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ORAL EMETINE IN THE TREATMENT OF INTESTINAL AMEBIASIS

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A previous paper (1) reported the trial use of emetine hydrochloride, orally, in the form of enteric-coated tablets, for the treatment of intestinal amebiasis. This study presents further observations on the use of this drug.

Emetine hydrochloride is known to be an effective amebicidal agent. Dobell and Laidlaw (2), St. John (3), and Bonnin and Aretas (4) have shown, by experimental methods, that emetine or its salts has a direct amebicidal action which is effective in very high dilutions; 1–1,000,000 to 1–5,000,000.

Table 1 summarizes the available information of the amebicidal activity, *in vitro*, of some of the drugs used in the treatment of amebiasis. It can be seen that emetine is a much more effective amebicidal agent than any of the newer drugs on which *in vitro* studies have been carried out.

Since emetine has a powerful, direct, amebicidal action, a property demonstrated in *in vitro* studies, oral therapy should eradicate the parasite. However, its concomitant powerful emetic action, resulting in severe salivation, nausea, and vomiting, has prevented administration of sufficient amounts to prove effective parasitologically. A few attempts have been made to provide protective coatings such as keratin or salol, or to combine the salt with other drugs in the form of emetine bismuth iodide, or emetine antimony iodide, in order to lessen the emetic effect. These results have, on the whole, not been successful.

Rogers, (8), in 1912, advocated the subcutaneous administration of the hydrochloride salt, thereby avoiding much of the nausea and vomiting which usually accompanied the oral administration. There was widespread acceptance of this method of therapy, and, in general, the results have justified the continued use of the drug. It has been shown by clinical experience, and animal experimentation, that it is a toxic drug with a cumulative action when administered in this manner.

Because of the toxicity of subcutaneous emetine, its therapeutic range has been limited, and according to Craig (9), the amount which can be safely given is, in the majority of cases, insufficient to permanently eradicate the parasite. Current opinion has limited its use to the control of symptoms, or as an adjuvant to the iodine and arsenic compounds for eradication of the parasite. Emetine subcutaneously is still the drug of choice in the management of extra-intestinal amebiasis.

The drug used in this study was emetine hydrochloride, prepared by Eli Lilly Company, and consisted of "enseals", or enteric-sealed tablets, to be administered orally. Each tablet contained one-third grain of alkaloid, and was designed to release its contents into the lower bowel approximately three to four hours after ingestion, thus avoiding the emetic effect of its presence in the stom-

ach, and upper intestinal tract. Little is known of the amount of absorption of emetine that can occur from the large bowel, but from the results of this study it is believed to be minimal.

TABLE 1

Amebicidal Activity, In Vitro, of Drugs Used in Treatment of Amebiasis

DRUG	AMEBICIDAL CONCENTRATION 48 HOURS	INVESTIGATOR
Chiniofon	1–500	Kessel (1928) (5)
Carbarsone	1–4,000	Leake (1932) (6)
Vioform	1–10,000	Leake (1932) (6)
Emetine hydrochloride	1–1,000,000	Dobell, Laidlaw and Bishop (1928) (7)
Emetine hydrochloride	1–1,000,000	St. John (1932) (3)

TABLE 2

	*DYSENTERY ACUTE	DYSENTERY CHRONIC	"CARRIER" STATE	TOTAL
Children.....	2	2	1	5
Adults.....	6	13	6	25
Total.....	8	15	7	30

PROCEDURES AND CLINICAL MATERIAL

A total of thirty cases of intestinal amebiasis were treated with emetine hydrochloride in the form of enteric-sealed tablets, orally, in this series. Included in this group are Latin Americans, British West Indians, and North Americans, of both sexes, and of age groups ranging from 17 months to 66 years. There were acute and chronic dysenteries, as well as "carriers," as given in Table 2.

The patients were all hospital admissions although not all were primarily for amebiasis. Some cases were discovered on routine stool examinations and some by proctoscopic examinations. There was no attempt at selection of cases, except that none were used if treatment with emetine hydrochloride subcutaneously had already been begun, and none were used unless the presence of *E. histolytica* in the stool was verified by the author. All cases, except one, were given a complete course of treatment, as hospital patients, under the authors' direct supervision. The exception was case No. 27 (Table 4), a colored female adult, employed as laundress by the author, and treated as ambulatory, but under daily direct observation.

A standardized dosage schedule was used throughout, as follows:

Children: One tablet (½ grain) of emetine hydrochloride, orally, three times a day for 12 days. Total: 12 grains in 12 days.

Adults: Two tablets (⅔ grain) of emetine hydrochloride, orally, three times a day for 12 days. Total: 24 grains in 12 days.

* Terminology of War Department Tech. Bull. 759, May, 1945—*Amebic dysentery:* Cases of amebiasis with intestinal symptoms and abnormal stools which contain motile amoebae. Carrier of *E. histolytica:* Cases in which there are no symptoms and cysts alone are found.

As the avoidance of the emetic effect depends entirely on the protective coating of the tablets, particular care was taken that no cracked, chipped, or disintegrated tablets were administered. The tablets are small enough to be swallowed whole by small children.

It was pre-supposed that some tablets would be passed through the entire intestinal tract without liberating their contents, especially in cases of acute dysentery. This was found to be true in two cases in which tablets were seen in the rectal lumen during a proctoscopic examination. The standard dosage was maintained throughout, however, as in ordinary treatment it would be impractical to determine exactly how many tablets had dissolved, of the total given.

All patients were observed daily on ward rounds and questioned closely as to symptoms of abdominal cramps, diarrhea, nausea or vomiting, insomnia, joint pains, malaise. Insofar as practicable the following routine was established.

(1) Daily microscopic examinations of stools for amebae. Specimens of all stools passed by each case were examined daily by the author before, during, and for a few days following, the course of treatment. Most cases harbored other intestinal parasites, notably helminths, and were given vermifuges and saline purges before and following the emetine. These stool specimens were also carefully examined for amebae.

(2) Daily cultures of stools for micro-organisms.

(3) Daily urinalysis.

(4) Blood pressure readings.

(5) Complete blood count every third day.

(6) Electrocardiogram every three days, except on infants.

(7) Proctoscopic examinations before and after treatment.

(8) Daily count of number of stools passed.

All cases were allowed out of bed as much as desired. No restrictions as to diet were followed, the patients usually taking the full diet.

IMMEDIATE RESULTS IN CHILDREN

There were five cases of intestinal amebiasis in children, (Table 3) of ages ranging from $1\frac{5}{12}$ to 9 years. There were two cases of acute dysentery, two of chronic dysentery, and one "carrier" state. All harbored other intestinal parasites, notably helminths, and presented the picture of malnourishment, underdevelopment and secondary anemia. They were given the usual vermifuges and purges as well as oral emetine hydrochloride. Case No. 3 was admitted critically ill with acute amebic dysentery, a sahli hemoglobin of less than 10 percent, and a total red cell count of 1,020,000. She required two blood transfusions prior to therapy for the parasites.

None of these children manifested vomiting or toxic manifestations during the administration of oral emetine. All showed a steady clinical improvement. The amebae disappeared from the stools between the third and fifth days of treatment, appetites improved, and the frequency of bowel movements diminished. A moderate diarrhea persisted in case No. 2. He was given a course of sulfaguanidine as pus cells were noted in the stool specimens. The diarrhea promptly subsided and the pus cells disappeared.

TABLE 3

CHILDREN

One grain daily for 12 days

CASE NO.	AGE	DIAGNOSIS, AND PARASITES FOUND	SYMPTOMS	Hb % SAHLI	IMMEDIATE RESULT	RE-EXAMINATION			
						Time since Rx	Stool Smears	Hb % Sahli	Comment
1	3	Amebic dysentery, chronic. Anemia, secondary *E. histolytica* troph. *S. stercoralis* *T. trichiuris*	Occasional convulsive attacks associated with listlessness and apathy for past 3 months. Grinds teeth.	50	No amebae after 3rd day. Appetite improved during hospital stay. No convulsions. No toxic symptoms.	4 mos.	Negative for amebae	60	Has been perfectly well since treatment, except for an attack of impetigo.
2	1½	Amebic dysentery, acute Anemia, secondary E. *histolytica* troph. *T. trichiuris* *G. lamblia*	Has had diarrhea for 3 months, but 4 days ago became worse, with blood and mucus. Pus noted in stools. Weighs 18 lbs.	38	Amebae disappeared after 5th day of Rx, but pus and mucus still present. Given course of sulfaguanidine following emetine. No toxic symptoms.	8 mos.	Negative for amebae *T. trichiuris* ova present	78	Father states child has been in excellent health since discharge. Appetite has been very good, child has gained weight. Has not had any diarrhea or fever. (Weight 25 lbs.)
3	5	Amebic dysentery, chronic severe. Anemia, secondary, severe. *E. histolytica*, troph. *E. coli*, troph. *N. americanus* *S. stercoralis* *T. trichiuris* *G. lamblia*	Child has been passing worms in stool for 7 months. Also has vomited "long worms." Only treatment has been "muy grande" purges 3 or 4 times in past few months. Child has gradually become weak and pale.	10	No amebae after 4th day of Rx. Critically ill on admission. Required 2 transfusions prior to therapy for parasites. No toxic symptoms manifested during emetine treatment. Early morning stools contained large numbers of *T. trichiuris* worms after 5th day of emetine.	4 mos.	Negative for *E. histolytica* Positive for: *N. americanus* *T. trichiuris* *S. stercoralis* *E. coli* cysts	58	Has had no diarrhea, fever, or abdominal pains, but has had "catarro." Has gained weight. Appetite is good.

4	9	"Carrier" of *E. histolytica* Vaginitis, gonorrheal Anemia, secondary *E. histolytica* cysts *N. americanus* *S. stercoralis* *T. trichiuris* *E. coli* cysts *G. lamblia*	Vaginal discharge for past month. No diarrhea, but has occasional abdominal cramps.	72	No cysts found after 5 days. Cultures for amebas negative after 3rd day. Averaged 1 stool daily, but on 6th day had 4 stools. No toxic symptoms.	6 mos.	Negative for *E. histolytica* Positive for: *S. stercoralis* *E. coli*, cysts	80	No symptoms. Has been perfectly well and happy.
5	4	Amebic dysentery, acute Anemia, secondary *E. histolytica*, troph. *E. coli*, troph. *T. trichiuris* *A. lumbricoides* *Trichomonas* sp.	About a month ago began to have bloody stools associated with a frequent diarrhea.	50	No *E. histolytica* trophozoites found in stools after 3rd day of Rx. Passed large numbers of *T. trichiuris* worms in early morning stools after 5th day of Rx. Frequency of stools diminished gradually. Gained 3 lbs. in weight during treatment. No toxic symptoms.	6 mos.	Negative for amebae. Positive for: *A. lumbricoides* *T. trichiuris* (few)	69	Since discharge child has been well. There has been no vomiting, diarrhea, or abdominal pains. Eats well, continues to gain weight, and is active.

Case No. 4, a nine year old colored girl, was admitted for gonorrheal vaginitis and was found to harbor a total of seven intestinal parasites, including *E. histolytica* cysts. She denied having had diarrhea, but did have occasional abdominal cramps. This was the only "carrier" state in children. She was treated with intramuscular penicillin, and oral emetine, concomitantly, without manifesting toxic symptoms. *E. histolytica* cysts or trophozoites could not be found in the stools, by smear or culture methods, after the fifth day of emetine treatment.

A noteworthy side effect in children treated with oral emetine, was the expulsion of large numbers of adult *Trichiuris trichiuris* in the early morning stools of cases No. 3, and No. 5, which were heavily parasitized with this worm. Both of these cases had persistent rectal prolapse occurring with each bowel movement. Large numbers of adult *Trichiuris trichiuris* could be seen on the rectal mucosa when it prolapsed. Consequent to the fifth day of oral emetine treatment, the early morning stools of these 2 children contained large numbers of these worms. As treatment continued, the frequency of the stools diminished, and there were noticeably fewer worms to be seen on the prolapsed rectal mucosa. The children gained weight gradually, and the rectal prolapse finally ceased. *Trichiuris trichiuris* ova were still present, however, in stool specimens examined several days following the course of oral emetine.

IMMEDIATE RESULTS IN ADULTS

Twenty-five adults, of ages from 18 to 66 years, were treated with a standardized dosage of two tablets of emetine hydrochloride, orally, three times a day for 12 days, a total of 24 grains in 12 days. (Table 4).

This series included 6 cases of acute dysentery, 13 of chronic dysentery, and 6 of the "carrier" state.

There were no serious toxic symptoms manifested in this group. No vomiting occurred in any case, care being taken to administer only complete, unbroken tablets. The diarrhea of the acute cases subsided rapidly, the number of stools reducing to 2 or 3 daily, then to none, or one, daily, by the end of the course of treatment. The abdominal cramps and tenesmus responded quickly, usually by the second or third day. Some of the chronic and "carrier" cases, who had not had diarrhea, began to have two or three soft stools daily during the treatment, but this was not accompanied by cramps or tenesmus. This was not considered a toxic effect. The trophozoites of *E. histolytica* could not be found in stool examinations, on the average, by the third day of treatment, but cyst forms could be found as late as the sixth day.

The patients having amebic ulcerations of the rectum were examined periodically by proctoscope and steady healing was evident. All cases, except two, showed complete healing at the end of treatment. One of these (No. 15), with large rectal ulcerations before treatment, showed a slight granularity in the appearance of the rectal mucosa at the end of treatment, but direct smears were negative for amebae. A recheck proctoscopic examination, one month later, showed a normal rectal mucosa throughout. The rectal lesions present in the other case (No. 25), were incompletely healed at the end of the oral emetine treat-

ment, but direct smears were negative for amebae. He was given a course of sulfadiazine for 10 days, and healing was complete.

There were no evidences of toxic effects of emetine on the myocardium. The blood pressure readings, pulse rates, and cardiac sounds showed no significant changes. No effects were noted on the electrocardiograms taken before, during, and after treatment. Case No. 26 had an electrocardiographic record of auricular fibrillation one year previous to emetine treatment. His electrocardiogram, taken prior to treatment, was essentially normal, and there was no demonstrable effect noted on repeated electrocardiograms taken during and following the administration of 24 grains of emetine, orally, in 12 days.

There were no significant changes in the urine during treatment. No evidence of albuminuria, glycosuria, acetonuria, gross changes in specific gravity, or cellular constituents occurred.

All patients were able to take the regular diet while under treatment without nausea or vomiting, and were entirely ambulatory. The one case (No. 27) allowed to continue her work as a laundress while taking 2 grains of emetine orally each day, felt well during the entire course of treatment. Her abdominal cramps, tenesmus, and diarrhea subsided by the second day of treatment and there was a definite increase in her appetite.

There were no complaints of joint pains, nervousness, insomnia, or neuritides. The absence of joint pains was particularly noted as it is often encountered when emetine is administered subcutaneously.

Other drugs, including oral atebrine, hexylresorcinol crystoids, sulfaguanidine, sulfadiazine, have been given, along with the oral emetine without interference or toxicity.

Most cases manifested secondary anemias to varying degrees. As there were often other intestinal parasites present, the amount of anemia caused by the amebae could not be accurately determined. All received treatment for the other parasites as well as the amebae and all showed improvement in the blood picture.

Aside from the mild irritative effect of the emetine in the intestine, producing two or three soft stools daily, but without cramps or tenesmus, in some cases, no toxic effects were noted in this series.

RECHECK STUDIES

The criteria of permanent cure of intestinal amebiasis are not definite. The inability to demonstrate cysts or trophozoites in the stools, plus clinical improvement, after a variable period of time since treatment is completed, is usually interpreted as a cure. The frequency of follow-up rechecks, and the method of stool examinations, has varied with different investigators. The possibility of re-infestation of the patient when he returns to his original environment cannot be eliminated. The longer the interval between recheck studies, the more possible it is that re-infestation may occur.

Twenty-four of the thirty cases treated with oral emetine were re-admitted as hospital patients for recheck studies, from 2 to 9 months after receiving the drug.

TABLE 4

ADULTS

Two grains daily for 12 days

CASE NO.	AGE	DIAGNOSIS, AND PARASITES FOUND	SYMPTOMS	PROCTOSCOPIC	Hb % SAHLI	IMMEDIATE RESULT	RE-EXAMINATION				
							Time since Rx	Stool Smears	Proctoscopic	Hb % Sahli	Comment
28	39	Amebic dysentery, chronic Hernia, right inguinal Sinusitis, chronic *E. histolytica*, troph. *S. stercoralis*	Was treated 4 months ago for amebic dysentery with Carbarsone. Since then has had diarrhea off and on, and pains in right inguinal region. Has 5 to 6 stools daily now.	Normal mucosa	80	No amebae found after 3rd day. Stools subsided to 2 or 3 daily. Had right inguinal herniorraphy after receiving emetine Rx. Stools checked periodically during 6 weeks hospitalization. All were negative for amebae.	8 months	Negative for amebae	Normal mucosa	80	Has had occasional pains in right inguinal region, at site of operation, but otherwise has been well. No abdominal cramps, or diarrhea.
29	36	Amebic dysentery, chronic Anemia, secondary *E. histolytica*, cysts & troph.	5 months ago was treated for amebic dysentery with carbarsone. At that time he had "ulcers in the rectum." For past 2 weeks he has had diarrhea and abdominal pains. Thinks he might have "amebas" again.	Several areas of small ulcerations with one long, shallow ulcer. *After Rx:* Normal mucosa.	78	No amebae found after 4th day of Rx. No toxic symptoms.	3 months	Negative for amebae	None	80	Has felt well. No further diarrhea. Has gained weight.

30	41	Amebic dysentery, chronic *E. histolytica*, cyst & troph.	Admitted only for recheck on previously treated amebiasis with emetine. *History:* Had acute amebic dysentery, with rectal lesions in 1944. Treated with oral emetine, 2 grains daily for 6 days. This repeated 6 days later. Rectal lesions healed. Symptoms disappeared. Rechecked in 1 month, cysts found. Denied symptoms. No rectal lesions. Given 2 grains daily for 8 days. Rechecked 5 months later. No symptoms. No rectal lesions. Gained 15 lbs. in weight. Trophozoites found after saline purge. Treated this time with 2 grains daily for 12 days.	Normal mucosa	85	No symptoms. No signs of toxicity.	5 months	Negative for amebae	Normal mucosa	98	Long history of amebiasis. Treated twice with oral emetine with dosage of less than 10 days, resulting in symptomatic cure, but parasite not eliminated. Last dosage of 2 grains daily for 12 days sufficient to eradicate parasite from stools up to 5 months following treatment.
23	32	Amebic dysentery, acute Syphilis, L-IV *E. histolytica*, troph.	For past 2 months has had constant diarrhea of watery, dark brown stools, sometimes with streaks of blood. Occasional sharp, shooting pains in abdomen.	Many small, pin-head sized lesions, with bloody, mucoid exudate present.	84	Diarrhea subsided on 5th day of Rx. No amebae found after 4th day. No toxic symptoms. X-ray of liver area normal. Heart enlarged in transverse diameter.	3 months	Negative for amebae	None	89	No symptoms. "Sleeps good, and eats good." Has gained 8 lbs. X-ray of liver and diaphragm normal. Heart enlarged in transverse diameter.
24	45	Amebic dysentery, chronic *E. histolytica* troph.	Onset 6 weeks ago, in Guatemala, of severe diarrhea. Received treatment of Carbarsone, and Vioform, of one week each, without effect. Since then has had repeated bouts of diarrhea at about weekly intervals.	One small linear ragged ulceration on inferior valve.	93	No toxic symptoms. Continued to have 3 to 4 stools daily throughout course of emetine. No abdominal symptoms. Appetite good.	4 months	Negative for amebae	Normal mucosa	90	Has had no symptoms since discharge. Has gained 20 lbs. in weight, and states he has a definite increased sense of well-being. X-ray of diaphragm normal.

TABLE 4—*Continued*

CASE NO.	AGE	DIAGNOSIS, AND PARASITES FOUND	SYMPTOMS	PROCTOSCOPIC	Hb % SAHLI	IMMEDIATE RESULT	RE-EXAMINATION				
							Time since Rx	Stool smears	Proctoscopic	Hb % Sahli	Comment
25	38	"Carrier" of *E. histolytica* *E. histolytica*, cysts	Admitted to hospital for operation on nose. Had history of amebiasis 3 years ago, and requested recheck of stools.	Few ragged ulcerations present.	98	Had 3 stools daily while on emetine Rx. Proctitis did not heal completely at end of emetine course. Given course of sulfadiazine, and healing was prompt. No toxic symptoms.	Not obtained				Seen outside hospital and stated he felt entirely well, but was unable to enter hospital for recheck studies.
26	42	"Carrier" of *E. histolytica* Myositis, chronic, cervical post-traumatic. *E. histolytica*, cysts.	For past 6 months has been extremely tired at end of working day. No history of abdominal pains or diarrhea.	Normal mucosa	88	No toxic symptoms. No increase in bowel movements.	3 months	Negative for amebae	Normal mucosa	92	Has felt generally better, but not entirely well. Has not had any abdominal symptoms, or diarrhea.
27	26	Amebic dysentery, acute Anemia, secondary *E. histolytica*, troph.	Has had severe diarrhea, abdominal pains, and vomiting for past 2 weeks. Never had this before.	Normal mucosa	69	Entire course of emetine Rx. given as outpatient while employed as laundress by author. Diarrhea subsided in 2 days of treatment. No further vomiting or abdominal cramps. Appetite improved.	2 months	Negative for amebae	None	80	This pt. employed as laundress by the author. Observed for 3 month period after emetine Rx., and had no recurrence of abdominal symptoms or diarrhea. Appetite good, and gain in weight and general health was noticeable.
17	25	Amebic dysentery, chronic Anemia, secondary *E. histolytica* troph. *N. americanus* *Trichomonas* sp.	Had "dysentery" lasting 6 months, about 2 years ago. For past 6 days has had 3 to 5 bloody stools daily.	Many varied sized ulcerations present. Direct smear positive for *E. histolytica*	50	Diarrhea subsided to 1 or 2 stools daily, by 3rd day of Rx. No amebae seen after 5th day. No toxic symptoms.	Not obtained				

18	36	Amebic dysentery, acute Anemia, secondary Syphilis, L-IV *E. histolytica* troph. *G. lamblia*	2 weeks ago developed epigastric pain, anorexia, malaise, associated with 4 to 5 watery stools daily. This has increased to 10 to 12 daily, with 4 to 5 at night. Stools are stained with blood.	Several large irregular ulcerations. *3 days after Rx:* Normal mucosa to 20 cm.	75	Diarrhea reduced to 3 stools daily by 4th day of Rx. No amebae found after 4th day. No toxic symptoms.	9 months	Negative for amebae	Normal mucosa	82	States he has felt very well since treatment. No symptoms of diarrhea whatever. Has gained weight.
19	44	Amebic dysentery, chronic Anemia, secondary *E. histolytica*, cyst & troph. *G. lamblia* *D. fragilis* *T. trichiuris* *C. mesnili*	Has had pains in R.U.Q. of abdomen, and flank, for past month, associated with gas pains. No diarrhea.	Granular appearing mucosa with several pinpoint easily bleeding areas.	72	Atabrine given for giardiasis, simultaneously with emetine, for first 5 days. No toxic symptoms developed. No amebae found after 6th day.	Not obtained				
20	24	Amebic dysentery, chronic *E. histolytica*, cysts & troph. *E. coli*, cysts	Ate some Casbews and developed sudden pains in R.U.Q. of abdomen, with vomiting.	Normal mucosa	90	No amebae found after 2nd day of Rx. No toxic symptoms.	3 months	Positive for: *E. coli* cysts Negative for *E. histolytica*	Normal mucosa	90	Has gained 8 lbs. in weight. Feels well. No diarrhea.
21	23	Amebic dysentery, acute Anemia, secondary *E. histolytica*, troph.	Onset 2 days ago of colicky abdominal pains with a persistent diarrhea. No blood noted in stools.	Normal mucosa	70	Had 2 or 3 stools daily up to 10th day of Rx., then 0 or 1 daily. No amebae found after 2nd day. No toxic symptoms.	Not obtained				
22	18	"Carrier" of *E. histolytica* *E. histolytica*, cysts *E. coli*, cysts *N. americanus* *S. stercoralis* *T. trichiuris*	Denies any, and all symptoms. Parasites found on routine pre-employment food-handler examination.	Normal mucosa	86	No cysts found after 6th day of Rx. No toxic symptoms.	7 months	Negative for amebae. Positive for: *N. americanus*	None	90	No symptoms. Gained weight. Blood picture improved.

TABLE 4—*Continued*

CASE NO.	AGE	DIAGNOSIS, AND PARASITES FOUND	SYMPTOMS	PROCTOSCOPIC	Hb % SAHLI	IMMEDIATE RESULTS	RE-EXAMINATION				
							Time since Rx	Stool smears	Proctoscopic	Hb % Sahli	Comment
13	43	Amebic dysentery, chronic *E. histolytica*, cysts & troph. *N. americanus* *S. stercoralis* *E. coli*, cysts *D. fragilis*, troph.	Has had "stomach trouble" for 4 years. Has epigastric pain associated with belching. No vomiting or diarrhea, but has lost weight.	Normal mucosa	86	No amebae found after 7th day of Rx. No toxic symptoms. No change in "stomach trouble."	Not obtained				
14	66	"Carrier" of *E. histolytica* Malaria, clinical Anemia, secondary *E. histolytica*, cysts *E. coli*, cysts	Fever, chills, and generalized aches and pains, for past 2 days. Vomited. Severe headache. *E. histolytica* cysts found on routine stool examination.	Several pinpoint easily bleeding areas scattered in rectum. *12th day of Rx:* Normal appearing mucosa	74	No ameba found after 3rd day. Fever responded to atabrine. No toxic symptoms.	4 months	Negative for amebae	Normal mucosa	78	Has had no symptoms since treatment. Feels good. Has gained 16 lbs. in weight.
15	54	Amebic dysentery, acute Diabetes mellitus *E. histolytica* troph. Anemia, secondary	Known diabetic. Recently had all teeth extracted and has been unable to eat properly, and has been having 3 to 4 watery stools daily. Has lost 10 lbs. in weight, and feels weak.	*Before Rx:* Large rectal ulcerations. *12th day of Rx:* Mucosa slightly granular in appearance. No ulcerations. Direct smear negative.	66	No amebae seen in stools after 3rd day of Rx. No toxic symptoms. Recheck proctoscopic one month after discharge showed normal mucosa.	4 months	Negative for amebae	Normal mucosa	80	No further diarrhea since treatment. Has gained weight, and feels good.

16	19	Amebic dysentery, chronic Malaria, tertian Syphilis, L-IV Anemia, secondary *E. histolytica*, cysts & troph. *E. coli*, cysts & troph. *E. nana*, troph. *N. americanus* *S. stercoralis* *T. trichiuris*	Has had chills, fever, headache and pains in back for past 5 days. No diarrhea or abdominal pains.	Normal mucosa	64	No amebae found after 2nd day of Rx. No toxic symptoms.	9 months	Negative for amebae. Positive for: *N. americanus* *S. stercoralis* *T. trichiuris*	None	76	Has had no symptoms since treatment. Has felt well. Appetite good.
10	22	Amebic dysentery, chronic Cellulitis, acute, supp. left leg. Tonsillitis, acute Anemia, secondary *E. histolytica* troph.	Admitted for treatment of cellulitis of leg. *E. histolytica* trophozoites found on routine stool examination. Denies abdominal symptoms or diarrhea.	Normal mucosa	68	No amebae found after 3rd day of Rx. No toxic symptoms.	5 months	Negative for amebae	Normal mucosa	80	No symptoms. Feels entirely well. Anemia improved.
11	55	"Carrier" of *E. histolytica* Hypertensive cardiovascular disease, with right hemiplegia. *E. histolytica* cysts *E. coli* cysts *G. lamblia* *Trichomonas* sp.	Had a "stroke" 5 days ago, and is unable to walk. States she has been constipated for years, and never has had abdominal pains or diarrhea. Blood pressure: 210/100.	Not done	75	No cysts found after 5th day of Rx. No toxic symptoms. No change in blood pressure.	6 months	Negative for *E. histolytica* Positive for: *E. coli*, cysts *Trichomonas* sp.	Mucosa mildly hyperemic. Suggestive of "strawberry" color.	80	No abdominal symptoms. Is still troubled wtih constipation. Blood pressure 180/105. Is able to "get around a little."

TABLE 4—*Concluded*

CASE NO.	AGE	DIAGNOSIS, AND PARASITES FOUND	SYMPTOMS	PROCTOSCOPIC	Hb % SAHLI	IMMEDIATE RESULTS	RE-EXAMINATION				
							Time since Rx	Stool smears	Proctoscopic	Hb % Sahli	Comment
12	33	Amebic dysentery, chronic Blepharo-conjuntivitis, bilateral *E. histolytica* troph. *E. coli*, cysts & troph.	Has had lacrimation and photophobia for 4 months. Has had abdominal pains and attacks of diarrhea for past 8 months. Has 5 bowel movements daily, with tenesmus and cramps every time he eats anything. Has lost 20 lbs. in weight.	*Before Rx:* Entire rectum covered with ulcerations, as large as 1 inch in length. *8th day of Rx:* Many ulcers present but appear to be healing. Mucosa bleeds easily. *12th day of Rx:* No ulcers seen. Few slightly erythematous areas present. Direct smears negative for amebae.	84	No amebae found after 4th day of Rx. Tenesmus subsided by 5th day of Rx. Pt. stated he felt steady improvement. No symptoms at all after 10th day of Rx. No toxic symptoms.	Not obtained				
6	44	Amebic dysentery, acute Anemia, secondary, severe *E. histolytica*, troph.	Has had periodic attacks of diarrhea, and abdominal cramps for past 3 years. Recently has become much worse, and is losing weight rapidly.	Many typical amebic ulcerations throughout lower bowel.	30	Diarrhea had subsided by 6th day. No amebae found after 6th day. Pt. stated he felt much better on second day of Rx, although diarrhea still present. Proctoscopic on 14th day showed no lesions. No toxic symptoms.	7 months	Negative for amebae	Normal mucosa	76	Has felt perfectly well. No further diarrhea or abdominal cramps. Has gained weight.

7	19	Amebic dysentery, chronic Malaria, clinical Anemia, secondary, severe *E. histolytica*, cysts & troph. *E. coli*, cysts *D. fragilis*, troph. *N. americanus* *S. stercoralis*	Has had fever, malaise, headache, for past 3 days. For past 2 years has had pale and yellow skin. Denies abdominal pains and diarrhea. Spleen enlarged.	No ulcerations. Mucosa pale.	89	Fever responded to atabrine. No amebae found after 3rd day of emetine Rx. Definite improvement of anemia while in hospital. No toxic symptoms noted.	7 months	Negative for amebae	None	80	No symptoms since discharge. Has been in good health. Marked improvement in anemia.
8	27	Amebic dysentery, chronic Yaws Cellulitis, suppurative, of abdominal wall Anemia, secondary *E. histolytica*, cysts & troph. *E. coli* cysts *N. americanus* *S. stercoralis* *G. lamblia*	Has had fever, chills, and joint pains for 5 days. No nausea, vomiting, or diarrhea. Has been constipated.	Normal mucosa	78	No amebae found after 3rd day of Rx. Fever subsided with cellulitis. No toxic symptoms.	6 months	Negative for amebae	None	85	No symptoms since discharge. Has one stool daily. Has gained 5 lbs. in weight and feels stronger. Blood picture improved.
9	31	Amebic dysentery, chronic Anemia, secondary *E. histolytica*, cysts & troph. *E. coli*, cysts & troph.	Has lost 16 lbs. in last 6 months. Feels run-down and chronically tired. No abdominal pains, but has periods of diarrhea.	Normal mucosa	69	No amebae found after 5th day of Rx. No toxic symptoms.	7 months	Positive for *E. histolytica* trophozoites following saline purge.	Normal mucosa	75	Has had no symptoms. Feels well, and has gained 12 lbs. in weight.

Complete interval histories and physical examinations were done, as well as laboratory studies. Proctoscopic examinations were done on adults, but not on children. Stool specimens were examined microscopically, using direct smear methods, by the author. Three smears, in saline suspension, from normally passed stools were each examined completely. If these were negative, a saline purge was administered, and three smears from each of several specimens were carefully examined. Cyst forms encountered were stained with iodine for identification.

If cysts or trophozoites of *E. histolytica* were found, irrespective of the time elapsed since original treatment, and irrespective of the presence or absence of symptoms, the case was considered a failure of oral emetine to cure.

The five children were rechecked in from 4 to 8 months following the original treatment. (Table 3). None were found to harbor *E. histolytica* cysts or trophozoites, but other intestinal parasites were present. Not one case had had any symptoms of diarrhea or abdominal pains in the interim. There was marked clinical improvement in all cases, manifested by increased activity and appetite, gain in weight, and improved general appearance. The blood picture showed marked improvement of the secondary anemia. The child (Case No. 3), who had had a hemoglobin of less than 10 percent at the time of treatment, showed a hemoglobin of 58 percent and a total count of 3,500,000, when rechecked 4 months later.

Nineteen of the twenty-five adults were obtained for recheck studies in from two to nine months following treatment with oral emetine. (Table 4). There was only one failure in this series. Case No. 9 was found to harbor *E. histolytica* trophozoites on examination of a saline purged stool. This was seven months following the original treatment. The patient denied any and all symptoms in the interim, had gained 12 pounds in weight, and felt so well he could not be convinced that he required further treatment.

All adults reported that they had felt entirely well since their treatment with oral emetine, and denied any symptoms of abdominal cramps or diarrhea. It was particularly noted that none complained of having had joint pains, and general feelings of tiredness, as is often noted when emetine is administered subcutaneously. All cases manifested normal findings on proctoscopic examinations, and the electrocardiograms manifested no changes. There was varying, but definite, improvement in the blood picture in all cases that had previously shown a secondary anemia.

There were no evidences of delayed toxic effects in either adults or children.

DISCUSSION

The present series of cases is small, but some conclusions can be drawn. Oral emetine, in the form used in this study, is a drug which is easy to administer, does not produce toxic symptoms in the dosage as reported herein, and provides effective results.

That the drug reaches the amebae in the ulcerated areas of the intestine can be demonstrated by following with the proctoscope the progress of a patient with

rectal ulcerations who is receiving the drug. A rapid decrease in the size of the ulcers, with healing, is evident. The presence of secondary infection of the amebic ulcerations will, however, prevent complete healing, although the amebae will disappear from mucosal scrapings, and the stools. The two cases in this series, whose rectal lesions failed to heal completely with oral emetine treatment, responded rapidly to sulfaguanidine and sulfadiazine, indicating a superimposed secondary infection of the amebic lesions.

There was no demonstrable evidence, in these cases, of absorption of sufficient amounts of emetine into the general system, from the large intestine to produce toxic symptoms. There were no cases of vomiting in the entire series, particular care being taken not to administer chipped or broken tablets, which would allow premature release of their contents into the stomach and upper intestinal tract.

The low or absent toxic effect of oral emetine in the dosage as used in these cases, is aptly demonstrated by the absence of toxic symptoms in the five children treated with oral emetine. The subcutaneous administration of one grain of emetine hydrochloride daily for twelve days, as was given orally, to these five children would have been dangerous, if not lethal. The adult dosage, although comparatively not as large as given to children, was twice the maximum recommended for subcutaneous administration, and failed to produce toxic effects.

It is thus possible, with the drug as used in this study, to administer orally, and without producing toxic effects, at least double the amount of emetine hydrochloride as could be done safely by subcutaneous administration.

The ability to administer a larger amount of emetine hydrochloride provides a method of maintaining a higher concentration of the drug in the intestinal tract, than was formerly possible by the subcutaneous route.

The results of this study indicate that the dosage used closely approaches the amebicidal concentration necessary to eradicate the parasite from the intestinal tract.

It is regretted that facilities were not available to study the concentration of free emetine hydrochloride obtained in the patients' stools by the dosage used in this series. The devising of a suitable method for determining the concentration obtained in the stools would facilitate the maintenance of adequate concentration of emetine in the intestinal tract to eradicate the amebae. The concentration of 1 to 1,000,000 is amebicidal *in vitro*, and the maintenance of this concentration should not be difficult with the drug as used in this series.

No difficulty was found in administering some other drugs to patients receiving emetine orally. Atabrine, hexylresorcinol crystoids, magnesium sulfate solution, ferric ammonium citrate solution, sulfaquanidine, sulfadiazine, and penicillin have all been given to patients in this series, without interference or toxicity.

There were no cases of extra-intestinal amebiasis encountered in this series. None of the cases restudied manifested any symptoms suggestive of liver infestation. X-rays of the liver and diaphragm were taken in some of the adults, but failed to show any demonstrable evidences of liver infestation, and was abandoned. It should be emphasized here that the drug, as used in this series, is probably not suitable for the treatment of extra-intestinal amebiasis.

It is possible that emetine hydrochloride enteric-sealed tablets may be an effective therapeutic agent against *Trichiuris trichiuris*. Two children in this series, receiving emetine orally, and heavily parasitized with this worm, passed large numbers of adult worms in their early morning stools. Controlled studies in a series of cases infested with this worm, and treated with oral emetine, would be of great value.

SUMMARY

Twenty-five adults and five children with intestinal amebiasis, including acute and chronic forms, were treated with emetine hydrochloride enteric-sealed tablets (Lilly), orally. Adults were given two grains daily for twelve days, and the children one grain daily for twelve days. No nausea or vomiting, nor other toxic symptoms were manifested. Nineteen of the adults, and all of the five children, were re-studied, as hosp tal patients, in from two to nine months following original treatment. Clinical cure was obtained in all cases, but parasitological cure failed in one adult, who was found to harbor *E. histolytica* trophozoites, seven months after receiving the drug.

The results obtained in this study indicate that emetine hydrochloride, in enteric-sealed tablets, administered orally, provides a concentration of emetine in the intestinal tract which closely approaches the amebicidal concentration necessary to eradicate the parasite, without producing toxic side effects.

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