The effects of antiparasitic medications on the nutritional status of children from a parish in rural Ecuador

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THE EFFECTS OF ANTIPARASITIC MEDICATIONS ON THE NUTRITIONAL STATUS OF CHILDREN FROM A PARISH IN RURAL ECUADOR

Marjorie S. Rosenthal

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1995
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The Effects of Antiparasitic Medications on the Nutritional Status of Children from a Parish in Rural Ecuador

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine

by Marjorie S. Rosenthal 1995

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Abstract

THE EFFECTS OF ANTIPARASITIC MEDICATIONS ON THE NUTRITIONAL STATUS OF CHILDREN FROM A PARISH IN RURAL ECUADOR. Marjorie S. Rosenthal, Michele Barry, Department of Internal Medicine, Yale University, School of Medicine, New Haven, Connecticut.

This thesis was designed to test the efficacy of two anti-parasitic medications, albendazole and praziquantel, administered as a single dose, in decreasing geo-helminth infection and improving nutritional status among children in an area endemic for both T. solium and geo-helminth infections. The one-year, prospective non-blind placebo-control interventional study with three arms (albendazole, praziquantel and placebo) involved 206 children from two neighboring parishes in rural Ecuador. Nutritional status was assessed by anthropometry measured at baseline and at one year; infection prevalence was assessed by fecal specimen analysis one month before, three months after and again six months after chemotherapy administration. The three interventional groups had significant differences among baseline variables for age, nutritional status and prevalence of geo-helminth infection. The mean height increment was significantly greater in children receiving praziquantel (4.70 ± SD 1.52 cm) than in those receiving a placebo (3.97 ± 1.17 cm), (p<0.05). The height increment of children receiving albendazole (4.28 ± 1.22 cm) was not significantly different from the other two groups. The mean weight increment of children receiving praziquantel (3.83 ± SD 1.74 kg) was greater than that of the children receiving a placebo (3.48 ± 1.66 kg), both of which were greater than that of children receiving albendazole (3.36 ±1.36 kg) but the differences were not significant. Three months after administration of albendazole and praziquantel, geo-helminth infection prevalence was reduced by 45.8% and 15.2%, respectively. Six months after the administration of albendazole and praziquantel, however, the infection
prevalence increased by 26.1% and 21.8%, respectively. Children taking albendazole neither grew statistically significantly more nor decreased their infection prevalence statistically significantly more than children taking praziquantel or a placebo. This may have resulted from the baseline differences of the intervention groups, from the prevalence of parasites untreated by the chemotherapeutic regimen or from the limited effects of a single mass chemotherapeutic intervention to effect change without the additional benefits of sanitation, education or a second chemotherapeutic intervention.
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INTRODUCTION

This study is one part of a larger research study on *Taenia solium* neurocysticercosis and intestinal helminthic infection in an Andean community in rural Ecuador. The goals of the larger study are to find the best way 1) to decrease neurocysticercosis morbidity, 2) to decrease *T. solium* intestinal carriage, 3) to decrease geo-helminth infection, 4) to improve the nutritional status of children and 5) to evaluate the cost-effectiveness of praziquantel and albendazole, two antiparasitic chemotherapeutic agents, in achieving the previous four goals. The larger study was performed by the Ecuador Academy of Neuroscience in collaboration with the Centers for Disease Control, the International Center for Developmental Research and the Yale School of Medicine.

The study was developed in an area endemic for these infections to address both the high morbidity and potential improvements with intervention. *T. solium* neurocysticercosis is the principle cause of late-onset epilepsy in the developing world (1, 2). By decreasing *T. solium* intestinal taeniasis, *T. solium* neurocysticercosis prevalence can be reduced (2, 3, 4). In children with helminthic infections, antihelminthic therapy not only reduces infection, it also has been shown to improve nutritional status (5, 6, 7, 8). The two antiparasitic medications were chosen for this interventional comparison because they have efficacy in reducing both intestinal taeniasis and helminth infection; albendazole is a broad-spectrum antihelminthic and praziquantel has a more limited spectrum (9, 10, 11). The larger research study aims to test the feasibility of a single intervention scheme against both *T. solium* and intestinal nematode infections in an area endemic for both.
This thesis is limited to my research in anthropometry, the follow up anthropometry one year later, socioeconomic data and parasitic data. This thesis, a prospective placebo-control study, concerns itself with the part of the larger study that tests the efficacy of praziquantel and albendazole in decreasing geo-helminth infection and improving nutritional status. It is hypothesized that children treated with albendazole, a broad spectrum antihelminth, will grow statistically significantly more, measured by height and weight, than those treated with praziquantel, a limited spectrum antihelminth.

I. BACKGROUND FOR THE LARGER STUDY

A. TAENIA SOLIUM

1. Prevalence of T. solium human infection

*T. solium* neurocysticercosis is the most common human cerebral parasite infection (12). According to the World Health Organization (WHO), 2.5 million people are infected with the intestinal tapeworm (13). When endemic, neurocysticercosis affects 2-4% of the population based on autopsy, 9% based on immunology and accounts for 50% of all late-onset epilepsy (14, 15, 16). *T. solium* is endemic in Southeast Asia, Micronesia, the Philippines, Mexico, Guatemala, Ecuador and eastern Europe (17). Most cases in the United States can be traced to travel in an endemic area or fecal-oral contact with a taenia tapeworm carrier from an endemic area (18).

In a study in southern Ecuador *T. solium* infections were shown to be more than two times as common in rural than urban settings. Infections were independent of such socio-economic indices as type of house, water source,
toilet availability and pig-rearing within the family (3). *T. solium* infections have been shown to cluster in some families and be more likely in larger families (2, 3, 18).

*T. solium* neurocysticercosis is hyperendemic in San Pablo del Lago. In a sample of individuals in San Pablo del Lago, 17% were diagnosed with neurocysticercosis by CT scan and 14.3% by enzyme-linked immunoelectrotransfer blot (EITB). The prevalence was 10.8% in children from an urban area in Ecuador. Of those diagnosed by CT or EITB, 60% were asymptomatic. Since the pathogenesis of neurocysticercosis is such that neurological infection may eventually become symptomatic, asymptomatic disease is an indication for therapy (19).

2. *T. solium* lifecycle
Humans are both intermediate and definitive host of *T. solium* while pigs are intermediate hosts, only. The life cycle of this cestode can occur only where pigs have access to human feces, humans consume poorly cooked pork and human food and water is contaminated by human feces. Since its lifecycle demands decreased hygienic standards, endemicity of neurocysticercosis is used as an indicator of socio-economic development (20, 21).

Taeniasis, intestinal infection of humans with the adult form of *T. solium* is acquired by eating undercooked pork infected with the larval form of the tapeworm. Taeniasis carriers pass *T. solium* eggs in their stool. Neurocysticercosis, the larval form of *T. solium*, is acquired by humans and pigs, the intermediate hosts, after eating food contaminated with feces containing *T. solium* eggs. As *T. solium* eggs pass through the digestive
system gastric and pancreatic enzymes catabolize the egg coat, releasing oncospheres. The oncospheres cross the intestinal wall, enter the bloodstream and are carried to the muscles or central nervous system where, within a few months, they evolve into cysticerci (14, 21). Whether auto-infection occurs when *T. solium* eggs are released from gravid proglottids and regurgitated into the stomach thus leading to larval invasion, is unclear (17).

Within two years of infection the cysticerci die and calcify. The inflammatory reaction around the dying cysticerci, consisting of lymphocytes, plasma cells and eosinophils, is variable but may lead to edema, reactive astrogliosis and displacement of neural structures (14, 17, 21).

3. Clinical manifestations of *taeniasis* and *neurocysticercosis*

Intestinal *taeniasis* usually does not cause clinical disease. Patients may become aware of their disease only when they find the tapeworm in their stool (17).

The clinical manifestations of *neurocysticercosis* are varied and may be non-specific. They are those of a space-occupying subcutaneous or visceral lesion and are therefore dependent upon the number, size and location of cysticerci. Most clinical manifestations arise when the mature cyst degenerates, regardless if death is by natural progression or by medication (12). The most frequent manifestation (up to 52% of patients in one study) is epilepsy (14). Other presenting signs may be increased intracranial pressure, meningoencephalitis, hydrocephalus, progressive dementia, abdominal pain or malabsorption. More than 50% of patients demonstrate a mixed picture and 25% exhibit a normal neurological exam (13, 17).
4. Diagnosis of taeniasis and neurocysticercosis

Diagnosis of intestinal taeniasis consists of finding gravid proglottids in stool. Finding *T. solium* ova in stool is less accurate; since *T. solium* eggs are released intermittently, ova identification is not sensitive and since all taenia species are morphologically similar, ova identification is not specific (17).

Diagnosis of neurocysticercosis is by CT scan and by EITB. EITB may have a low specificity in endemic regions because it will be positive if the patient is infected with either the adult or larval form. If the EITB is positive, clinical evaluation, stool examination and/or CT scan are indicated. Correct diagnosis is important because most patients respond to albendazole or praziquantel (15). When present, subcutaneous nodules may be biopsied and *T. solium* hooklets may be identified (17). Subcutaneous nodules, however, are less common in Latin American *T. solium* than elsewhere (22).

II. BACKGROUND FOR STUDY

A. GEO-HELMINTHS

1. Prevalence of geo-helminths

Geo-helminths are highly prevalent throughout the world; greater than one-third of the world’s population is infected with one or more species (9). More specifically, over one billion people have a hookworm (*Ancylostoma duodenale* or *Necator americanus*) infection (17), over one billion people have an *Ascaris lumbricoides* infection and over 750 million people have a *Trichuris trichiura* infection (9, 17). Most studies demonstrate that infection with multiple parasites, polyparasitism, is more prevalent than infection with a single parasite (9, 23, 24). These three geo-helminths are distributed
throughout the world, especially in tropical and subtropical regions (17, 25).

Geo-helminth infection prevalence is increased within lower socio-economic groups. The association between infections and poor water supply, poor hygienic facilities and overcrowding has been well demonstrated (25, 26, 27). According to the World Bank, *Ascaris* and *Trichuris* and *T. solium* are "closely associated with socio-economically depressed communities" (9). A number of studies have shown that helminth infections cluster within families (19, 28).

Children are at increased risk for geo-helminth infections and their sequelae (7, 9, 28, 29). Helminth infections aggregate within children: more than 70% of all helminths infect less than 30% of the population, most of whom are children (9, 29). Hookworm infections are more common in school-age children than any other age group and *Ascaris* infections are more common in pre-school-age children than any other age group (6). In some parts of the tropics, more than 90% of children are infected with *Ascaris* (5). Infected children are more likely to have a greater worm burden than infected adults, increasing the intensity of symptoms and sequelae (24, 30).

2. Effects of geo-helminths: short-term
The three most common geo-helminths, *Ascaris*, hookworm and *Trichuris*, all cause some form of malnutrition; about 10% of all intestinal parasitic infections are sufficiently intense to cause decreased levels of growth and development (9, 24). The consequences of the infection are in proportion to the size of the worm burden. That is, the fecal egg count intensity is related to the deficits in growth and hemoglobin level (9, 23, 28).
Ascaris, via malabsorption of nutrients, lactose intolerance, decreased intestinal permeability and anorexia, causes impaired growth and development (31). Ascaris also causes abdominal obstruction and has been shown to cause decreased physical fitness (28, 32).

Hookworm causes iron-deficiency anemia and resultant fatigue. Severe infections causes protein malnutrition, exertional dyspnea, headache, pallor and tachycardia; chronic infections cause growth retardation, both physical and intellectual (5, 8, 10, 17, 23, 28, 33). Hookworm infections have been shown to cause decreased physical fitness and increased susceptibility to other infections (5, 8, 32).

Trichuris causes dysentery and may cause iron-deficiency anemia. Chronic infection causes chronic colitis and its sequelae: malnutrition, finger clubbing and growth retardation (17).

3. Pathophysiology and diagnosis of geo-helminths
Hookworm, Ascaris and Trichuris are all transmitted by improper disposal of feces from infected individuals. Hookworm embryonated eggs are deposited in soil from contaminated feces. They grow, molt and when they come into contact with human skin they enter through hair follicles or in places of decreased skin integrity. Both A. duodenale and N. americanus may enter through skin and A. duodenale may enter via oral ingestion, also. Ascaris and Trichuris fertilized eggs are both deposited in soil from contaminated feces. They embryonate and are then swallowed by a human host. The larvae hatch in the small intestine (17).
There are two likely mechanisms by which geo-helminths cause decreased growth, physical fitness and cognitive ability in human hosts. One mechanism, iron deficiency anemia, may be due to increased loss or decreased uptake. Hookworms cause increased loss by secreting an anticoagulant that blocks human factor Xa and by sucking blood from the small intestine villi; the anticoagulant causes bleeding even after the hookworms move to a new site. *Trichuris* causes increased loss by capillary damage in the small intestine and all three geo-helminths can cause vomiting, diarrhea or GI bleeding from inflammation of intestinal mucosa. *Ascaris* causes decreased uptake via induction of small intestine inflammation and the resulting decreased nutrient absorption (5, 9, 17, 29).

The second likely mechanism by which geo-helminths cause decreased growth is the production of cytokines by the human host. Cytokines act centrally to depress appetite and peripherally to increase catabolic enzymes of both muscle and adipose tissue. Specifically, in response to parasitic infection, macrophages release TNF-alpha which increases the synthesis of catabolic enzymes. TNF-alpha autocrinally activates macrophages to synthesize IL-1 which induces anorexia, fever and cortisol release (5, 34, 35).

Diagnosis of geo-helminths is by stool exams. Hookworm, *Ascaris* and *Trichuris* all have characteristic eggs, identified microscopically (17). Since diarrhea, abdominal complaints and other acute symptoms may or may not be part of the clinical picture, a geo-helminth infection may be clinically apparent only when its sequelae are present (4).
4. Effects of geo-helminths: long-term sequelae

The long-term effects of continuous geo-helminth infection are the long-term effects of decreased physical fitness, increased fatigue and decreased growth. That is, since “the peaks of intensity, and thus morbidity, occur at an age which is crucial for physical and intellectual development,” (9) chronically infected children, even controlling for socioeconomic status, suffer increased absenteeism and poor performance at school, are less able to benefit from primary education and less able to develop healthy adult bodies (32, 36).

Multiple studies have demonstrated not only that children with parasitic infections perform statistically significantly worse in cognition tests, but also that test performances improve after antiparasitic therapy (37, 38, 39). Since education level and occupational productivity are highly correlated, (40) the decreased intellectual and growth potential creates a decreased ability to support a family and a vicious cycle of poverty and infection (9, 23, 24).

B. ANTHROPOMETRY

1. Anthropometry as an indicator of malnutrition

More than one-third of the world’s children suffer from some form of malnutrition. Children in developing countries more often suffer from chronic malnutrition (43%) than acute (9%) (5, 36).

Anthropometry is the use of body measurements to assess nutritional status. Since any insult to a child’s health will affect growth and maturation, assessment of growth is assessment of health (36, 41). Anthropometry may be used to assess individuals or entire populations. In assessing individuals, it may be used as a screening device to identify children at risk of malnutrition.
In assessing populations, it may be used to identify groups at risk for the sequelae of malnutrition and help determine which interventions may be most beneficial to those groups (43).

Anthropometry helps to distinguish between different types of malnutrition: when there is a high prevalence of very thin, wasted children, an etiology of famine or an acute infectious disease is likely; when there is a high prevalence of short stature, or stunting, however, indicators of poor socioeconomic status—poor hygiene, inadequate supplies of potable water, chronic infectious disease—are likely etiologies (42, 44). A 1994 WHO analysis demonstrates that there is little correlation between stunting and wasting, indicating that the anthropometric indices can distinguish between the kind of malnutrition with some certainty (42).

Anthropometry, criticized for being less accurate than biochemical assays is invaluable in the field for the ease with which indices can be obtained and compared (43, 45, 46).

2. Mechanics of Anthropometry
Anthropometry may be used as an indicator of both acute and chronic nutritional status; weight reflects both the present and past nutritional experience while height "within the genetic range of the individual" reflects only the past (44).

After height and weight are measured, the numbers are generally compared to those of a reference population. Since the reference population is generally not from the same population as the study population, it is used to determine
relative nutritional status and not necessarily desired growth (42). A commonly used reference population is the International Growth Reference Curves, established by the Centers for Disease Control and Prevention (CDC) and the WHO in 1977. The National Center for Health Statistics (NCHS) derived the curves from a representative group of United States children, ages 2-18 years. The children included both caucasians and non-caucasians and children from all levels of income status. For statistical purposes, when the curves were established they were normalized for each indice (41, 42).

Regardless of the reference population used, each child is assigned a number that describes his/her nutritional status in relation to the reference median. A z-score, a proportion of the standard deviation, is generally preferred to a percentage of the reference median because the z-score’s normalization around the mean makes its interpretation more straightforward. By definition, the proportion of individuals who have z-scores >2 is the same as the proportion who fall >2 standard deviations from the mean; in the normalized reference population that proportion is 2.3%. A z-score facilitates this comparison between the study population (the proportion with z>2) and the reference population (2.3%). A z-score is also preferred to a percentile for describing the extremes of the distribution. Finally, a z-score facilitates the performance of the analytical procedures, i.e., t-tests and regression analysis, that require normalization (41, 42).

Height-for-age (HA) is a reflection of long-term growth; (36) low height-for-age therefore represents “continuous poor overall economic conditions and/or repeated exposure to adverse conditions“(47). Low HA, also called stunting or short stature, may be secondary to micronutrient deficiency,
protein deficiency or parasitic infection (42). HA may be used for evaluating long-term conditions or intervention efficacy (26, 42).

Weight-for-height (WH) reflects proportions, "harmony of growth" (36) or current nutritional experience (26). A low WH is often synonymous with wasting or thinness. Its field-work advantage is that no birth record is necessary. This indice’s disadvantage is that the increased variability in weight and height as children enter puberty makes WH no longer independent of age; WH cannot be used with girls greater than ten years old and boys greater than 11.5 years old (42).

Weight-for-age (WA) is a somewhat more controversial measurement. Whereas some authors argue it represents a synthesis of the long-term growth of HA and the body proportion of WH (36), some authors argue that WA is not a good indicator of nutritional status because a low WA, considered underweight, does not differentiate between children who are tall yet too thin and those who are short yet well-proportioned (42, 43, 47).

Most authors agree that WH and HA are the most useful indices in evaluating the nutritional level of a pre-school age population (42, 47). For a school-age/early pubescent population, however, WH is less useful. The studies that have found a strong association between low WH and low WA (48, 49) offer greater significance to WA as an indice of school-age nutrition (42).

3. Anthropometry and associations with socio-demographic status
Correlation between socio-demographic indices and nutritional status may
vary by location; any attempt to extrapolate correlation must be tempered by the limitations of place (26). Nonetheless, certain socio-demographic indices that are frequently associated with poor anthropometric outcomes include poor housing, mothers with low levels of education, female gender, latrine absence and minimal water use (23, 26, 50).

4. Using anthropometric indices

Anthropometric indices may be used as indicators for etiology of malnutrition, and as indicators for morbidity and mortality.

As was previously discussed, intestinal helminth infections impair growth. Children with hookworm, *Ascaris* and *Trichuris* infections have anthropometric indices indicative of chronic malnutrition: they are at increased risk for low HA and WA (5, 23, 28, 33). The consequences of the infection are in proportion to the size of the worm burden. That is, the fecal egg count intensity is related to the deficits in WA and HA (9, 23, 28). Children with more intense infection have lower anthropometric indices than their less intensely infected counterparts (23, 28).

Anthropometric indices have been associated with mental development. In a Jamaican study, developmental scores were significantly related to HA and WA, but not WH. Reduced development was significant even with mild and moderate malnutrition (26). A Guatemalan study similarly found poor HA and WA scores correlated with poor behavioral development. The Guatemalan study also found that improvements in HA or WA were correlated with improvements in behavioral performance (51). These findings demonstrate that poor mental and behavioral development is
associated with anthropometric indices chronic malnutrition.

Anthropometric indices have been widely used for predicting mortality. Bairagi demonstrated that all anthropometric indices studied (WA, weight change, HA and height change) were each more powerful indicators of mortality than were socio-economic indices (45). A number of studies found that low WA is the best anthropomorphic predictor of mortality; that is, with declining WA, mortality increased exponentially (45, 52, 53). None of these studies appeared to demonstrate a threshold effect on mortality; even mild to moderate malnutrition (up to 79% of mean WA) was associated with increased mortality. Of those deaths attributable to malnutrition, 45-83% occurred in children only mildly to moderately malnourished (52).

**C. INTERVENTIONS**

Thus taking into consideration the socio-economic factors that increase the likelihood of both nematode and *T. solium* infection and the sequelae of these infections, it is incumbent upon society, for reasons as linked to economics as to altruism (5, 23, 40), to find cost-effective ways of prevention.

1. Primary prevention of transmission

Most world health organizations agree that the long term solutions to malnutrition and geo-helminth control are eradication of poverty, an increase in health care, sanitation and education (9). Interventions that result in increased use of clean water and sanitation, especially in areas endemic for *Ascaris*, hookworm and infectious agents of diarrhea, have been shown to improve the health of children (27).
The interventions must be community-wide and multi-faceted. The World Bank cautions that in communities where only some families have sanitation facilities there is generally no correlation between the infection rate in a family and the presence of a latrine (9). Community-wide sanitation programs have been successful in reducing enteric helminth transmission to U.S. levels in post World War II Northern Italy, Israel and Japan (24). Others hypothesize that the failure of some latrine-building interventions has been the lack of concurrent water-improvement interventions; they argue that one without the other cannot significantly reduce the fecal-oral transmission rates (50).

For effective intervention, education needs to be a salient aspect, also. In Indonesia new latrines did not alter geo-helminth infection because the children continued to defecate outdoors and in Iran farmers were pleased that the latrines provided them with a central location to gather human excretement to spread as fertilizer (9). The Rockefeller Sanitary Commission, on the other hand, reduced transmission of hookworm through a population-wide education campaign about transmission of hookworm via barefeet (17).

While environmental interventions to interrupt transmission are the ultimate goal, in the short-term, building community-wide hygienic facilities and a safe water supply as well as educating the public is too time-consuming (the rate of infection in post World War II Italy took over 15 years to decline (9)) and expensive (9, 24, 29). The enormous financial and temporal difficulties of community-wide sanitation improvements make population-based broad-spectrum chemotherapy the best means of reducing parasitic
infection in the short-term.

2. Chemotherapy for taeniasis and geo-helminths

In communities without sanitation facilities, antiparasitic chemotherapy may be considered prevention as well as cure (6). For, as it reduces the prevalence of intestinal taeniasis, it reduces the chance of disseminating neurocysticercosis throughout the community. Likewise, as it reduces prevalence of geo-helminth infections, it reduces the chance of fecal-oral transmission throughout the community.

The WHO has advocated antihelminthic chemotherapy wherever the prevalence of helminthic infection is >50% (30) Other authors have advocated mass anti-cestode chemotherapy whenever the prevalence of taeniasis is >1% in humans and cysticercosis is >5% in pigs (3).

Two drugs used widely for *T. solium* are praziquantel and albendazole. Praziquantel, a piperazinone-isoquinolone, works by decreasing tegumental integrity in the parasite. Less than one minute after exposure each parasite contracts, allowing the ingress of Ca ions. The parasite’s muscles go into tetany, sucker control is lost and it is swept down the host digestive tract. The integument undergoes disintegration, previously inaccessible antigentic sites are exposed allowing the host immune system to attack (9). Praziquantel is the drug of choice for cestodes (11).

Albendazole, a benzimidazole, works by interference with polymerization of worm tubulin. It is the drug of choice for nematodes (11). Albendazole is not approved for use in the United States.
The side effects of praziquantel are malaise, headache and dizziness (frequently), sedation, abdominal discomfort, fever, sweating, nausea, eosinophilia and fatigue (occasionally) and pruritis and rash (rarely). The side effects of albendazole are diarrhea, abdominal pain and Ascaris migration to the nasopharynx or oralpharynx (occasionally) and leukopenia, alopecia and increased transaminases (rarely) (11). Benzimidazoles are embryotoxic and teratogenic in animals and their safety in infants and pregnant females has not been established (10).

3. Chemotherapy for T. solium
Praziquantel in single high doses (50 mg per kg body weight) and single low doses (5 mg per kg) has been shown to be effective against larval and adult T. solium infections, respectively (1, 2, 3, 54). Treating infected humans with low-dose praziquantel not only reduces the prevalence of intestinal taeniasis, it also has the added effect of decreasing its prevalence in pigs (3). Similarly, albendazole, in high doses (15 mg per kg for 8-30 days) and low doses (400 mg QD for 1-3 days) has been shown to be effective against larval and adult T. solium infections, respectively (4, 14, 55).

For treatment of cerebral larval T. solium (neurocysticercosis) high dose albendazole appears to be more efficacious than praziquantel. For example, when outcome is measured as a reduction in neurocysticercosis symptoms and/or a decrease in cysticerci seen on CT scan, albendazole has been shown to have greater efficacy than praziquantel (12, 57, 58, 56). In reducing neurocysticercosis-associated seizures, moreover, Vasquez demonstrated that albendazole had a greater efficacy than praziquantel and a combination of
albendazole and praziquantel had greater efficacy than either alone (14).

For prevention of neurocysticercosis via decreased prevalence of adult *T. solium* (intestinal taeniasis), however, albendazole and praziquantel both appear to be efficacious and have not been compared directly. Multiple studies have shown the efficacy of a single low-dose of praziquantel in reducing intestinal taeniasis (2, 3) and a single 400 mg dose of albendazole has reduced intestinal taeniasis in some studies (4) and been ineffective in others (59). The larger study, more concerned with preventing neurocysticercosis than treating it, attempts to answer which of the two antiparasitic medications better reduces intestinal taeniasis prevalence.

4. Chemotherapy for geo-helminths
A comparison of praziquantel and albendazole as anti-helminthic medications reveals that both have been shown to reduce certain helminths and increase anthropometric indices as individual interventions and in combination (24) but have not been compared directly in this manner.

Praziquantel reduces childhood infection with schistosomes but not hookworms (8, 60). In areas endemic for schistosomes, praziquantel has been associated with an increase in anthropometric indices including weight increment, height increment, WA, WH, arm circumference, triceps skinfold and subscapular skinfold (60). Albendazole reduces intestinal infection with hookworm (32), hookworm and *Ascaris* (6) and, in some studies, hookworm, *Ascaris* and *Trichuris* (33, 61). Increased growth with albendazole has been measured by improved height increment, weight increment, HA, WA and WH (6, 32, 33).
Most antihelminthic chemotherapeutic studies demonstrate increased growth after intervention (8, 32, 33, 60) even when growth is not associated with decreased helminthiasis (6). The limited sensitivity and specificity of conventional stool examinations may account for some of this incongruence (18).

5. Chemotherapeutic regimen

Mass chemotherapy is the most cost-effective way in which to prevent geo-helminths and T. solium infections whenever the prevalence or intensity is high or there is evidence of associated morbidity or mortality (9). Diagnostic testing and treatment of infected individuals only, is unreasonable in these situations given the low sensitivity and high cost of periodic fecal exams (18, 24). Mass chemotherapy increases compliance: when medication is given to all children at school they are more likely to take it (24). Thus as long as the medications are without significant side effects, population-based chemotherapy is recommended for antihelminthic and taeniacidal interventions.

D. SAN PABLO DEL LAGO, ECUADOR

Ecuador has a total area of 276,840 kilometers$^2$; it is slightly smaller than Nevada. The population in 1994 was 10,677,000 and by the year 2,000, it is estimated to grow to 11,945,000. The population density (persons per square miles) is 101, the birth rate 26 per 1,000, and the death rate 6 per 1,000. Ethnically, 55% are Mestizo, 25% are Indian, 10% are of European descent and 10% are of African descent. Almost 95% are Roman Catholic. Spanish is the official language but many Indian languages, especially Quechua, are
prominent. Forty-three percent of adults have completed primary school; the illiteracy rate is 14% (62).

The labor force in Ecuador is 35% agriculture, 21% manufacturing and 16% commerce. Petroleum, bananas, shrimp, cocoa and coffee are, in descending order, the most commonly exported commodities (62). Pig husbandry practices in Ecuador are a risk factor for disease: 61% of pigs are bred mostly outdoors on small farms and only 48% of pigs are inspected at slaughter by a veterinarian (19).

As for health care resources in Ecuador, there are 1.04 doctors and 3.12 nurses per 1,000 people. There are 1.7 hospital beds per 1,000 people. Health care expenditures are 4.1% of the GNP and 31 million dollars are received in foreign aid. Low birth weight babies are 10% of total and infant mortality is 4.7% of live births. Children <1 year old have a vaccination rate of 89.0% (62).

Children in Ecuador have a high prevalence of malnutrition. Ecuadoranean children are more stunted than wasted, indicating a predominance of chronic over acute malnutrition. A WHO study of both rural and urban children in 1993 demonstrated 34.0% stunting and 1.7% wasting (36).

San Pablo del Lago is in the province of Imbabura in the country of Ecuador. High within the Andes, San Pablo is 2,600 meters above sea level. Its land mass is about 150 square kilometers. In 1992 there were 6,951 residents in San Pablo del Lago. There were 1,782 <9 years old and 1,640 between 10-19 years making 49.4% of the population <20 years old. Greater than 85% of families owned their own homes and greater than 90% of homes were made of brick.
The illiteracy rate was 32% (19).

San Pablo del Lago remains a traditional agrarian town, largely unchanged by the influx of tourism and industrialization to other parts of Ecuador in the past few decades. While the WHO has cautioned that the rapid industrialization of many developing countries is leading them, unprepared, to health care problems of more developed countries (coronary artery disease, adult onset diabetes, hypertension, etc.), San Pablo's health care problems remain those of a poor, agrarian-based community.

III. SUMMARY

Children in developing countries have a high prevalence of malnourishment. School children in developing countries, whose habits are conducive to fecal-oral transmission of parasites, are at increased risk for infection with geo-helminths and taeniasis. Infected children suffer decreased physical growth and intelligence. Their community suffers increased potential transmission as well as decreased contributions through work and leadership.

In the short-term, the most cost-effective manner of controlling both intestinal parasites and *T. solium* neurocysticercosis is through population-based, broad-spectrum chemotherapy. By choosing school children in a community endemic for geo-helminths, hyperendemic for *T. solium* and with a high prevalence of malnutrition, this thesis attempts to determine which of two medications, praziquantel or albendazole, is more effective in decreasing geo-helminth infection and of increasing nutritional status. Given the greater anti-helminth spectrum of albendazole, it is hypothesized
that the children treated with albendazole will have greater growth increments than the children treated with praziquantel.
MATERIALS AND METHODS

The design, results and discussion of the larger study, on *T. solium* taeniasis and neurocysticercosis in an Andean community in rural Ecuador, have been published previously (19, 20, 56, 64, 65, 63).

I. Study Population

Third, fourth and fifth graders, (ages 8.67 to 14.17 years) from San Pablo del Lago and Gonzalez Suarez, neighboring parishes in Ecuador, South America were chosen as the subjects. The age-group was chosen for its high incidence of helminthic infection (24) and the serious sequelae of such infections (9, 23, 32). The age-group was also chosen for their maturity to participate in the psychiatric evaluation aspect of the larger study and for their stability in primary school throughout the study. The study was designed to exclude pregnant females, severely ill children and children with a history of seizures but there were none to exclude. Every child enrolled in school in the two parishes at the beginning of the study was a potential participant. The parents of each child were asked to consent to participate and all were free to withdraw at any time. Agreement to consent was 100% (65).

The two parishes, about 100 kilometers north of Quito, Ecuador were selected for the endemic prevalence of both *Taenia solium* and soil-transmitted nematode infections (3) as well as the local authorities' willingness to participate in the study.

The study was reviewed and approved in Ecuador by an Ethical Review Committee (constituted by members of the Ministry of Health and the
Ecuadorean Academy of Neuroscience), the Human Subjects Review Board at the Centers for Disease Control and the Human Investigations Committee at the Yale School of Medicine.

Two hundred and six students, all of the grade-appropriate children from the five primary schools in San Pablo del Lago and Gonzalez Suarez, were enrolled in June 1992.

II. House-to-House Surveys
In the Spring of 1992, consenting heads of household were interviewed regarding family members and socioeconomic data. Permission was obtained to measure family members at school. Interviews were conducted in Spanish by students from the Catholic University in Quito, Ecuador.

III. Anthropometry
Children were measured for baseline data in June 1992. Height and weight were measured for each child. Height and weight were first normalized according to UNICEF’s plan “How to Weigh and Measure Children.” (66)

Height was measured using a height meter (a metal measuring tape with a precision to 5 mm. glued into a groove of a piece of wood measuring 180 cm.), a wooden right-angled triangle (that fit into the groove of the height meter) and a plum line (a screw-driver tied to the end of a 100 cm-long string.) Before each group of measurements an adequate place to install the height meter was obtained and the height meter was installed according to the “Manual for the Implementation of Height Census of School Entrants.” (67)
Each student was measured in the position indicated by the manual: without
shoes and socks, with his/her body (heels, shoulder blades and back) straight against the height meter, with the knees straight, the head erect, looking horizontally at a fixed point. The measurer placed the triangle flat on the student's head and flush with the groove in the height meter. The student was asked to step forward, the measurer read and then recorded the height. The measurer measured a group of five students once and then, without looking at the number recorded previously, measured the same group a second time. The average of the two measurements was recorded as the result.

Weight was measured using a Health-O-Meter standing scale which has precision to 100 grams. Each student was weighed wearing their gym outfit (a t-shirt and shorts) or as few clothes as possible within the realm of cultural sensitivity (i.e. indigenous girls who do not wear underclothing were weighed in their skirts and shirts while those who do wear underclothing were weighed in their underclothing, only.)

Date of birth was determined by the official record at the civil register in San Pablo, when available. When the official record was unavailable (for children who moved to San Pablo after birth and for all the children from Gonzalez Suarez) the classroom teacher’s record was used.

The anthropometry enumerator and birth date collector in 1992 was Marjorie S. Rosenthal, a Yale Medical Student.
IV. Mass Chemotherapy

The children from San Pablo del Lago were divided geographically into two interventional groups. To improve compliance the division was made so that every child from any one school was receiving the same medication. In December 1992, six months after the baseline data was collected, one group received a single 150 mg dose of praziquantel and the other group received a single 400 mg dose of albendazole. At the termination of the study, in an effort to clear all helminthic infections from participants, both groups received a single 400 mg dose of albendazole.

The children from Gonzalez Suarez were all in the non-intervention group. In December 1992 they received a placebo. At the termination of the study they received a single 400 mg dose of albendazole.

Chemotherapy was administered by Dr. Marcelo Cruz, Dr. Ivan Cruz and Yale medical students Jack Maypole and Erik Shmookler.

V. Coproparasitology

In November 1992, stool specimens were collected from 127 children, 69 from the albendazole group, 46 from the praziquantel group and 12 from the non-intervention group. In March 1993 and June 1993 stool specimens were collected and analyzed from 69 children from the albendazole group and 46 from the praziquantel group, only. The 79 children whose stool was not analyzed (38% of the original cohort) were not available during the days the team was in the field.
At each collection, stool specimens were collected in the field and brought to Quito (a two hour drive) for analysis that day. Specimen were examined for eggs from *Ascaris lumbricoides*, *Trichuris trichiura*, *Taenia solium* and hookworm by Kato-Katz method (68) at the Ecuador Academy for Neuroscience.

VI. Anthropometry after chemotherapy

Children were measured for the one-year follow-up in June 1993. One hundred and fifty-eight students (77%) of the original 206 were measured. Identical protocols for measuring and recording height and weight were employed in the follow-up.

The anthropometry enumerator at that point was Jack Maypole, a Yale Medical Student.

VII. Statistical Analysis

The results of each student’s height and weight were compared to the growth reference curves for weight-for-age (WA) and height-for-age (HA) established by the NCHS and the CDC on the Epi. Info program (versions 5.01 and 6.01). Each child was assigned one z-score for WA and one for HA. (16) A z-score of 1 (a measurement falling one standard deviation below the mean or greater) was considered high or normal, a z-score of 2 (less than or equal to two standard deviations below the mean but greater than one standard deviation below the mean) was considered slightly malnourished, a z-score of 3 (less than or equal to three standard deviations below the mean but greater than two standard deviations below the mean) was considered moderately
malnourished and a z-score of four (greater than three standard deviations below the mean) was considered severely malnourished (47).

The data was analyzed on a DECpc using Epi. Info program (versions 5.01 and 6.01) at the computer room in the Yale School of Medicine and on a Macintosh IIci using StatCalc in the office of Kim Freudigman, Ph.D. Statistical tests included two-factor repeated measures ANOVA, Kruskal Wallis one way ANOVA chi-squared tests and student’s t-test for association. Repeated measures ANOVA was used to determine the significant difference between growth slopes over one year by intervention group.

The data was analyzed to characterize socio-economic status, anthropometry and infection prevalence variables for the three interventional groups. HA and WA were reported as the percentage of children in the interventional group >2 standard deviations below the mean of the reference data. Thus the greater the percentage of children with a z score >2, the worse the nutritional status of that group. The data was then analyzed for the associations between intestinal helminths infection and both anthropometric and socio-economic status variables. Finally, the two intervention groups were statistically combined into one to compare the difference between intervention and none.
RESULTS

I. Study Population

Of the 206 children in the original cohort, 158 children (77%) were measured in the one-year follow-up. Explanations for those lost to follow-up included the family had relocated or the child had changed schools. Of the original cohort 127 children (62%) participated in the first stool exam and 115 (56%) in the second stool exam. Explanations for those lost to follow-up included the family had moved, the child was at the market with the family, the child had changed schools and unknown.

II. Comparison of Intervention and Non-intervention Groups

A. Demographics (see Table I)

The percentage of females was greatest in the praziquantel (PRZ) group (52.2%) then the albendazole (ALB) group (51.4%) then the non-intervention (NON) group (44.7%). The differences were not significant.

The mean age (in years) was greatest in the PRZ group (10.90 ± 1.15), then ALB group (10.65 ± 0.97), then the NON group (10.39 ± 0.98). The differences were significant between the PRZ and NON group (students’ t-test=4.562, p<0.05).

The family size (mean ± standard deviation) was greatest in the ALB group (6.64 ± 1.58), followed by the NON group (6.61 ± 1.87), then the PRZ group (6.39 ± 1.58). The differences were not statistically significant.

The percentage of children with a toilet--including one attached to plumbing and one attached to a drain and tank--was greatest in the NON group (65.8%),
then the PRZ group (63.0%), then the ALB group (56.8%); the differences were not statistically significant.

The percentage of children who have their water supply piped into or near their house was greatest in the PRZ group (97.8%), then the NON group (92.1%) and then the ALB group (85.2%). The difference was significant between the PRZ and ALB groups ($X^2=5.034, p<0.05$).

The percentage of children with a mother who had some formal education was greater in the ALB group (75.7%) than the PRZ group (63.0%) but the difference was not statistically significant. The data was not collected in the NON group.

The percentage of children who came from a home where the head of the household had some formal education was greatest in the ALB group (87.8%), then the NON group (84.2%), then the PRZ group (76.1%); the differences were not significant.

B. Anthropometry

1. Baseline (see Table I)

The three groups of children had significant differences concerning anthropometric indices (Table 1). The percentage of children with >2 nutritional status by HA was 52.2% in the PRZ group, 55.3% in the NON group and 72.9% in the ALB group. The differences were significant between the PRZ and ALB groups ($X^2=5.349, p<0.01$) but not between the other groups.
The percentage of children with >2 nutritional status by WA was 2.6% in the NON group, 8.7% in the PRZ group and 14.9% in the ALB group. The differences were significant between the NON and ALB groups ($X^2=3.893$, $p<0.05$).

2. At One Year

At one year the height increment (mean ± standard deviation) was greatest in the PRZ group (4.70 ± 1.52 cm.), then the ALB group (4.28 ±1.22 cm.) and then the NON group (3.97 ± 1.17 cm.). The difference was significant between the PRZ and NON groups (student's t-test = 5.902, $p<0.05$). At one year the weight increment was greatest in the PRZ group (3.83 ±1.74 kg), followed by the NON group (3.48 ± 1.66 kg) and then the ALB group (3.36 ± 1.36 kg). The differences were not significant.

The slope of height increment over the year showed no significant difference between the three intervention groups (figure 1). The slope of weight increment over the year showed no significant difference between the three intervention groups (figure 2).

At one year the height increment was greatest in the children with HA=1 at baseline, then HA=2, then HA=4, then HA=3. Height increments (mean ± standard deviation) were 5.36 ±1.56, 4.26 ± 1.53, 4.19 ± 1.40 and 4.14 ± 1.56, centimeters respectively. The differences were statistically significant ($F_{stat}=4.795$, $p<0.01$). At one year the weight increment was greatest in the children with WA=1 at baseline, then WA=2, then WA=3, then WA=4. Weight increments were 3.90 ± 1.72, 3.40 ± 1.43, 2.74 ± 0.97, 1.80 ± 0.0,
kilograms respectively. The differences were statistically significant (F
stat=3.223, p<0.05).

C. Helminthic Infection

1. Baseline (November 1992)

Stool exams were performed in 69 children in the ALB group, 12 children in
the NON group and 46 children in the PRZ group. (Table I) The percentage of
children whose stool demonstrated eggs of *A. lumbricoides* or *T. trichiura* at
baseline was 48.4% (Figure III). Other parasitic eggs (*T. solium* and
hookworm) were not recovered from stool. The greatest infection prevalence
was in the ALB group (58.8%), followed by the NON group (58.3%), followed
by the PRZ group (30.4%). The differences were significant between the ALB
and PRZ group ($X^2=8.329$, $p<0.01$).

The percentage of children infected with *A. lumbricoides* was 46.0% (Figure
IV). The greatest infection prevalence was in the NON group (58.3%),
followed by the ALB group (57.4%), followed by the PRZ group (26.1%). The
differences were significant between the NON and PRZ groups ($X^2=4.415$,
$p<0.05$), and the ALB and PRZ groups ($X^2=10.754$, $p<0.01$).

The percentage of children infected with *T. trichiura* was 18.9% (Figure V).
The greatest infection prevalence was in the NON group (25.0%), followed by
the ALB group (21.7%), followed by the PRZ group (13.0%). The differences
were not significant.
2. March 1993
Three months after the first dose of mass chemotherapy (March 1993), stool from 46 children in the PRZ, 69 in the ALB group and none in the NON group was evaluated. The percentage of children infected with *A. lumbricoides, T. trichiura, T. solium* or hookworm was 13.9% (Figure III). The PRZ group had a greater infection prevalence (15.2%) than the ALB group (13.0%). The differences were not significant.

At the three month coproparasitology exam, 5.2% of the children were infected with *A. lumbricoides*; 8.7% in the PRZ group and 2.9% in the ALB group (Figure IV). At that point 9.6% of the children were infected with *T. trichiura*; 11.6% in the ALB group and 6.7% in the PRZ group (Figure V). There were no significant differences between the medication groups.

3. June 1993
Six months after the first dose of mass chemotherapy (June 1993), stool from 46 children in the PRZ, 69 in the ALB group and none in the NON group was evaluated. The percentage of children infected with *A. lumbricoides, T. trichiura, T. solium* or hookworm was 38.3%. The infection prevalence was greater in the ALB group (39.1%) than the PRZ group (37.0%) (Figure III). The differences were not significant.

At the June exam, 34.8% of the children were infected with *Ascaris*: 34.8% in the PRZ group and 34.8% in the ALB group (Figure IV). At that point 20.0% of the children were infected with *T. trichiura*: 26.1% in the ALB group and 10.9% in the PRZ group (Figure V). The difference in *T. trichuria* infection prevalence was statistically significant ($X^2=3.960$, $p<0.05$).
III. Helminthic Infection and Socioeconomic Status

There was a significant difference of infection rates between large and small family size. Children from families with greater than five people had a greater baseline infection prevalence (54.5%) than those from families with five or fewer people (34.2%), ($X^2=4.359, p<0.05$).

There was a significant difference in rates of baseline infection between those less than ten years old and those ten years old or older. The younger group had a greater infection prevalence (64.5%) than the older group (43.2%), ($X^2=4.429, P<0.05$).

There was no significant difference of infection prevalence rates between those who have bathrooms and those who do not, the kind of water supply, the level of education of the mother or the level of education of the head of household. Finally, there was no significant difference between the rate of infection in girls and boys.

IV. Comparison of intervention and non-intervention groups after combining the two intervention groups into one

A. Anthropometry

1. Baseline

Combining the two intervention groups (those treated with albendazole and those treated with praziquantel) into one group and comparing it to the non-intervention group creates sample size groups of 120 and 38, respectively. Between the combined intervention (INT) and NON groups there was no significant difference for HA or WA. The percentage of children with HA>2 was less for the NON group (55.3%) than the INT group (65.0%). The
percentage of children with WA>2 was less for the NON group (2.6%) than the INT group (12.5%).

2. At one year

At one year the incremental height change (mean ± standard deviation) of this combined sample was greater in the INT group (4.44 ± 1.35 cm.) than the NON group (3.97 ± 1.17 cm.). The difference between the INT and NON groups was borderline-significant (student’s t-test=3.680, p=0.053717).

The mean incremental weight change in this combined sample was greater in the INT group (3.54 ± 1.53 kg) than the NON group (3.48 ± 1.66 kg). There was no significant difference between the two groups.

There was no significant difference between the slopes of height growth or weight growth (Figures VI and VII).

V. Secondary Effects of Antiparasitic Medications

All of the secondary effects of the medications, abdominal pain, headache and diarrhea, were ones listed as frequent or occasional by the Medical Letter (11). The effects, experienced by 10.3% in the praziquantel group and 15.6% in the albendazole group, did not deter any school-children from continued participation in the study.
## COMPARISON OF BASELINE VARIABLES

(Table 1)

<table>
<thead>
<tr>
<th>Variable</th>
<th>non-intervention</th>
<th>PRZ</th>
<th>ALB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=38</td>
<td>N=46</td>
<td>N=74</td>
</tr>
<tr>
<td>sex -no. of males (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-no. of females (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age (years) mean ± SD</td>
<td>10.39 ±0.98&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.90 ±1.15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10.65 ±0.97</td>
</tr>
<tr>
<td>mean family size ± SD</td>
<td>6.61 ±1.87</td>
<td>6.39 ±1.58</td>
<td>6.64 ±1.58</td>
</tr>
<tr>
<td>latrine type-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-toilet or bowl with drain, tank</td>
<td>25 (65.8)</td>
<td>29 (63.0)</td>
<td>42 (56.8)</td>
</tr>
<tr>
<td>-bowl with drain, no tank</td>
<td>6 (15.8)</td>
<td>5 (10.9)</td>
<td>3 (4.1)</td>
</tr>
<tr>
<td>-no latrine</td>
<td>7 (18.4)</td>
<td>10 (21.7)</td>
<td>26 (35.1)</td>
</tr>
<tr>
<td>water source-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-piped into or near house</td>
<td>25 (92.1)</td>
<td>45 (97.8)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>63 (85.2)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>-ditch, well or spring</td>
<td>3 (7.9)</td>
<td>--</td>
<td>7 (9.5)</td>
</tr>
<tr>
<td>Head of Household-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-formal education*</td>
<td>32 (84.2)</td>
<td>35 (76.1)</td>
<td>65 (87.8)</td>
</tr>
<tr>
<td>-farmer,shepherd</td>
<td>4 (10.5)</td>
<td>4 (8.7)</td>
<td>3 (4.1)</td>
</tr>
<tr>
<td>Mother in Household-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-formal education*</td>
<td>**</td>
<td>29 (63.0)</td>
<td>56 (75.7)</td>
</tr>
<tr>
<td>&gt;2 nutri status-no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-height for age</td>
<td>21 (55.3)</td>
<td>24 (52.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>54 (72.9)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>-weight for age</td>
<td>1 (2.6)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4 (8.7)</td>
<td>11 (14.9)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Prevalence of Parasites-no. (%)***</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-&lt;i&gt;A. lumbricoides&lt;/i&gt;</td>
<td>7 (58.3)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>12 (26.1)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>39 (56.5)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>-&lt;i&gt;T. trichiura&lt;/i&gt;</td>
<td>4 (25.0)</td>
<td>6 (13)</td>
<td>15 (21.7)</td>
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<tr>
<td>-&lt;i&gt;T. solium&lt;/i&gt;</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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<tr>
<td>-hookworm</td>
<td>0 (0)</td>
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<td>0 (0)</td>
</tr>
<tr>
<td>-any parasite</td>
<td>7 (58.3)</td>
<td>14 (30.4)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>40 (58.3)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

*Attended primary school and may or may not have continued

**No data for the non-intervention group in this category was collected.

***Parasitology was performed on only 69 children in the albendazole group and only 12 children in the non-intervention group.

<sup>a</sup>=significant difference between two groups (p<0.05)
<sup>b</sup>=significant difference between two groups (p<0.01)
<sup>c</sup>=significant difference between more than two groups (p<0.05)
Figure I

Height Increment by Intervention Group
Figure II

Weight Increment by Intervention Group

<table>
<thead>
<tr>
<th>Intervention Group</th>
<th>Weight 1</th>
<th>Weight 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-intervention</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Praziquantel</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Albendazole</td>
<td>31</td>
<td>34</td>
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</table>
Figure III

Helminth Infection Prevalence by Intervention Group (all helminths)
Figure IV

*A. lumbricoides* Infection Prevalence by Intervention Group
Figure V

*T. trichuria* Infection Prevalence by Intervention Group
Figure VI

Height Increment for Intervention v. Non-Intervention
Weight Increment for Intervention vs. Non-Intervention

![Graph showing weight increment for intervention vs. non-intervention. The graph compares weight at two time points (Weight 1 and Weight 2) for both intervention and non-intervention groups.]
DISCUSSION

I. EFFECTS OF INTERVENTION ON ANTHROPOMETRY
The hypothesis, that the children in the albendazole group would grow more than the children in the praziquantel group, was disproven and the null hypothesis, that there is no statistically significant difference in growth, is accepted.

A WHO study of children from Ecuador reveals a predominance of chronic over acute malnutrition (36). Similarly, results from this thesis found more children stunted (62.7% had HA>2) than wasted (10.1% had WA>2).

In this thesis the albendazole group children grew more in height and less in weight than the NON group; the albendazole group grew less than the praziquantel group in both height and weight. Figures I and II demonstrate how similar the slope of growth of the albendazole group is to the other two groups.

The height increment at one year was significantly greater in the praziquantel group than the NON group and borderline-significant in the combined intervention group than the NON group. Both of these two pairs had HA and WA baseline variables that were not significantly different. They did have baseline differences of *Ascaris* infection rate and age, either of which may have accounted for the difference at one year.

Albendazole is a relatively new medication; some of its antiparasitic effects have been evaluated only once. Improved growth after a single 400 mg dose
of albendazole therapy has been demonstrated in a Kenyan study. In that study, six months after therapy, despite continued exposure to infection, growth rates (WA, HA and WH) were significantly greater in the albendazole group than in the placebo group (33). The existence of a significant difference in growth improvements in the albendazole group in the Kenyan study and not in this thesis may be accounted for by baseline data, age or microorganism prevalence.

The baseline data in this thesis demonstrates that the albendazole group had a significantly lower WA than the placebo group and a significantly lower HA than the praziquantel group. When the intervention groups were created geographically, the risk of potentially biased baseline data was considered and accepted in return for the benefit of increased compliance. Unfortunately, the combination of biased baseline data and significantly greater growth increments in children with better baseline nutritional status may have negated the possibility that the albendazole group could have overcome the anthropometric differences in one year: the baseline data may reflect deep inter-group differences that necessitate more than one dose of chemotherapy to effect change. The Kenyan study had no significant differences in the baseline anthropometry (33).

Secondly, the mean age in this thesis (10.66 ± SD 1.04 years) is old enough that more children may have completed their growth spurt before the study began, thus reducing the likelihood that the change in growth would be significant; the mean age for the Kenyan study was 8.55 years.
Finally, the lack of a growth difference may have been accounted for by microorganism prevalence of *Giardia lamblia*, hookworm or *Trichuris*. San Pablo has a *Giardia lamblia* infection prevalence of 3.5% (20). *Giardia* has been shown to be detrimental to nutritional status and where endemic, anti- giardial chemotherapy has been shown to improve nutritional status (69, 70). Albendazole has been shown to be effective in treating *Giardia* in vitro (71) and at a dose of 400 mg each day for five days (72) but not at a dose of 400 mg once (73).

The prevalence of hookworm and *Trichuris* in this thesis (0% and 18.9%, respectively) was far less than that in the Kenyan study (79-95% and 97-98%, respectively) where a single 400 mg dose of albendazole improved growth. The prevalence of *Ascaris* in this thesis (46.0%) was within the range of that from the Kenyan study (44-54%) (33). The malnutrition of the children of San Pablo, less likely to have been caused by chronic hookworm and *Trichuris* infection, is less likely to have been relieved by albendazole.

Thus the design of the study may have been such that significant improvements were less likely to be demonstrated or the etiology of the poor nutritional status may be factors untreatable by a single dose of albendazole, only.

II. EFFECTS OF INTERVENTION ON INFECTION PREVALENCE
The results of the three parasitology exams indicate that there was a decrease in infection prevalence and then an increase that approached, if not superseded, the original prevalence. Three months after administration of albendazole and praziquantel, geo-helminth infection prevalence was
reduced by 45.8% and 15.2%, respectively. Six months after the administration of albendazole and praziquantel, however, the infection prevalence increased by 26.1% and 21.8%, respectively (see figures III, IV, V). Since the non-intervention group was not examined at the second and third exams, it is impossible to compare the parasitology of the intervention with the non-intervention groups. The causes of the shape of the infection prevalence curve can therefore by hypothesized, only.

The most likely hypothesis is that the antiparasitic medications, administered once, were not enough to contain the rate of reinfection in this community. The reinfection rate indicates that the medication needs to be administered more frequently or additional antiparasitic measures, such as increased education and sanitation, need to be included.

Albendazole and praziquantel, administered between parasitology exams one and two, can account for the decrease in infection prevalence at exam two. Since children have a propensity to become reinfected at the same rate they were previously infected (33), the increase in infection prevalence between exams two and three may be a result of the natural process of reinfection after medication. Recommended dosage schedules for albendazole and praziquantel are varied. The Medical Letter recommends a single 400 mg dose of albendazole for treatment of geo-helminths and a single 5-10 mg/kg dose of praziquantel for treatment of T. solium taeniasis (11). There is no recommendation for praziquantel treatment of geo-helminths.

Studies in Thailand, Bolivia and Kenya, in areas endemic for Ascaris, Trichuris and hookworm, demonstrate that a single 400 mg dose of
albendazole decreases geo-helminths infection (33, 61, 74). In Thailand and Bolivia, however, the follow-up parasitology exams were within four weeks of medication (61, 74). In Kenya the follow-up exam was six months after chemotherapy; it demonstrated a decrease in intensity of infection but not in prevalence (33). Thus none of the studies demonstrate a decreased prevalence of geo-helminth infection six months after 400 mg of albendazole chemotherapy.

Building latrines, building facilities for a clean water supply and educating the community have each been shown to decrease the prevalence of geo-helminth infection (17, 24, 27). The eradication of poverty and illiteracy has also been shown to decrease the prevalence of infection (9). For this thesis, one may hypothesize that, had these children and their families had latrines, clean water, and infection-control education, the decrease in infection prevalence after the chemotherapy may have been maintained throughout the year.

III. INFECTION AND SOCIOECONOMIC STATUS

Children in developing countries have a high prevalence of parasitic infections and the children studied here are no exception. A United Nations study estimates that the infection prevalence for children in developing countries is 40% for *Ascaris*, 30% for *Trichuris* and 17% for hookworm (12). The infection prevalence in the children in this study was 48.4% for all parasites, 46.0% for *Ascaris*, 18.9% for *Trichuris* and 0% for hookworm.

Greater infection rate occurred in larger families and younger children. Infection rate was unrelated to water source, latrine type, education of the
mother, education of the head of the household or the kind of housing material. These findings are consistent with previous studies. Geo-helminth infection prevalence is increased in more crowded dwellings and among younger children (26, 69). Although many studies find an association between certain socioeconomic indices (water supply, latrine type, housing and education level) and parasitic disease prevalence, (26, 50), due to the infectious nature of parasitic disease, the association exists only when entire communities are compared to other communities and not within communities (9, 50).

IV. METHODOLOGICAL PROBLEMS

The design problems of this thesis are common in field studies of large populations in developing countries. The intervention groups were created geographically (as opposed to randomly or randomly by baseline data) because the principle investigators felt the best way to achieve chemotherapy compliance was to give everyone within a specific area the same therapy. The resulting significant differences among the intervention groups at baseline, however, are problematic for interpreting the growth increments and infection rates. Baseline variables with statistically significant differences include water source, HA, WA, age, infection rate overall and *Ascaris* infection rate.

Also problematic for the interpretation of the data is the enumerator variability and the transportation of the fecal specimens. Each year, the anthropometry was performed by a different enumerator. Since training and standardization were identical for the two enumerators but they were, nonetheless, two different individuals, the precision was decreased but not
the accuracy (66, 67). The fecal specimens had to be transported from the field to the city, a two hour drive. The delay and potential loss may have caused errors in specimen interpretation.

Despite the methodological problems, certain trends could be detected comparing the effects of intervention on both anthropometry and infection prevalence as well as correlating infection and socio-economic status.

V. CONCLUSION

Solving malnutrition in school-age children remains a dilemma of the developing world. The malnourishment of school-age children is largely mild to moderate; mortality and acute morbidity are therefore less common than in the severe malnutrition more frequently experienced by pre-school age children. Yet since it is less likely to be brought to the attention of medical personal, school-age malnutrition may be more likely to cause long-term effects of chronic malnutrition. The WHO and United Nations have continued to demonstrate that the sequelae of malnutrition are felt as much by the nation as the family and the individual.

The long-term goal of eradicating the endemicity of geo-helminths must continue. This thesis provides evidence that a single dose of chemotherapy is not enough; eradication will be achieved only through a combination of chemotherapy, education and improved hygiene. Sustaining a parasitic-free population in rural Ecuador necessitates long term changes that include eradicating poverty and improving education to assist a disempowered community out of the vicious cycle of parasitic infection.
ENDNOTES


Hygiene, 87(5): 576-77.


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