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Anemia and Intestinal Parasites

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During the last 10 years, scientists working on helminths have been looking at the impact of antihelminthic treatment on nutrition, both in terms of child growth and micronutrient status. This interest stemmed from pioneering work conducted mostly in East Africa by Stephenson (1987). An inherent assumption in the ongoing research on the impact of helminths on morbidity is that the latter is related to the intensity of intestinal nematode infections and treatment, which reduces helminth intensity, and would have an impact on growth, nutritional status, and school performance; thus, the consequences of helminth disease may be controlled using regular antihelminthic treatment. The challenge for WHO is to find a low-cost generic antihelminthic drug that can be produced in developing countries.

This paper describes the use of antihelminthic chemotherapy as a tool to control anemia and draws on work in Zanzibar, supported by both USAID and WHO. Specifically, the research is looking at the long-term effect of a regular single dose, 500 mg mebendazole tablet on morbidity in school children. Initially, some 3,600 primary school children were followed for one year, during which fecal blood loss and hookworm egg counts were monitored. The dominant hookworm species in the area is *Necator americanus*.

Preliminary results showed a highly significant intensity-related effect of infection on fecal blood loss, iron stores, and severe anemia. This suggests that if the intensity of infection could be reduced to a level that is not associated with blood loss and morbidity, regular deworming would probably be the appropriate approach for morbidity control. In other words, the first objective of regular antihelminthic chemotherapy would be to reduce morbidity by reducing the intensity of infection, even though individuals may not be completely cured and will continue to be exposed to reinfection. The latter is because none of the antihelminthic drugs available are 100 percent effective, especially against hookworms and *Trichuris trichiura* (Albonico et al., 1994; Albonico et al., 1995). In the late 1960s, the Belgian pharmaceutical company Janssen developed mebendazole as the drug of choice for treating worm infections. The initial recommended regimen against *T. trichiura* and hookworm infection was 100 mg twice a day for 3 days. In the late 1970s, Janssen developed the 500 mg preparation for use in large-scale interventions against intestinal nematodes and for long-term treatment against alveolar echinococcosis, a relatively rare infection that requires high-dose, long-term therapy with antihelminthics. Two small studies, one in Thailand (Johgsuksuntigul, pers. com.) and the other in Sri Lanka (Ismail, Premaratne, and Suraweera, 1991) have compared the effect of a single dose of 500 mg mebendazole on the intensity of intestinal nematodes with other drugs, such as the commonly used and inexpensive pyrantel.

Because mebendazole is a generic drug that can be purchased for about US\$0.02 per single 500 mg dose, it is important to know whether it is as efficacious as a single dose of albendazole, a commonly

used single-dose antihelminthic, which is significantly more expensive.

A trial was designed to compare the efficacy of Janssen's original 500 mg mebendazole, a generic 500 mg mebendazole produced in Malta by Pharmamed, and the original 400 mg albendazole produced in the United Kingdom by SmithKline Beecham. The results showed that both the albendazole and mebendazole were very effective in eliminating *Ascaris lumbricoides* eggs after 21 days of treatment (see [figure 5.1](#)), but this was expected because most antihelminthics are very effective against *A. lumbricoides*. In contrast, the effect of albendazole treatment on *T. trichiura* was much less significant (see [figure 5.2](#)). Indeed, the number of children that had no *T. trichiura* eggs was quite small but, more interesting, most of the children had egg counts below 500 eggs/g feces. In other words, the intensity of infection was significantly reduced. Mebendazole, both the original and cheap generic product, was found to be slightly more effective against *T. trichiura* than albendazole. Although albendazole was significantly more effective than mebendazole in curing hookworms (see [figure 5.3](#)), the majority of children treated with mebendazole had egg counts below 500 eggs/g feces and many were cured.

The results of this study have important program implications for public health planners. The question is whether to use a drug that is more expensive, that is, albendazole, which has a greater effect on hookworm infection and a similar effect for the other two parasites (*Ascaris* and *Trichuris*), or a drug that is twenty times less expensive, that is, mebendazole, that also has a very significant impact on reducing the intensity of infection. Given that the amount of blood lost from the gut is similar in a child whose worm intensity is very low and a noninfected child, it seems logical that a more sustainable program would be one that uses mebendazole, which has a more frequent retreatment interval, than one that uses albendazole.

The efficacy trial was continued, and the same children were followed up again at four and six months. The results of the follow-up study showed that, regardless of whether a child was cured of helminths or not, most got reinfected after treatment; thus, the post treatment reinfection rate is an important aspect of large-scale, chemotherapy-based helminth control programs. The results also showed that after four months, the difference in the efficacy of the two drugs on hookworm egg counts was less evident than at 21 days; at 6 months the intensity of hookworm infection was exactly the same as before the intervention (see [figure 5.4](#)).

A similar pattern to that for curing hookworm infection was observed for *T. trichiura*, but neither mebendazole or albendazole were as effective (see [figure 5.4](#)). Because both drugs are highly effective against *A. lumbricoides*, egg count levels fell close to zero, but reinfection took place and preintervention levels were reached after six months. These results show that even if a more effective drug is used, in this area of very high transmission, egg counts revert to pretreatment levels six months after treatment. This means that in areas of high transmission, the retreatment schedule has to be quite frequent.

A large-scale trial, which includes an untreated control group, is currently under way to look at the impact of retreatment schedules on egg count intensities at 4- versus 6-month intervals, using all three chemotherapies. Several issues are being monitored, including differences in worm intensities and the impact this has on iron stores, vitamin A status, and undernutrition.

Figure 5.1: Efficacy of Albendazole and Mebendazole treatment on eliminating *Ascaris* eggs

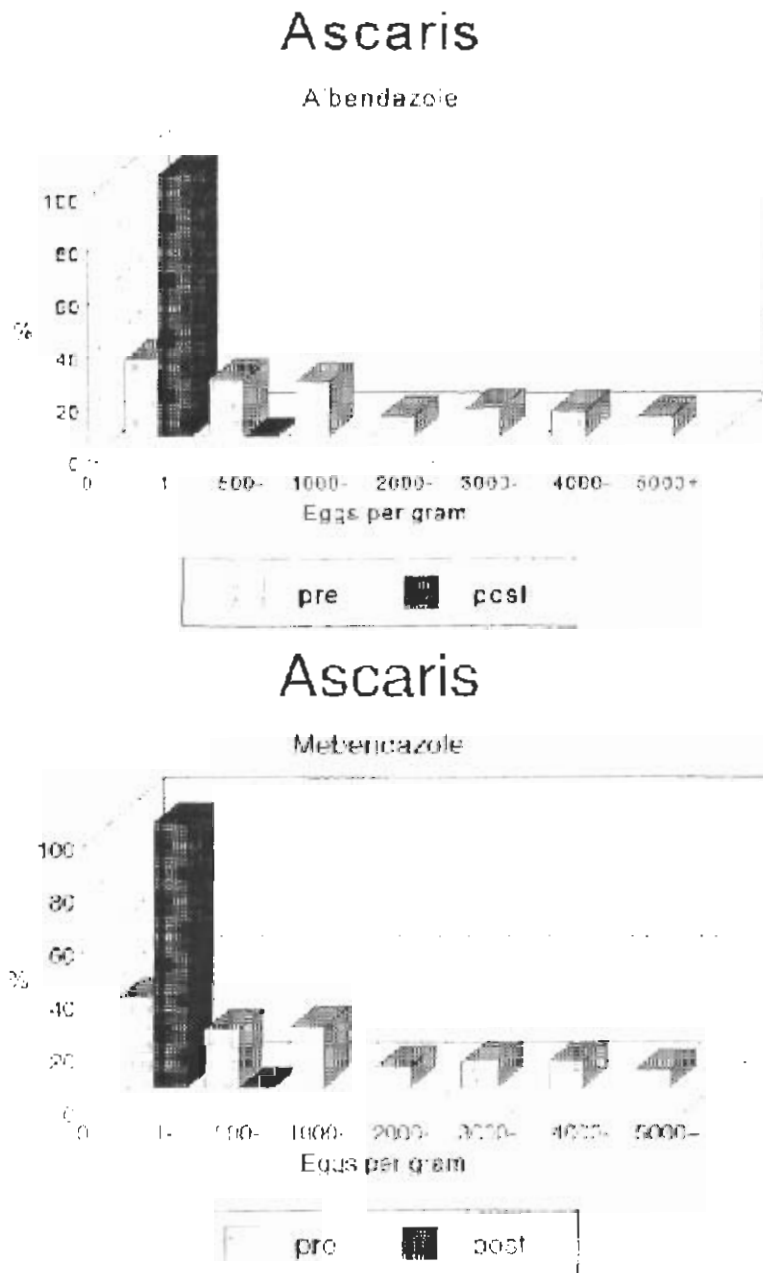


Figure 5.2: Efficacy of Albendazole and Mebendazole treatment on eliminating Trichuris eggs

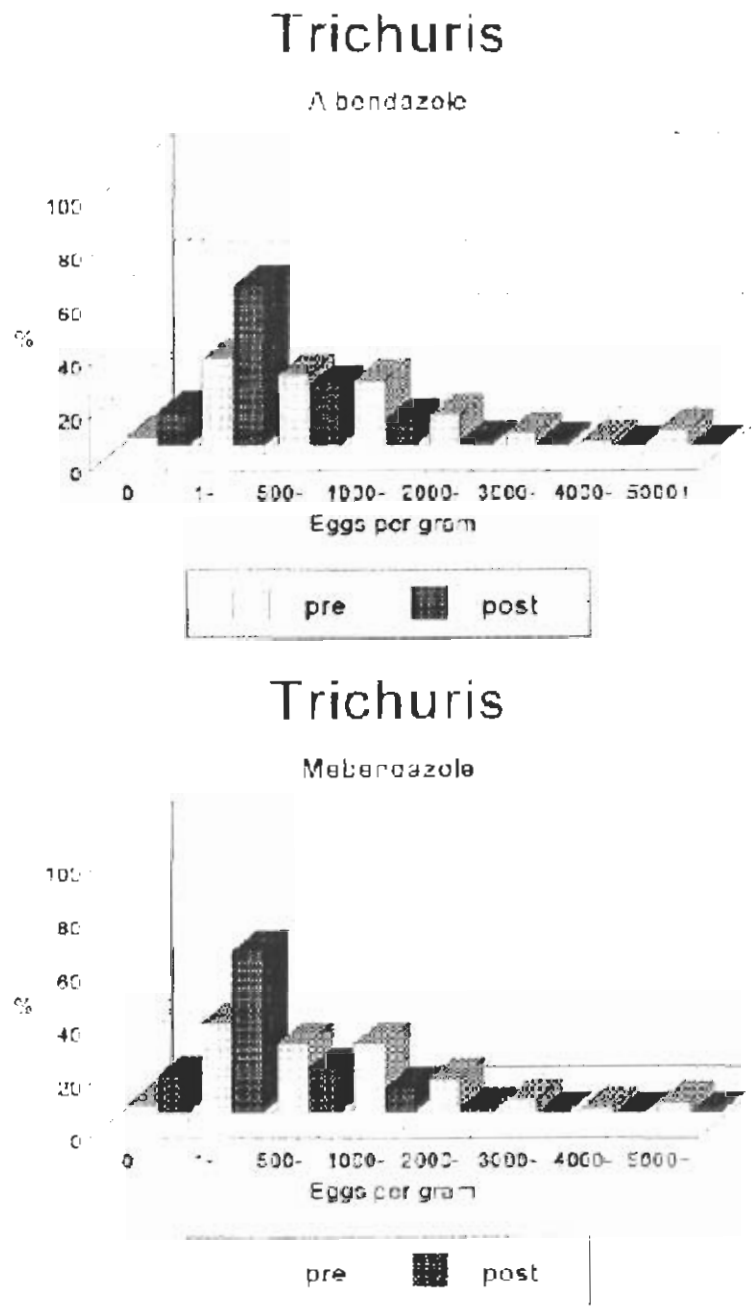


Figure 5.3: Efficacy of Albendazole and Mebendazole treatment on eliminating hookworm eggs

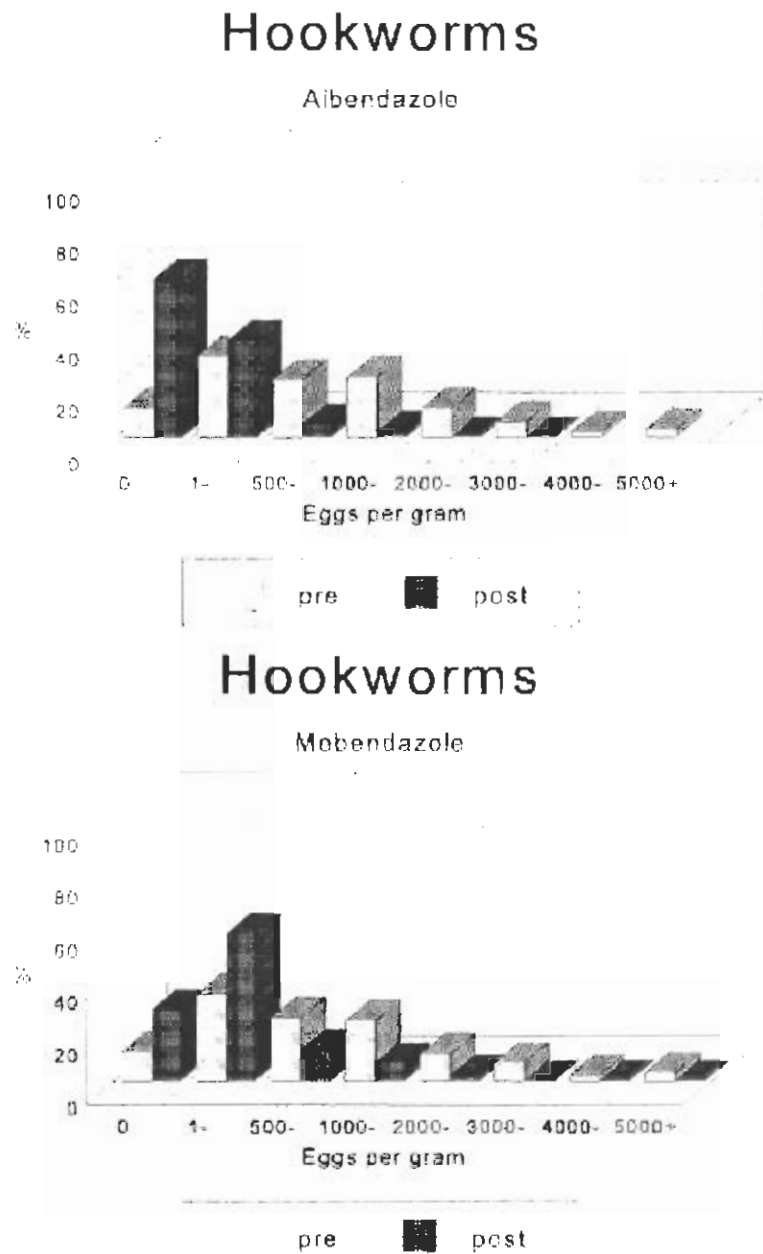
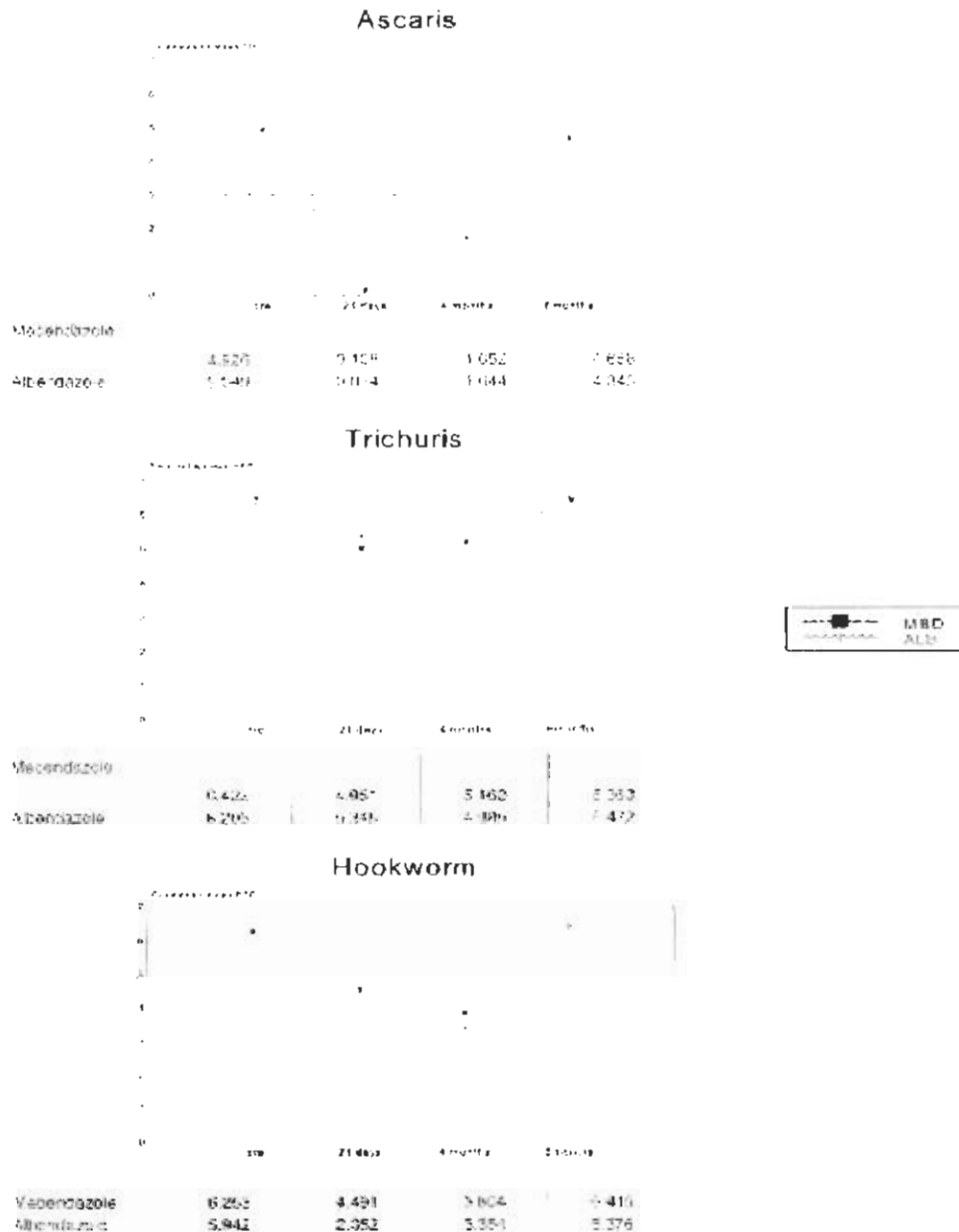


Figure 5.4: Egg count distributions in Mebendazole and Albendazole groups before treatment, and after 21 days, 4 months, and 6 months of treatment



In summary, a single dose of 400 mg albendazole is more effective against hookworm than a single 500 mg dose of mebendazole; the difference attenuates at four months. Both drugs are similarly and extremely effective against *Ascaris*. Mebendazole is more effective than albendazole against *Trichuris*, although the cure rates are low for both drugs. Both the egg production rate and intensity of infection may be sufficient for disease control in endemic areas; at four months, efficacy is similar for both drugs. Although data comparing the generic with the original mebendazole are not shown, the results indicate that both formulations had similar efficacy against hookworms *Ascaris* and *Trichuris*.

The recommendations arising from the above studies were that in areas where hookworms are the main parasites, albendazole may be recommended, whereas in *Trichuris* and *Ascaris* transmission areas, mebendazole is the drug of choice. Where mixed infections are prevalent, the dose should be based on the local epidemiological and financial situation, given that the efficaciousness of the drugs is similar at four months. In high transmission areas, the prevalence and transmission of *Trichuris* and hookworms

return to pretreatment levels after six months.

Both drugs are very safe for school children; a one-half tablet mebendazole (i.e., 250 mg) is safe for children under two years old. This means that a tablet must be manufactured in a form in which it can be broken into two. Albendazole is not recommended for children under two years old. Another advantage of both albendazole and mebendazole is that the recipient's weight does not need to be known when prescribing the drug—unlike for levamisole and pyrantel, which are two commonly used antihelminths.

References

Albonico, M., P. G. Smith, L. Salvioli, et al. 1994. A randomized controlled trial comparing mebendazole and albendazole against *Ascaris*, *Trichuris*, and hookworm infection. *Trans. Soc. Trop. Med. Hyg.* 88(5):585-89.

----. 1995. Rate of reinfection with intestinal nematodes after treatment of school children with mebendazole or albendazole in a highly endemic area. *Trans. Soc. Trop. Med. Hyg.* 89(5):538.

Ismail, M. M., U. N. Premaratne, and M. G. Suraweera. 1991. Comparative efficacy of single dose antihelminthics in relation to intensity of geohelminth infection. *Ceylon Med. J.* 36:162-67.

Stephenson, L. S. 1987. *The Impact of Helminth Infections on Human Nutrition*. London: Taylor and Francis.

Discussion

Dr. Tomkins asked if the use of albendazole and mebendazole had any impact on iron status. Dr. Savioli replied that this is not yet known. Small-scale studies, conducted over the last fifteen years in East Africa using a single dose of albendazole in school children, have shown a significant impact on iron status after six months. Other studies have shown an improved school performance. Dr. Stoltzfus commented that the purpose of the ongoing Zanzibar study is to look at the long-term effect on the shift of the hemoglobin distribution in a population of school children that were hookworm endemic and who were then dewormed. The baseline data show that iron requirements are doubled because of blood loss due to hookworm infestation, which has implications for iron balance in children; however, hookworm loads will be lower in preschool children, but at the same time, their iron needs are relatively high and a smaller hookworm load could have a similarly dramatic effect on iron requirement.

Dr. Brabin asked if there are any hematologic criteria or prevalence figures for anemia that could be used as guidelines for initiating an antihelminthic program. Dr. Savioli replied that the priority setting for deworming programs has never been based on scientific criteria. Indeed, the purpose of the Zanzibar trial is to develop tools for setting priorities.

Dr. Nestel asked Dr. Savioli to comment on the safety of antihelminths for children under two years old, for example, albendazole is not recommended. Dr. Savioli responded that 250 mg mebendazole, piperazine, pyrantel, and levamisole are safe and have been widely used. The Sick Child Initiative recommends mebendazole treatment in a single 250 mg dose for all ages in areas where helminths are widespread for all ages.

Dr. Mascie-Taylor asked about the consequences of bilharzia on blood loss. Dr. Savioli responded that the overriding factor for blood loss is hookworm. The Zanzibar study in school children has not shown an association between Schistosoma infection and anemia, but this may be due to the long-term positive effect of Schistosoma treatment. Nevertheless, Schistosoma haematobium is unlikely to be a big problem in children under five years old.

Dr. Schultink commented on a Brazilian study in children heavily infected with Ascaris and Trichuris. Serum retinol levels of children given a vitamin A supplement did not increase, unlike in the control group who were dewormed but not given vitamin A at the outset. Dr. Schultink asked whether there is an increase in acute-phase response indicators in children infected with Ascaris and Trichuris, because several studies on the effect of deworming on iron status show no effect on hemoglobin status. The acute phase response may play a role in vitamin A metabolism, and serum ferritin is an acute-phase response protein. Dr. Filteau responded that preliminary data from Tanzania show that deworming with albendazole did decrease levels of some acute phase proteins.

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