Effect of intestinal parasite treatment on the efficacy of oral iodized oil for correcting iodine deficiency in schoolchildren[1–3]

Carina A Furnée, Clive E West, Frits van der Haar, and Joseph GAJ Hautvast

ABSTRACT Oral supplementation with iodized oil for correction of iodine deficiency in a population has advantages over intramuscular injection but the duration of effect is shorter. The relation of intestinal parasite treatment and efficacy of oral iodized oil was examined in an intervention study in 8–10-y-old schoolchildren in Malawi. Severely iodine-deficient schoolchildren with a single parasitic infestation of *Ascaris lumbricoides* (n = 44), hookworm (n = 42), or *Entamoeba histolytica* (n = 24) were randomly allocated to receive or not receive treatment before taking a 1-mL oral supplement (490 mg I) of iodized ethyl esters from poppy seed oil. The urinary iodine concentration was measured at various time points after supplementation to define the time intervals before urinary iodine concentrations returned to 0.40 μmol/L, indicating moderate iodine deficiency. Treatment with metronidazole for *E. histolytica* increased the protection period from 2.0 to 21.0 wk ($P < 0.05$). For all untreated children together, the duration of effect was 9.2 wk shorter ($P < 0.001$) than that for their treated peers (16.8 wk). We conclude that intestinal parasitic infestations reduce the efficacy of oral supplementation with iodized ethyl esters by interfering with absorption. *Am J Clin Nutr* 1997;66:1422–7.

KEY WORDS Iodine deficiency disorders, iodized oil, parasites, *Entamoeba histolytica*, *Ascaris lumbricoides*, hookworm, urinary iodine excretion, Malawi, lipid absorption, schoolchildren

INTRODUCTION

Iodine deficiency occurs in populations living in areas where the soil has been depleted of iodine and the diet consists predominantly of locally grown foods (1). Salt iodization is the most efficient, low-cost means to reduce the incidence of iodine deficiency disorders in such populations (2). An alternative iodine supply is required when implementation of universal salt iodization is delayed or iodized salt coverage in remote areas is inadequate, and iodized oil may be applied in such situations (3). There is considerable experience with injections of iodized oil, which provide protection against recurring iodine deficiency for up to 5 y (4). Oral supplementation with iodized oil has economic and many practical advantages over injections. However, high variations in effect have been reported (5–9) and the average duration of protection is shorter, often ranging from 6 mo to 1 y. A review of 10 studies in various age and sex groups with widely varying oral doses from different iodinated vegetable oils suggested that the observed periods of effect were roughly related to the severity of initial iodine deficiency (10).

Factors that may influence the absorption and retention of oral iodized oil supplements have received little attention. It has been shown that in children infected with *Ascaris lumbricoides*, the absorption of oral vitamin A supplements is affected (11–13). Thus, parasitic infestation in apparently healthy children may also reduce the absorption of iodized oil supplements. Because intestinal parasitic infestations are often coendemic with iodine deficiency in developing countries, the present study examined the effect of antiparasitic treatment in schoolchildren infested with *A. lumbricoides*, hookworm, or *Entamoeba histolytica* on the efficacy of oral iodized oil for correcting iodine deficiency.

SUBJECTS AND METHODS

Subjects

Subjects were selected from 8-, 9-, and 10-y-old schoolchildren (n = 502) attending four primary schools in Ntcheu District, Malawi. Approval for the study was obtained from the National Council for Medical Research, Malawi. Schools were chosen on the basis of having a sufficient number of schoolchildren and their easy access from the main highway in the country. Prior consent was obtained from a parent or guardian of each child. Because only apparently healthy subjects were considered eligible, all schoolchildren were examined by a medical assistant from Ntcheu District Hospital. Schoolchildren with a significantly enlarged liver or spleen, indicative of disease that may interfere with fat or protein metabolism, or with a midupper-arm circumference < 15.5 cm, indicative of

[1] From the Division of Human Nutrition and Epidemiology, Wageningen Agricultural University, Netherlands, and the Department of International Health, Emory University School of Public Health, Atlanta.

[2] Supported by the Netherlands Foundation for Advancement of Tropical Research (WOTRO), The Hague, Netherlands (file number W91–172).

[3] Reprints not available. Address correspondence to CE West, Division of Human Nutrition and Epidemiology, Wageningen Agricultural University , PO Box 8129, 6700 EV Wageningen, Netherlands. E-mail: clive.west@staff.nutepi.wau.nl.

Received November 12, 1996.
Accepted for publication May 22, 1997.

protein-energy malnutrition, were excluded from the study (n = 16).

Study design

Data were collected as part of a series of studies in apparently healthy schoolchildren on factors that may affect the efficacy of oral iodized oil for correcting iodine deficiency (14). *A. lumbricoides*, hookworm, and *E. histolytica* infestations were studied because of the relevance of these pathogens in the country.

Two stool and urine samples were taken from each child on 2 consecutive days. Each stool sample was examined immediately in duplicate to detect parasite ova directly in 50 mg sieved feces by microscope in the field using the Kato-Katz thick smear technique (15, 16). Eosin dyeing (2% eosin in saline) and potassium iodo-iodide coloring (3 g KI and 2 g I in 100 mL water) was applied to detect and determine flagellates or amebae. A record was kept of egg counts of *A. lumbricoides* and hookworm. Other parasites and species of ameba, particularly *E. histolytica* (10× objective; cysts 10–15 μm in diameter, round, 2–4 nuclei), were diagnosed qualitatively. A subject was classified as a cyst passer if *E. histolytica* cysts were noticed in both colored smears, taken on 2 consecutive days. Stools were examined by an experienced laboratory technician from the Bilharzia Research Institute, Lilongwe. One in every 10 stools was cross-examined by a parasitologist of the Department of Intestinal Parasitology, Kamuzu Central Hospital, Lilongwe, to ensure a correct diagnosis.

Stool examination identified 150 schoolchildren to be infested by a single parasite species only. One-half of those identified with *A. lumbricoides* only (n = 55), with hookworm only (n = 60), or as *E. histolytica* cyst passers only (n = 35) were randomly allocated to drug treatment, which took place in accordance with national guidelines. Children positive for *A. lumbricoides* received a single dose of 400 mg albendazole (Alzental; Shin Poong Pharmaceutical Co Ltd, Seoul, South Korea). Children with hookworm were treated with 400 mg albendazole for 3 consecutive days. Medication of children in these groups took place at school under supervision of a field assistant. *E. histolytica* cyst passers received 200 mg metronidazole (Sterling Products International Ltd, Blantyre, Malawi) three times daily for 5 consecutive days. On each treatment day, the early morning dose was supervised by a field assistant, the second dose was taken under supervision of the class teacher just before the child left school, and the third dose was given daily to the subjects as they left school with the instruction to take the dose at home before going to bed.

Two weeks after completion of drug therapy, all children received orally 1 mL iodized oil (Lipiodol Ultrafluide, 490 g I/L; Laboratoire Guerbet, Aulnay-sous-Bois, France) by dispenser (Englass Dispensing Devices, The English Glass Co, Ltd, Leicester, United Kingdom). One week after oral iodized oil administration, two stool samples were collected and examined in duplicate as before to assess the cure rates of albendazole and metronidazole.

Schoolchildren with less common parasites or multiple infestation (n = 306) received appropriate treatment but were not included in this study. A placebo group (n = 35), pretreated with both albendazole and metronidazole because of mixed infections, received 1 mL neutral poppy seed oil to monitor for possible unidentified sources of iodine. Children without parasites (n = 30) were not included in the study.

Urinary iodine excretion was based on the concentration of iodine in casual urine samples because it was not feasible to collect 24-h urine samples (14). Urine samples were collected before 1100 at school under supervision of field assistants. The iodine status at baseline was assessed from the average iodine concentration in urine collected on 2 consecutive days before iodized oil supplementation. Subsequent values were based on the average iodine concentration in casual urine samples collected on 3 consecutive days at the 4th, 8th, 20th, 40th, and 44th wk of follow-up.

Urinalysis

Urine samples preserved with thymol were sent to the Department of Human and Animal Physiology of Wageningen Agricultural University, where they were stored at −20 °C before laboratory analysis. Iodine was assayed after alkaline digestion by using the Sandell-Kolthoff reaction (17–19) adapted for use with a microtiter plate reader (Thermomax; Molecular Devices Corporation, Palo Alto, CA) coupled to a personal computer equipped with special software (SOFTMAX; Molecular Devices Corporation). All samples were assayed in duplicate and when results differed by > 10% from their average, the duplicate analysis was repeated. The average result was used in data analysis. The smallest concentration detectable by the method was 0.04 μmol/L and the precision was 0.012 μmol/L. Recoveries of added iodate and iodide were 100% and 97%, respectively.

Statistical analysis

The urinary iodine data included for analysis were from subjects with at least one observation at three or more of the time points during follow-up (n = 26, 16, and 16 for treated children and n = 18, 26, and 8 for untreated children with *A. lumbricoides*, hookworm, and *E. histolytica*, respectively); the average iodine concentration was used at each time point with more than one observation (14).

A K-sample median test was applied to compare urinary iodine concentrations of the treated and untreated groups for each parasite species (20). In short, the 95% CI around the median was calculated for the treated groups by using ± 2 SDs and when a median urinary iodine concentration in the untreated group did not fall within the respective interval, the difference for that time point was considered significant (P < 0.05).

Changes in urinary iodine concentration after oral iodized oil supplementation were analyzed by a hyperbolic equation that describes the relation between the rate of iodine excretion and the time passed after oral administration of iodized oil without making a prior assumption about the processes involved in iodine retention and elimination (21):

$$I(T, x) = (\alpha_0 + \alpha_1 \times x)T^{-(\beta_0 + \beta_1 \times x)} \qquad (1)$$

where I is the urinary iodine concentration (μmol/L) at time T, T is time (wk) after supplementation, x is the dummy variable for untreated (0) and treated (1) subjects, α is iodine retention (μmol/L) for untreated (α_0) or treated (α_1) subjects, and β is the iodine elimination rate ($\mu mol \cdot L^{-1} \cdot wk^{-1}$) for untreated ($\beta_0$) or treated ($\beta_1$) subjects.

TABLE 1
Intestinal parasites and baseline urinary iodine concentrations in apparently healthy schoolchildren in Ntcheu, Malawi[1]

	No parasites	*Ascaris lumbricoides*	Hookworm	*Entamoeba histolytica*
Age (y)[2]	9.5 ± 0.8	9.5 ± 0.8	9.4 ± 0.9	9.4 ± 0.9
Overall prevalence (n)[3]	29 (6.0)	126 (26.0)	306 (63.2)	327 (67.6)
Urinary iodine concentration (μmol/L)[4]	0.17 (0.12, 0.26)	0.17 (0.11, 0.26)	0.17 (0.06, 0.26)	0.16 (0.12, 0.26)

[1] n = 484.
[2] $\bar{x}$ ± SD.
[3] Percentage in parentheses.
[4] Median; 25th and 75th percentiles in parentheses.

The coefficients α and β were calculated by using the maximum likelihood technique (22) to estimate the iodine retentions and elimination rates in treated and untreated schoolchildren, separately for each of the parasite groups. These estimates were then used to calculate the time (T^*) that the urinary iodine concentration remained elevated above a given concentration (I^*) in a respective group. In this study, I^* was selected at 0.40 μmol/L, the concentration suggested as indicating moderate iodine deficiency (23).

Asymptotic Student's t values were computed to test the significance of a difference between the iodine retention and elimination rate for treated and untreated groups. The goodness of fit of the model (adjusted r^2) was computed to assess the strength of the correlation between urinary iodine concentrations and time for each study group.

RESULTS

The prevalence of *A. lumbricoides*, hookworm, and *E. histolytica* found in the study population is shown in **Table 1**. Egg counts for *A. lumbricoides* were all < 7000/g feces whereas egg counts for hookworm varied between 3000 and 8000/g feces. Cure rates for albendazole and metronidazole were 96% and 89%, respectively. Median urinary iodine concentrations in the groups at baseline indicated severe iodine deficiency in the population (23). Ages and baseline urinary iodine concentrations were comparable among the study groups. The urinary iodine concentration in the placebo group remained low throughout the study.

Patterns of urinary iodine concentration after oral iodized oil supplementation in the different groups qualifying for statistical analysis are given in **Table 2**. All treated groups had significantly higher urinary iodine concentrations ($P < 0.001$) at the 4th week of follow-up. This was also the case at the 8th week of follow-up for schoolchildren initially infested with hookworm or *E. histolytica*, as well as for the total group ($P < 0.05$). During weeks 20, 40, and 44, urinary iodine concentrations between the study groups were not significantly different although they remained slightly higher for treated children than for untreated children.

The efficacy coefficients iodine retention, iodine elimination rate, and the protection period found for the different groups are shown in **Table 3**. The apparent increases in iodine retention and elimination rate associated with treatment were not significant for any of the group comparisons. However, the duration of protection in children passing *E. histolytica* cysts who were untreated and treated for the infection was 2.0 and 21.0 wk, respectively ($P < 0.05$; **Figure 1**). The adjusted r^2 for *E. histolytica* cyst passers was 0.24. No significant differences were found in protection periods associated with treatment in the *A. lumbricoides* and hookworm groups. The period that urinary iodine concentrations remained elevated > 0.40 μmol/L in the total group of untreated (T_0^*) and treated (T_1^*) children was 9.2 and 16.8 wk, respectively—a difference of 7.6 wk ($P < 0.001$).

DISCUSSION

Because intestinal parasites are important causes of diarrhea in which fat absorption can be reduced significantly (24), they may also interfere with the absorption of orally administered iodized oil. Reduced efficacy of iodized oil because of intestinal parasite infestation is also biologically plausible because malabsorption of vitamin A has been shown in children in-

TABLE 2
Urinary iodine concentrations after oral iodized oil supplementation in Malawian schoolchildren, treated or untreated for intestinal parasites[1]

	Ascaris lumbricoides		Hookworm		*Entamoeba histolytica*		Total group	
Time	Untreated (n = 18)	Treated (n = 26)	Untreated (n = 26)	Treated (n = 16)	Untreated (n = 8)	Treated (n = 16)	Untreated (n = 52)	Treated (n = 58)
	μmol/L							
0 wk	0.16 (0.11, 0.23)	0.17 (0.12, 0.26)	0.15 (0.06, 0.23)	0.17 (0.10, 0.25)	0.17 (0.11, 0.24)	0.19 (0.12, 0.27)	0.17 (0.09, 0.25)	0.16 (0.11, 0.25)
4 wk	0.57 (0.16, 1.11)	1.10[2] (0.42, 3.41)	0.85 (0.39, 1.79)	1.88[2] (0.63, 3.41)	0.27 (0.17, 0.63)	1.52[2] (0.54, 2.83)	0.59 (0.14, 1.29)	1.20[2] (0.46, 3.80)
8 wk	0.45 (0.27, 0.72)	0.55 (0.31, 0.87)	0.28 (0.21, 0.91)	0.89[3] (0.40, 1.36)	0.17 (0.12, 0.76)	0.42[3] (0.21, 1.02)	0.34 (0.13, 0.89)	0.72[3] (0.17, 1.03)
20 wk	0.30 (0.19, 0.54)	0.34 (0.27, 0.61)	0.22 (0.15, 0.69)	0.29 (0.23, 0.89)	0.18 (0.13, 0.49)	0.33 (0.17, 0.63)	0.27 (0.13, 0.59)	0.32 (0.18, 0.72)
40 wk	0.32 (0.11, 0.57)	0.34 (0.11, 0.58)	0.32 (0.11, 0.58)	0.29 (0.14, 0.53)	0.18 (0.13, 0.46)	0.35 (0.16, 0.61)	0.24 (0.13, 0.47)	0.28 (0.13, 0.58)
44 wk	0.17 (0.09, 0.39)	0.27 (0.13, 0.82)	0.18 (0.09, 0.39)	0.25 (0.13, 0.47)	0.17 (0.12, 0.48)	0.25 (0.13, 0.43)	0.19 (0.13, 0.38)	0.23 (0.08, 0.43)

[1] Median; 25th and 75th percentiles in parentheses.
[2,3] Significantly different from untreated: [2] $P < 0.001$, [3] $P < 0.05$.

TABLE 3
Efficacy coefficients of oral iodized oil supplementation in Malawian schoolchildren, treated or untreated for intestinal parasites[1]

Efficacy coefficient	*Ascaris lumbricoides*	Hookworm	*Entamoeba histolytica*	Total group
Iodine retention (μmol/L)				
Untreated children	1.11[3]	0.98[3]	0.48[2]	0.91[3]
Treated children	2.43	1.24[2]	3.37[3]	1.81[2]
Iodine elimination rate ($\mu mol \cdot L^{-1} \cdot wk^{-1}$)				
Untreated children	0.42[4]	0.38[4]	0.31	0.38[4]
Treated children	0.63[2]	0.49[3]	0.71[2]	0.52
Protection periods (wk)[5]				
Untreated children	12.1[4]	11.4[4]	2.0	9.2[4]
Treated children	18.4[4]	10.8[3]	21.0[2]	16.8[3]
Difference	6.3	−0.6	19.0[2]	7.6[4]
Goodness of fit (r^2)	0.15	0.09	0.24	0.16

[1] *See* Table 2 for the number of subjects.
[2–4] Significance calculated from asymptotic Student's t values: [2] $P < 0.01$, [3] $P < 0.05$, [4] $P < 0.001$.
[5] 0.40 μmol/L was the urinary iodine concentration selected indicating moderate iodine deficiency.

fected with *A. lumbricoides* (11–13). Until now, however, no study has reported the relation between intestinal parasite infestation and the effect of oral iodized oil supplementation for correction of iodine deficiency.

A. lumbricoides, hookworm, and *E. histolytica* were common in the schoolchildren in this study. Egg counts for *A. lumbricoides* were < 7000/g feces, which indicated a low severity of infestation. The hookworm burden was moderate but worms were not recovered after treatment, making a specific diagnosis impossible. *Necator americanus* is, however, the predominant nematode reported by the Ntcheu District Hospital, as in Malawi generally. Albendazole cure rates for *A. lumbricoides* and hookworm, both nematodes of the small intestine, were high.

E. histolytica, a parasite of the colon, is widely distributed and occurs characteristically in endemic form. The prevalence in schoolchildren is about the same as that in the general population (25). Infested schoolchildren in this study were so-called chronic *E. histolytica* cyst passers even though they did not have clinical symptoms. Although the diagnostic quality control provided confidence that the diagnosis of *E. histolytica* was correct in this study, we are aware that what is currently called *E. histolytica* may in fact have been two species, one of which is invasive and the other noninvasive (26). Unfortunately, the cysts of the two are indistinguishable by microscope. Because the trophozoites were not examined for blood corpuscles to differentiate between the two species, we could not be certain which of the species was observed. The 89% cure rate achieved with metronidazole was high considering the complex schedule of treatment.

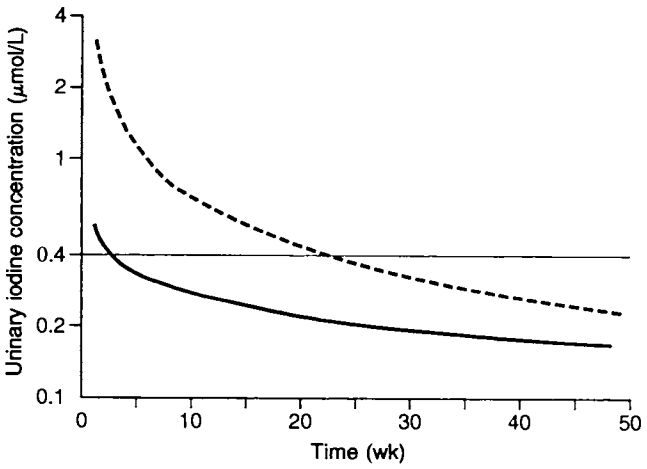

FIGURE 1. Urinary iodine concentrations after oral iodized oil supplementation in apparently healthy schoolchildren treated (broken line) and untreated (unbroken line) for *Entamoeba histolytica* in Ntcheu District, Malawi. The cutoff concentration for moderate iodine deficiency (I*; 0.40 μmol/L) is indicated by the horizontal line.

In all treated groups, the urinary iodine concentrations during the 4th week after oral iodized oil supplementation were significantly higher (Table 2), which suggests that the absorption of iodized oil improved after treatment for intestinal parasites. The iodine retention coefficients were also consistently higher for the treated groups (Table 3), although these differences were not significant because of the high variation in urinary iodine concentrations in the children and the small number of observations in each group. Whereas iodine retention was better in all groups of treated schoolchildren, the iodine elimination rate also increased, which resulted for *A. lumbricoides* and hookworm in comparable periods of protection in the treated and untreated groups. The protection period for treated schoolchildren in the *E. histolytica* group was, however, significantly longer than in untreated children.

The possible effect of *A. lumbricoides* or hookworm infestation on the efficacy of iodized oil may have been undervalued in this study because the worm burdens were not severe (15). It may also be that these parasites of the small intestine have a limited effect or no effect on the absorption of iodized ethyl esters, as used in this study, or that the iodine dose, compared with the initial severity of iodine deficiency, was too low to detect a difference. Further research is needed to verify more reliably the effect of parasite infestation of the small intestine on the efficacy of oral iodized oil.

E. histolytica is a parasite of the colon and because fats are normally digested and absorbed in the small intestine it is not immediately clear what the mechanism may have been by which the efficacy of the oral iodized oil supplement was affected. The iodine retention rates, elimination rates, and

protection periods observed in untreated *E. histolytica* cyst passers were lower than those of the other groups. It may be that the ameba infestation stimulated bowel movement generally, causing a swift passage time through the gut, thus affecting absorption. The urinary iodine concentration in the *E. histolytica* group remained elevated for 21 wk after treatment with metronidazole, exceeding the protection period in the other groups. Metronidazole is a broad-spectrum antimicrobial agent acting against a wide range of anaerobic bacteria as well as intestinal protozoa. Bacterial overgrowth of the small intestine is common in children in developing countries, leading to deconjugation of bile salts and poor fat absorption in general (27). The observed increase in efficacy after treatment with metronidazole may, therefore, be the result of treating general bacterial overgrowth in the small intestine, in addition to a specific improvement after removal of *E. histolytica*.

Only two cases of *Giardia duodenalis* were identified in the study population, making it impossible to study its relation with the efficacy of oral iodized oil supplementation. *G. duodenalis* is a flagellate with a worldwide distribution and an important cause of chronic diarrhea accompanied by impaired fat absorption in developing countries (28–30). It may be that like *E. histolytica*, *G. duodenalis* reduces the efficacy of oral iodized oil.

In areas where iodine deficiency and intestinal parasites coexist in endemic forms, antiparasitic therapy may be advisable for its additional benefit in combination with oral iodized oil supplementation. For the severely iodine-deficient children who were infested with *E. histolytica*, metronidazole treatment appeared particularly valuable. In hyperendemic areas such as the location in this study, screening for the ameba would be inefficient. Generally, however, a decision for universal metronidazole treatment in combination with oral iodized oil supplementation involves a tradeoff against its teratogenicity: possible side effects and costs. The expenditure for parasite treatment to improve iodine retention might be compared with the cost of giving a larger dose of iodized oil. Possible deleterious effects may be induced by the administration of large doses of iodine, however. Such effects have been observed in adults (9), but to our knowledge not in children (5, 6–8).

Compared with the study of patients with intestinal parasitic infection, the present design in which infested, nonsymptomatic schoolchildren were studied, is less efficient in distinguishing an effect of common intestinal parasites on the efficacy of oral iodized oil supplementation. The high variability of urinary iodine concentrations after oral iodized oil supplementation and the low numbers of infested children who completed the field study period without treatment were also limitations to the likelihood of detecting an effect. Results of this study nevertheless showed that intestinal parasitic infestation in apparently healthy schoolchildren can reduce the efficacy of oral iodized oil for correcting iodine deficiency.

REFERENCES

1. Koutras D. Iodine: distribution, availability, and effects of deficiency on the thyroid. In: Dunn JT, Pretell EA, Daza CH, Viteri FE, eds. Towards the eradication of endemic goitre, cretinism, and iodine deficiency. Washington, DC: Pan American Health Organization, 1986:15–27. (Scientific publication no. 502.)
2. Bhrgi H, Rutishauser R. Iodization of salt and its surveillance. In: Dunn JT, Pretell EA, Daza CH, Viteri FE, eds. Towards the eradication of endemic goitre, cretinism, and iodine deficiency. Washington, DC: Pan American Health Organization, 1986:155–69. (Scientific publication no. 502.)
3. Dunn JT, Thilly CH, Pretell EA. Iodized oil and other alternatives to iodized salt for the prophylaxis of endemic goitre and cretinism. In: Dunn JT, Pretell EA, Daza CH, Viteri FE, eds. Towards the eradication of endemic goitre, cretinism, and iodine deficiency. Washington, DC: Pan American Health Organization, 1986:170–81. (Scientific publication no. 502.)
4. Thilly CH, Bourdoux P, Swennen B, et al. Overall worldwide strategy of goitre control. In: Dunn JT, Pretell EA, Daza CH, Viteri FE, eds. Towards the eradication of endemic goitre, cretinism, and iodine deficiency. Washington, DC: Pan American Health Organization, 1986:130–53. (Scientific publication no. 502.)
5. Watanabe T, Moran D, El-Tamer E, et al. Iodized oil in the prophylaxis of endemic goitre in Argentina. In: Dunn JT, Medeiros-Neto GA, eds. Endemic goitre and cretinism: continuing threats to world health. Washington, DC: Pan American Health Organization, 1974:231–41. (Scientific publication no. 292.)
6. Bautista A, Barker PA, Dunn JT, Sanchez M, Kaiser DL. The effects of oral iodized oil on intelligence, thyroid status, and somatic growth in school-age children from an area of endemic goiter. Am J Clin Nutr 1982;35:127–34.
7. Eltom M, Karlsson FA, Kamal AM, Boström H, Dahlbreg PA. The effectiveness of oral iodized oil in the treatment and prophylaxis of endemic goiter. J Clin Endocrinol Metab 1985;61:1112–7.
8. Benmiloud M, Chaouki ML, Gutekeunst R, Teichert H-M, Wood WG, Dunn JT. Oral iodized oil for correcting iodine deficiency: optimal dosing and outcome indicator selection. J Clin Endocrinol Metab 1994;79:20–4.
9. Elnagar B, Eltom M, Karlson FA, Ermans AM, Gebre-Medhin M, Bourdoux PP. The effects of different doses of oral iodized oil on goiter size, urinary iodine, and thyroid-related hormones. J Clin Endocrinol Metab 1995;80:891–7.
10. Dunn JT. Iodized oil in the treatment and prophylaxis of IDD. In: Hetzel BS, Dunn JT, Stanbury JB, eds. The prevention and control of iodine deficiency disorders. Amsterdam: Elsevier, 1987:127–34.
11. Sivakumar B, Reddy V. Absorption of vitamin A in children with ascariasis. J Trop Med Hyg 1976;78:114–5.
12. Mahalanabis D, Jalan KN, Maitra TK, Agarwal SK. Vitamin A absorption in ascariasis. Am J Clin Nutr 1976;29:1372–5.
13. Mahalanabis D, Simpson TW, Chakraborty ML, Ganguli C, Bhattacharjee AK, Mukherjee KL. Malabsorption of water miscible vitamin A in children with giardiasis and ascariasis. Am J Clin Nutr 1979;32:313–8.
14. Furnée CA, Van der Haar F, West CE, Hautvast JGAJ. A critical appraisal of goiter assessment and the ratio of urinary iodine to creatinine for evaluating iodine status. Am J Clin Nutr 1994;59:1415–7.
15. WHO/UNICEF. Field studies on the relationship between intestinal parasitic infestations and human nutrition. Report of an informal WHO/UNICEF consultation. Geneva: WHO/UNICEF, 1981.
16. Bailey W. Laboratory diagnosis of parasitic disease. In: Manson-Bahr PEC, Bell DR, eds. Manson's tropical diseases. Appendix IV. 19th ed. London: Bailliere Tindall, 1987:1490–1.
17. Sandell EB, Kolthoff IM. Microdetermination of iodine by catalytic method. Mikrochim Acta 1937;1:9–25.
18. Benotti J, Benotti N, Pino S, Gardyna H. Determination of total iodine in urine, stool, diet, and tissue. Clin Chem 1965;11:932–6.
19. Moxon RED, Dixon EJ. Semi-automatic method for the determination of total iodine in food. Analyst 1980;105:344–52.
20. Mood AM, Graybill FA, Boes DC. Introduction to the theory of statistics. Tokyo: McGraw-Hill, 1974:373–80.
21. Furnée CA, Pfann GA, West CE, van der Haar F, van der Heide D, Hautvast JGAJ. New model for describing urinary iodine excretion: its

use for comparing different oral preparations of iodized oil. Am J Clin Nutr 1995;61:1257–62.

22. Kleinbaum DG, Kupper LL, Muller KE. Applied regression analysis and other multivariate methods. Boston: PWS-Kent Publishing Company, 1988.
23. WHO/UNICEF/ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodization. Geneva: WHO, 1994. (Document WHO/NUT/94.6.)
24. Molla A, Molla AM, Sarker SA, Khatoon M, Mujibur Rahaman M. Effects of acute diarrhoea on absorption of macronutrients during disease and after recovery. In: Chen LC, Scrimshaw NS, eds. Diarrhea and malnutrition. New York: Plenum Press, 1983:143–54.
25. Wilcocks C, Manson-Bahr PEC. Manson's tropical diseases. London: Bailliere Tindall, 1980.
26. Sargeaunt PG. *Entamoeba histolytica* is a complex of two species. Trans R Soc Trop Med Hyg 1992;86:348 (letter).
27. Hall A. Intestinal parasitic worms and the growth of children. Trans R Soc Trop Med Hyg 1993;87:241–2.
28. Farthing MJG. Giardiasis: pathogenesis of chronic diarrhea and impact on child growth and development. In: Lebenthal E, ed. Chronic diarrhea in children. New York: Raven Press, 1984:253–67.
29. Hartong WA, Gourley WK, Arvanitakis C. Giardiasis: clinical spectrum and functional-structural abnormalities of the small intestinal mucosa. Gastroenterology 1974;66:16–21.
30. Ament ME, Rubin CE. Relation of giardiasis to abnormal intestinal structure and function in gastro-intestinal immuno-deficiency syndromes. Gastroenterology 1972;62:216–26.