child.[37] Of 154 children with giardiasis diagnosed in a hospital in Melbourne, Australia, 31% had suffered recent weight loss or failure-to-thrive.[56] Weight loss and reversible failure-to-thrive also were found in 10 of 11 children with symptomatic giardiasis at the University of Kansas Medical Center.[57] In both series, eradication of the protozoal infection was accompanied by catch-up growth and restoration of normal nutritional status.

The cases of gastrointestinal parasitosis with a sufficient magnitude of symptomatology to merit medical intervention represent only the tip of the iceberg. Less evident is the effect on the growth of children of the endemic roundworm and protozoal infections that affect up to 30%-70% of disadvantaged populations in various parts of the world. Even in the United States, Centers for Disease Control field workers in rural Louisiana found that only 36% of 193 children aged two to 10 years had no evidence of intestinal parasites in their stools. Roundworms, whipworms, giardia, and amebae were found in the remaining population, and 28% of the children examined had more than one parasitic species in the intestinal tract.

Recent investigations have focused on the relationship of parasitosis to growth in a public health context. Some studies have demonstrated a beneficial effect on growth velocity after periodic treatment of ascariasis in preschool children.[58-60] Other studies could not demonstrate a positive effect on the growth of preschool children after the eradication of roundworms.[61,62] The conclusions of the various studies are not definitive. The studies have been criticized variously for small sample size, for the fact that a few patients responding in the opposite fashion would have changed the statistical conclusions, for the broad spectrum of the antihelminthic drugs used, for the variable criteria for growth, and for the short observation periods.

A field trial of antiparasitic treatment and prophylaxis in a population of preschoolers in a rural Guatemalan village has been recently concluded.[63] Treatment was administered at three-month intervals for one year to four equal groups. One group received placebo; a second group received only piperazine, a drug specific for ascaris; the third group received only metronidazole, an agent effective against protozoal pathogens; and the final group received a combination of both drugs. No dramatic effect on growth was observed with any regimen, but a slight increase in ponderal growth (300 gm) and in linear growth (1 cm) was seen in both groups receiving metronidazole as compared with the two groups in which only piperazine or placebo had been administered. This suggests a *biologic* effect of protozoa—most likely giardia—on protein-energy nutriture, but the public health significance of this limited effect of eradication of intestinal protozoa remains to be assessed in a cost-benefit analysis.

Effect of Host Nutritional Status on Gastrointestinal Parasitic Infection

In the foregoing sections, we discussed the multiple nutritional effects that gastrointestinal parasites can have on the host. However, Scrimshaw et al[64] initially affirmed that the interaction of nutrition and infection could be *synergistic* or *antagonistic*. With respect to the effect of host nutriture on susceptibility to parasitic infestation, malnutrition could either favor or retard the parasitic infection. Resistance to and resolution of a parasitic infection is mediated by the host immune defense system.

In the context of intestinal parasitoses, studies in experimental animals have shown that niacin-deficient,[65] ascorbic acid-deficient,[66] and protein-energy-deficient[67] diets increase the pathogenicity of *E histolytica*, implying a synergistic relationship. A poor general diet has been implicated as a factor in human susceptibility to amebiasis,[68,69] but the association has not been rigorously confirmed. Similarly, in infantile protein-energy malnutrition (PEM), giardiasis appears to be common.[70,71] In PEM, hypochlorhydria, immune deficiency, and bacterial contamination of the upper gut could all be factors predisposing to giardial infection.

Antagonistic interactions between nutritional status and gastrointestinal parasites also have been identified. Amebae have a high iron requirement. Diamond et al[72] showed that relative iron deficiency was protective against the establishment of hepatic abscesses after the injection of *E histolytica* in golden hamsters. They speculate that the high prevalence of fulminant, lethal amebiasis in the South African Bantu is related to their notoriously high iron consumption and total-body iron reserves. The implied consequence of these observations is that iron deficiency offers relative protection against the severe complications of amebiasis.

Conclusions

We have focused on the importance of nutritional implications in considering the clinical and public health consequences of intestinal parasites. Intestinal parasites can impair host nutriture in a number of ways. A variety of pathogens of the small intestine and, notably, the amebae in the large bowel, affect specific nutrients. The influence of subclinical intestinal parasitosis on growth is less well defined. Much evidence points to an important relationship between host nutriture and the expression of parasitic illnesses. In addressing the issue of intestinal parasitoses, one should adopt a holistic approach that includes a consideration of the nutrition of the host.

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Nonulcer Dyspepsia

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Dyspepsia, a common human complaint, occurs in approximately 33% of patients clinically believed to have peptic ulcer. Its cause may be gastroduodenal dysmotility, related perhaps to reflux of duodenal contents into the stomach. In some patients, dyspepsia is aggravated by ingestion of fat, caffeine, tobacco, or analgesic drugs, and it is affected adversely by emotion. Dyspepsia is characterized by epigastric discomfort, which often is burning or gnawing in character. Flatulence, a feeling of postprandial fullness, heartburn, and nausea are related symptoms. Epigastric discomfort may result from the irritable bowel syndrome. Any association with gallbladder disease is coincidental.

The diagnosis of dyspepsia is based on the clinical history. In most cases, upper gastrointestinal tract disease may be excluded by x-ray examination of the esophagus, stomach, and duodenum. Bleeding, weight loss, anemia, or dysphagia may be signals of organic disease and signify further investigation. The management of dyspepsia is effected by explanation, reassurance, simple dietary advice, and administration of antacids and simethicone. In exceptional circumstances, cimetidine or metoclopramide may be administered for short periods.

Dyspepsia is the scourge of men who wish to accomplish things. Hitler and Churchill suffered from it during critical periods of their careers, and it affects the lives of 7% to 15% of ordinary citizens.[1] In spite of its prevalence, it is unlikely that any one definition would satisfy everyone. Most would agree that it is characterized by epigastric pain, discomfort, fullness, and bloating, often following a meal. "Gas," "nausea," "heartburn," and "indigestion" are common accompanying complaints. These symptoms may be caused by a peptic ulcer, acute gastritis, esophagitis, or other visceral disease, in which case the treatment is well defined. We are concerned here with those dyspeptic patients in whom no organic disease can be demonstrated.

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Incidence and Relation to Duodenal Ulcer

The problem of *ulcer* versus *nonulcer* dyspepsia has troubled physicians since the turn of the century, when Lord Moynihan reported that ulcer pain could occur in the absence of an ulcer. From 1943 to 1978, 18 studies were undertaken involving 15,000 "dyspeptic" patients.[1] With wartime exceptions, the proportion of patients in whom no organic disease could be demonstrated has remained at about 30% to 50%. It might be believed that those patients with "x-ray-negative dyspepsia" simply had a nondemonstrable ulcer, but the addition of endoscopy to four of the most recent studies did not greatly alter the prevalence of nonulcer dyspepsia. One Danish study[2] diagnosed x-ray-negative dyspepsia in 47% of 181 patients. Endoscopy reduced the number of nonulcer dyspepsia cases by only 9%. Thus, nonulcer dyspepsia is present in roughly 33% of patients clinically believed to have a peptic ulcer, and may be present in 2% to 8% of the general population.[1,3]

Relation to Acid Peptic Disease

We know little about peptic ulcer pain. Silent ulcers exist, and there is a discordance between ulcer healing and symptomatic improvement. Injection of acid through a gastroscope into an ulcer fails to reproduce the pain. Evidence exists that pyloroduodenal dysmotility with reflux of bile into the stomach may be responsible for gastric ulcer and the discomfort of nonulcer dyspepsia.[4,5]

Gastric acid secretion does not appear to be increased