Control of ascariasis through age-targeted chemotherapy: impact of 6-monthly chemotherapeutic regimens

Thein-Hlaing,[1] Than-Saw,[2] & Myat-Lay-Kyin[3]

A field trial of 6-monthly ascariasis chemotherapeutic regimens targeted at 1–19-, 1–14-, and 5–19-year-olds was carried out in three communities in rural Myanmar to observe the effects on the prevalence, intensity, and morbidity indicators over 2 years.

After periodic chemotherapy, the prevalence and intensity of Ascaris *infection in age-targeted and non-age-targeted groups fell in all the study areas, more markedly among the 1–19- and 1–14-year-olds. There was also a decrease in the frequency of vomiting of worms, passing of worms per anus, coughing, abdominal pain and treatment of bowel complaints, especially among the treated groups. In addition, there were reductions in the frequency of fever from nonbowel complaints and protrusion of the abdomen among children in the targeted group.*

Introduction

Ascaris lumbricoides infection is still highly prevalent in countries with poor socioeconomic conditions and inadequate environmental sanitation, especially in Africa, Asia, and Latin America, where it affects over 1000 million people (*1*). WHO has advocated chemotherapy as an immediate and effective measure for controlling ascariasis in communities (*2, 3*). Community-oriented chemotherapy has been studied in two main forms: mass chemotherapy at the population level, in which a proportion of the community is treated, irrespective of their age and other characteristics (*4, 5*); and targeted chemotherapy, which is confined to a group of individuals characterized by age (*4, 6, 7*). In contrast, studies on periodic chemotherapy have employed various intervals of time (*5, 8, 9*). A more rational cost-effective and pragmatic chemotherapeutic regimen should be sought and examined for its possible application in most endemic areas. We therefore carried out a field trial of 6-monthly chemotherapeutic regimens targeted at three age groups in three communities in rural Myanmar (Burma) in order to determine the following: the degree of reduction in the prevalence and intensity of *A. lumbricoides* infection and some of its indicators in the targeted and nontargeted age groups under each regimen; the changes in stomach girth measurements of children following repeated chemotherapy; and the effectiveness of a surveillance system in the control area.

Study area and population

The study area was selected for the reasons outlined below. It was highly endemic for *Ascaris* infection, consisting of three rice-farming communities each with a relatively stable population of about 1000; it was accessible throughout the year; and the local health and administration personnel were cooperative. The area is located in Letpadan township, about 145 km north of Yangon. The study village communities were Gwetaukwin (area A), Kinetawsu (area B), and Kunchan (area C), with populations of 853, 857, and 1116, respectively. The villages were randomly allocated so that each received an age-targeted chemotherapeutic regimen. The field study consisted of surveys at 6-month intervals (surveys 1–5 (S1–S5)) over a period of 2 years, beginning in December 1986.

Study methods

The following procedures and methods were carried out in the three villages: stool specimens were collected from all inhabitants before chemotherapy and from a fixed cohort of 202 individuals from area A, 101 from B, and 102 from C, one week after treatment (efficacy group) at the initial (S1), middle (S3), and final (S5) surveys. The specimes were examined for *Ascaris* eggs by direct microscopy on three glass smears of stool samples. Stool specimens were also taken at each

[1] Deputy Director (Sociomedical Research), Department of Medical Research, Ministry of Health, Ziwaka Road, Yangon 11191, Myanmar. Requests for reprints should be sent to this address.

[2] Research Officer, Parasitology Research Division, Department of Medical Research, Ministry of Health, Yangon, Myanmar.

[3] Senior Research Officer, Epidemiology Research Division, Department of Medical Research, Ministry of Health, Yangon, Myanmar.

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survey (S1–S5) from a fixed number of randomly selected households (192 persons from area A, 159 from B, and 165 from C) and the number of *A. lumbricoides* eggs per gram of stool determined using the cellophane thick smear method (*10*). Children and teenagers in the targeted age groups, i.e., those aged 1–19 years in village A, 1–14 years in B, and 5–19 years in C (S1–S4) and those in the efficacy groups (S1–S5) were given tablets of the anthelmintic drug levamisole (Ketrax),[a] according to the manufacturer's instructions.

Household surveys were conducted every 6 months beginning at S1, using a structured questionnaire to record, by recall, ascariasis morbidity indicators among under-20-year-olds, such as coughs and abdominal pain that had lasted for 2 weeks prior to the interview, bowel and other complaints and their treatment, vomiting, and any worms passed per anus over the previous 6 months. During the household visits, also the abdominal girth of 2–9-year-olds was determined by having the child stand to attention and placing the measuring tape close to the skin, making sure that it passed horizontally across the umbilicus. Finally, in village A from S3 onwards, a fortnightly surveillance that was continued over a 1-year period was carried out by a paid female voluntary health worker to monitor some of the morbidity indicators. The ages of the study cohorts were updated at 6-monthly intervals.

Results

Drug efficacy and side-effects

Cure rates after mass treatment with levamisole in villages A, B, and C at S1, S3, and S5 were about 90% (Table 1) and the drug efficacy was maintained in individuals after five successive treatments. About 12% of the individuals treated ($n=396$) at S3 and 9% ($n=337$) at S5 had one or more of the following symptoms of ascariasis (in descending order of frequency): fever, giddiness, vomiting, and loss of appetite.

Prevalence of Ascaris *infection*

The overall prevalence of *Ascaris* infection in each study community was greater than 75%, and among persons aged at least 45 years was about 60% or more (Table 2). After repeated age-targeted mass chemotherapy with levamisole, the overall and age-specific prevalences in both the targeted and nontargeted groups became lower in all the villages. The reduction was more prominent at the end of the first year than at the end of the second, and was greater in area A than B, and in B than C. In area C, the reduction in the prevalence among under-5-year-olds and over-45-year-olds at the end of the second year was negligible (Table 3).

Table 1: **Efficacy of levamisole on a fixed cohort of individuals who completed successive 6-monthly treatments: percentage of persons unaffected by treatment**

Village area	Survey 1		Survey 3		Survey 5	
	No.	%	No.	%	No.	%
A[a]	66	7.6	51	2.0	42	11.9
B[b]	88	10.2	70	2.9	54	5.6
C[c]	91	13.2	81	3.8	65	3.5
Total	245	10.6	202	3.0	161	6.2

[a] Target age group: persons <20 years of age.
[b] Target age group: children <15 years of age.
[c] Target age group: persons aged 5–19 years.

Intensity of Ascaris *infection*

The overall and age-specific numbers of eggs per gram of stool in village B were higher than those in village A or C, except among under-5-year-olds (Table 4). After repeated chemotherapy, however, the percentage reduction in egg count in village A or B was much greater than that in C (Table 5).

Ascariasis morbidity

The indicators for ascariasis morbidity at S1, the pattern of worms being passed per anus, the history of coughing and abdominal pain in the three study villages, and of vomiting of worms and treatment of bowel complaints in areas A and B were similar. The findings are shown in Table 6 for the same month of different study years to avoid any seasonal influences.

Table 2: **Prevalence of *Ascaris* infection in the three rural areas at the baseline survey (S1), Letpadan township, Myanmar**

Age group (years)	Area A[a]	Area B[b]	Area C[c]
	No.	No.	No.
<5	82 (80.49)[d]	48 (75.00)	96 (79.17)
5–9	103 (83.50)	57 (80.70)	114 (90.35)
10–14	111 (86.49)	46 (91.30)	98 (80.61)
15–19	79 (79.75)	22 (90.90)	80 (82.50)
20–44	242 (78.10)	89 (75.28)	259 (79.15)
⩾45	160 (73.13)	85 (58.82)	177 (63.84)
All ages	777 (79.41)	347 (75.22)	824 (77.91)

[a,b,c] See corresponding footnotes to Table 1.
[d] Figures in parentheses are percentages.

[a] I.C.I. Pharmaceuticals Division, Macclesfield, Cheshire, England.

Table 3: **Reduction in the prevalence of *Ascaris* infection from baseline pretreatment levels as a result of age-targeted chemotherapy with levamisole in the three study communities**

Age group (years)	% reduction in prevalence:					
	Area A[a]		Area B[b]		Area C[c]	
	S3[d]	S5[e]	S3	S5	S3	S5
<5	23.72	34.53	13.61	5.99	14.65	0
5–9	30.51	15.17	32.23	8.54	29.21	9.91
10–14	47.97	37.57	47.06	23.66	37.19	21.30
15–19	45.73	41.84	33.99	22.99	48.43	21.96
20–44	43.42	27.55	39.85	29.38	28.93	18.36
⩾45	38.97	33.90	26.08	17.53	6.99	6.44
All ages	38.97	30.73	32.25	19.50	25.70	12.09

[a, b, c] See corresponding footnotes to Table 1.
[d] S3 = survey 3, carried out on the 12th month of the study.
[e] S5 = survey 5, carried out on the 24th month of the study.

Table 4: **Baseline intensity (S1) of *Ascaris* infection in the three rural areas in Letpadan township, Myanmar**

Age group (years)	Area A[a]		Area B[b]		Area C[c]	
	No.	Mean ± S.D. ($\times 10^3$)[d]	No.	Mean ± S.D. ($\times 10^3$)[d]	No.	Mean ± S.D. ($\times 10^3$)[d]
<5	30	3624 ± 9.25	12	1918 ± 2.82	21	3098 ± 5.66
5–9	36	2803 ± 5.61	22	3810 ± 6.67	29	927 ± 1.21
10–14	40	1170 ± 1.67	22	3262 ± 4.69	11	983 ± 1.71
15–19	34	798 ± 1.49	11	1234 ± 1.67	19	676 ± 1.19
⩾20	38	1075 ± 2.02	13	2832 ± 3.87	16	529 ± 0.67
All ages	178	1528 ± 3.97	80	2862 ± 4.71	96	1292 ± 2.96

[a, b, c] See corresponding footnotes to Table 1.
[d] Refers to the number of eggs per gram of stool.

Table 5: **Percentage reduction in the intensity of *Ascaris* infection from baseline pretreatment levels following age-targeted chemotherapy with levamisole in Letpadan township, Myanmar**

Age group (years)	% reduction in prevalence:											
	Area A[a]				Area B[b]				Area C[c]			
	S2[d]	S3[e]	S4[f]	S5[g]	S2	S3	S4	S5	S2	S3	S4	S5
<5	90.23	93.41	76.60	77.18	71.22	93.48	29.92	66.42	81.86	91.41	51.94	75.60
5–9	86.59	92.69	70.43	88.26	87.95	97.09	89.74	78.24	40.02	55.66	0	50.81
10–14	86.07	92.05	77.09	80.17	90.53	97.76	84.12	85.16	32.25	87.59	49.44	76.70
15–19	83.46	78.95	56.27	66.29	71.64	90.92	28.89	85.33	18.64	37.57	57.40	81.51
⩾20	83.54	89.77	53.49	78.05	81.78	96.75	77.54	94.85	0	57.66	20.04	34.03
All ages	83.64	89.53	61.85	78.27	84.31	96.44	72.71	81.27	54.41	77.25	30.19	70.74

[a, b, c] See corresponding footnotes to Table 1.
[d, e, f, g] S2, S3, S4, and S5 represent the surveys carried out at the 6th, 12th, 18th, and 24th months of the study, respectively.

Table 6: **Effect of age-targeted chemotherapy with levamisole on some variables of ascariasis morbidity in Letpadan township, Myanmar**

Age group (years)	Frequency (%)								
	Area A[a]			Area B[b]			Area C[c]		
	December:			December:			December:		
	1986	1987	1988	1986	1987	1988	1986	1987	1988
Vomiting of worms									
<5	11.49 (87)[d]	– (87)	8.54 (82)	11.76 (102)	2.38 (92)	– (103)	4.80 (125)	6.50 (123)	6.77 (133)
5–14	4.05 (222)	1.89 (203)	0.99 (201)	3.82 (157)	2.38 (169)	– (179)	3.67 (245)	2.92 (255)	2.29 (262)
15–19	1.23 (81)	– (98)	– (88)	1.72 (58)	– (66)	– (64)	2.17 (92)	1.11 (90)	1.10 (91)
Worms passed per anus									
<5	31.03 (87)	12.00 (87)	10.98 (82)	29.41 (102)	9.52 (92)	4.85 (103)	21.60 (125)	17.07 (123)	15.79 (133)
5–14	22.97 (222)	4.43 (203)	2.99 (201)	25.48 (157)	3.55 (169)	2.23 (179)	26.53 (245)	3.92 (255)	4.58 (262)
15–19	9.88 (81)	2.04 (98)	2.27 (88)	22.41 (58)	3.03 (66)	7.81 (64)	27.96 (93)	4.44 (90)	3.29 (91)
History of coughing									
<5	58.62 (87)	47.13 (87)	50.00 (82)	57.84 (102)	34.78 (92)	33.98 (103)	53.60 (125)	39.84 (123)	33.83 (133)
5–14	41.89 (222)	20.69 (203)	25.87 (201)	42.04 (157)	18.34 (169)	12.85 (179)	44.49 (245)	34.51 (255)	23.28 (262)
15–19	23.46 (81)	21.43 (98)	13.64 (88)	31.03 (58)	25.76 (66)	26.56 (64)	33.33 (93)	28.89 (90)	16.48 (91)
History of abdominal pain									
<5	35.63 (87)	18.39 (87)	19.51 (82)	29.41 (102)	11.96 (92)	22.33 (103)	28.80 (125)	21.14 (123)	18.05 (133)
5–14	34.68 (222)	17.73 (203)	19.40 (201)	35.03 (157)	14.79 (169)	13.41 (179)	53.47 (245)	20.78 (255)	17.94 (262)
15–19	29.63 (81)	14.28 (98)	19.32 (88)	34.48 (58)	7.57 (66)	17.18 (64)	37.63 (93)	22.22 (90)	16.48 (91)
Treatment of bowel complaints[e]									
<5	13.79 (87)	4.00 (87)	4.88 (82)	12.75 (102)	7.14 (92)	3.88 (103)	8.00 (125)	6.50 (123)	3.01 (133)
5–14	6.31 (222)	1.48 (203)	0.99 (201)	8.28 (157)	2.96 (169)	0.56 (179)	4.08 (245)	3.53 (255)	1.91 (262)
15–19	6.17 (81)	2.04 (98)	1.14 (88)	1.72 (58)	1.51 (66)	– (64)	5.38 (93)	2.22 (90)	1.10 (91)

[a, b, c] See corresponding footnotes to Table 1.
[d] Figures in parentheses are the number of persons interviewed.
[e] Including abdominal pain, dyspepsia, peptic ulcers, diarrhoea, and dysentery.

As a result of the 6-monthly age-targeted chemotherapy, a marked progressive reduction occurred in such indicators among the targeted age groups and a moderate reduction in nontargeted individuals. Similarly, the incidence of fever (from nonbowel ailments) among treated children also declined over successive periods in all the study areas (Table 7).

Table 7: **Frequency of treatment for fever (nonbowel complaints)[e] among the 5–14-year-old target group**

Survey	Frequency (%)		
	Area A[b]	Area B[c]	Area C[d]
S1 (December 1986)	23.8 (222)[e]	8.3 (157)	10.2 (245)
S3 (December 1987)	6.4 (203)	6.5 (169)	7.8 (255)
S5 (December 1988)	8.9 (201)	3.4 (179)	6.1 (262)

[e] Other complaints pertaining to the respiratory system, skin, eyes and ears were also monitored. The percentage rate for each group ranged from 0 to 2.
[b, c, d] See footnotes *a, b, c,* respectively, in Table 1.
[e] Figures in parentheses are the number of children interviewed.

Abdominal girth measurements

After successive rounds of chemotherapy, there was a general decrease in abdominal measurements among 4–8-year-olds of the same age at different sampling times (Table 8). It should be noted that, because one of the medical officers who was responsible for measuring girths left after the S4 survey, girth measurements for S5 are not shown in Table 8 in order to avoid the effects of observer variations.

Surveillance of ascariasis morbidity

Data for 184 children who had completed chemotherapy from S1 to S5 (December 1986 to December 1988) in village A were analysed. The findings on the chemotherapy given to test the efficacy of levamisole in December 1988 (S5) were also used in the surveil-

Table 8: **Mean abdominal girths for children of the same age, according to the number (from zero to three) of 6-monthly treatments with levamisole they had received**

Age (years)	Mean girth ± S.D. (cm)			
	Zero	One	Two	Three
4	50.7 ± 3.1 (20)[a]	49.3 ± 3.5 (22)	50.4 ± 2.7 (28)	49.1 ± 3.2 (21)
5	50.6 ± 2.6 (36)	49.8 ± 3.4 (35)	49.8 ± 3.2 (18)	48.7 ± 2.9 (20)
6	50.9 ± 3.3 (32)	50.6 ± 3.4 (37)	50.8 ± 3.1 (27)	49.8 ± 2.9 (28)
7	50.9 ± 3.3 (32)	51.7 ± 2.8 (31)	51.1 ± 3.0 (31)	49.9 ± 2.9 (31)
8	51.9 ± 3.1 (34)	52.9 ± 3.2 (27)	51.6 ± 3.0 (28)	51.4 ± 2.8 (27)
9	52.2 ± 3.7 (29)	52.2 ± 2.9 (23)	52.3 ± 3.1 (30)	52.4 ± 3.3 (26)
Total	51.2 ± 3.2 (183)	51.1 ± 3.5 (175)	51.1 ± 3.1 (162)	50.3 ± 3.2 (153)

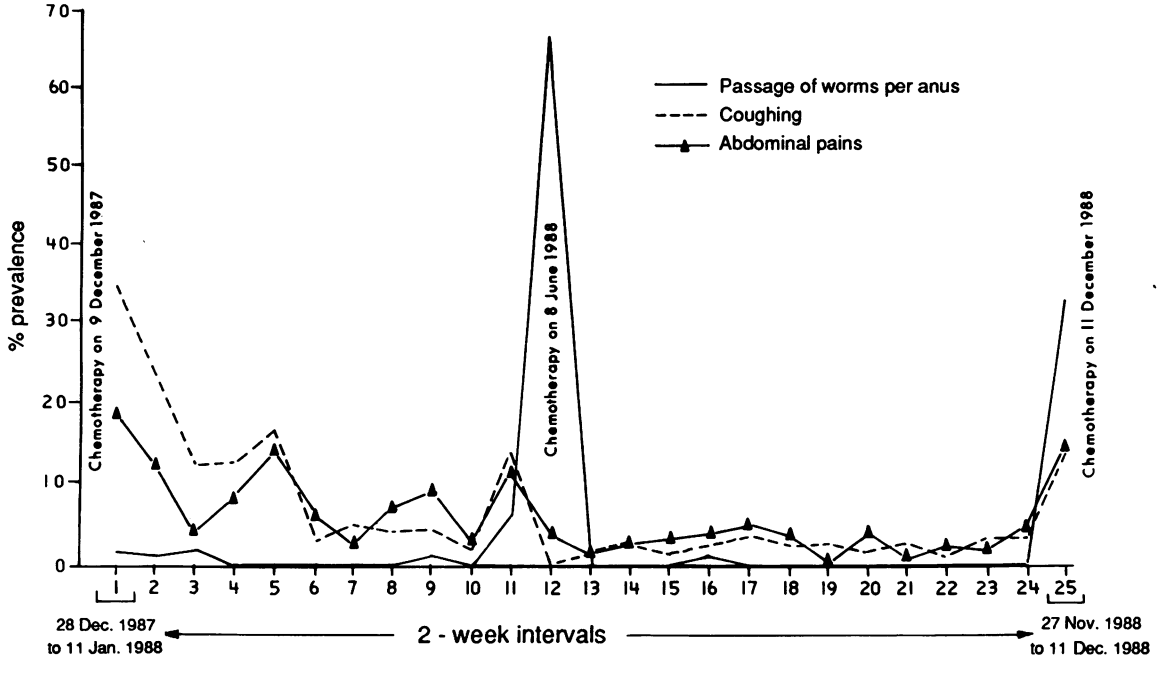
[a] Figures in parentheses are the number of children examined.

lance study. A clear reduction in the passage of worms per anus, abdominal pain, and coughing occurred in the 2 weeks following chemotherapy, and the frequency of these indicators of ascariasis began to increase just before the next dose of chemotherapy was due (Fig. 1). Vomiting of worms almost ceased during the surveillance period.

Discussion

The efficacy of levamisole in individuals was unchanged after they had received five successive doses of the drug, and the cure rate was over 90% (*11*). Of the three 6-monthly chemotherapeutic regimens, the one targeted at 1–19-year-olds was the most effective in reducing the overall and age-specific prevalences and intensities of *Ascaris* infection in the targeted and nontargeted groups. Although this regimen might not be as effective as 4-monthly, 3-monthly, or 2-monthly doses (*4–7*), it is much more so than annual chemotherapy, which at the end of the year resulted in a return to the pretreatment worm prevalence and mean

Fig. 1. **Prevalence of coughing, abdominal pain, and passage of worms per anus by 2-week surveillance interval among treated children in village A.**



worm burden per child (*5, 9*). The second most effective regimen was that targeted at under-15-year-olds. These results indicate that chemotherapy at 6-monthly intervals targeted at various age groups could have an impact on controlling ascariasis morbidity in the entire population in endemic areas. This is particularly true if the age–intensity curve in the communities is convex, e.g., if children and teenagers are harbouring a large portion of the total adult worm population (*11, 12*). Moreover, repeated age-targeted chemotherapy should have an augmented impact because of the predisposition of individuals to acquire heavy (children) or light (adults) burdens of *Ascaris* infection (*9, 13*). All these phenomena explain the fall in ascariasis morbidity indicators such as coughing, abdominal pain, and treatment of bowel disorders, especially among those who received chemotherapy. The reduction in the frequency of fever illnesses among treated children may be due to a decrease in the immunosuppression caused by long-standing *Ascaris* infection (*2*). In addition, the decline in abdominal protrusion, which is often regarded as a sign of ascariasis among children in endemic areas, was caused by a reduction in the mass of worms in their abdomens. Thus, the fall in ascariasis morbidity brought about by age-targeted chemotherapy in communities could result in a reduction in the number of cases of the disease that are hospitalized (*14, 15*) and in the costs of surgical interventions and other treatments (*16*). Finally, there should be an improvement in the nutritional status of children in communities after periodic chemotherapeutic treatments (*7, 17*).

Control of ascariasis by community-oriented chemotherapy is compatible with the elements of primary health care (*18*). Hence, such control efforts should be adopted in health programmes in areas that are highly endemic for ascariasis.

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Résumé

Lutte contre l'ascaridiose par chimiothérapie axée sur certains groupes d'âge: impact d'une posologie semestrielle

Les infestations à *Ascaris lumbricoides* sont encore fortement prévalentes dans les pays de faible niveau socio-économique et où l'hygiène du milieu est insuffisante. Pour élaborer une mesure d'intervention contre la maladie qui soit plus logique et plus rentable, un essai sur le terrain d'une chimiothérapie donnée tous les 6 mois, visant les groupes d'âge de 1–19 ans, 1–14 ans et 5–19 ans, a été effectué dans 3 communautés du Myanmar (Birmanie) rural, pendant une période de deux ans ayant commencé en décembre 1986. Des échantillons de selles ont été examinés pour connaître la prévalence et l'intensité des infestations à ascaris et quelle était l'efficacité du lévamisole, un anti-helminthique. Des visites à domicile ont été effectuées pour enregistrer les indicateurs de morbidité ascaridienne chez les moins de 20 ans et pour mesurer la circonférence abdominale des enfants âgés de 2 à 9 ans. Un système de surveillance bimensuelle a été organisé au cours de la seconde année de l'étude pour suivre certains des indicateurs de morbidité.

L'efficacité du lévamisole était supérieure à 90% et est restée inchangée après 5 traitements successifs. La prévalence totale de l'ascaridiose dans chaque communauté étudiée était supérieure à 75% et était $\geqslant$60% chez les personnes âgées de $\geqslant$45 ans. Des posologies semestrielles axées sur certains groupes d'âge, celle visant les sujets de 1–19 ans était la plus efficace pour réduire la prévalence totale et spécifique de l'âge et l'intensité de l'infestation dans les groupes visés et non visés. Venait ensuite la posologie visant les sujets de 1–15 ans. Dans les groupes visés, il y a eu une diminution marquée des indicateurs de morbidité ascaridienne comme l'expulsion de vers par l'anus, le vomissement de vers, la toux, les douleurs abdominales et la demande de traitement de troubles intestinaux, alors que chez les individus non visés, il n'y a eu qu'une réduction modérée de ces indicateurs. Les diminutions de ces indicateurs chez les enfants traités étaient confirmées par les données de surveillance. De plus, une chute du nombre des troubles non intestinaux, comme la fréquence des épisodes fébriles et celle de la protrusion abdominale, a été observée chez les enfants traités.

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