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ORAL EMETINE IN THE TREATMENT OF INTESTINAL AMEBIASIS

A Preliminary Report

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Emetine, one of the several alkaloids contained in the root of *Cephaelis ipecacuanha*, was first used in the treatment of dysentery by Helvetius in 1685 in the form of the powdered dried root. Over a hundred years later Pelletier (1) succeeded in separating emetine from the other alkaloids and as such it was successfully employed as a therapeutic agent by Bardsley in 1829 (2). In 1891 Walsh (3) treated cases of dysentery with the mercuric iodide salt of the drug and claimed good results. At first, emetine was used in all types of dysentery and as a consequence there were many failures. When amebic dysentery was established as an entity, the effectiveness of the alkaloid as a therapeutic agent for amebic dysentery was firmly established.

Vedder (4) in 1911, published a report covering preliminary experiments undertaken to test the efficacy of the alkaloid, and stated that in dilutions of 1 to 100,000 it was lethal to the amebae *in vitro*. Further studies carried out by Vedder in 1912 (5) and also in 1914 (6) have given similar results. Most noteworthy of the investigations in this particular field have been those of Dobell and Laidlaw (7), Dobell, Laidlaw and Bishop (8), St. John (9), and Bonnin and Aretas (10). These authors, in agreement with Vedder, have shown by a variety of experimental methods that emetine or its salts have a direct amebacidal action which is effective in very high dilutions (1 to 1,000,000 to 1 to 5,000,000).

Due to its powerful emetic action the oral administration of emetine has been unsatisfactory. Rogers (11) advocated the subcutaneous administration of the hydrochloride salt to avoid the nausea and vomiting caused by preparations of emetine taken orally. There was an immediate widespread acceptance of this method of therapy and in general, the results have justified the continued use of the drug. Unfortunately, treatment with emetine parenterally is not without its dangers. Clinical experience, autopsy findings, and animal experimentation have shown emetine to be a toxic drug when administered by hypodermic injection, (12), (13), (14).

Because of the toxicity of subcutaneous emetine, its therapeutic dosage has been limited. Craig (15) states that the amount which can be safely given is, in the majority of cases, insufficient to permanently eradicate the parasite. Therefore, it is used as an adjuvant with other drugs such as chiniofon, carbarsone,

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TABLE I

1 grain daily for 12 days—total 12 grains

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
1	33	Amebic dysentery.* Other intestinal parasites: *N. americanus*, *T. trichiuris*.	Diarrhea, mod. severe for one month, sensation of weakness, abdominal cramps and tenesmus. Heavy feeling in back.	Small ulcerations lower ⅓ of rectum	75	*E. hist.* trophozoites. Other parasites	Not done	Neg.	Before treatment. Normal limits. 3, 6, 11th days of treatment. Normal limits.	Symptoms subsided in 3 days. No amoebae after 3rd day. Rectal ulcers healed on 11th day Rx.	No toxic symptoms. Gained 4 lbs. in weight.	7 mo.	Neg.	Neg.	Neg.	84	Neg.	No symptoms since original Rx.
2	52	Amebic dysentery. Carrier of *E. typhosa*. Other intestinal parasites: *E. coli*, *C. mesnili*, *N. americanus*,	Periodic attacks of diarrhea and abdominal pain for past year. 2 weeks prior to admission began to have	Normal findings	75	*E. hist.* trophozoites. Other parasites.	Not done	Several positive for *E. typhosa*.	Before Rx: Normal limits. 3, 6, 10th days of Rx: Normal limits.	Symptoms subsided in 3 days. No amebae after 4th day.	None	9 days	Cysts & trophozoites of *E. hist.*					Given another course of 12 grs. in 12 days. No amebae found after 2 days of Rx. Rechecked in 3 mos. and again in 5 mos. No symptoms in interim.

		T. trichiuris, S. stercoralis	8–10 stools per day with abdominal cramps.															Direct smears, cultures, proctoscopic, negative for *E. hist.* Positive for cysts of *E. coli.* Hb. 96%.
3	31	Amebic dysentery. Other intestinal parasites: *E. coli, E. nana, I. williamsi, S. Stercoralis, N. americanus, T. trichiuris.*	8 days prior to admission developed cramping pains in lower abdomen and slight diarrhea of 2x daily. History of amebiasis 1 year previous.	Normal findings	80	*E. hist.* trophozoites. Other parasites.	Not done	Neg.	1, 5, 9th days of Rx: Normal limits. 10th day T_F slightly lower than previous, Ess. normal limits.	No amebae after 2 days.	None	5 mo.	Neg.	Neg.	Neg.	78	Neg.	No symptoms.

TABLE 1—*Continued*

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
4	35	Amebic dysentery. Other intestinal parasites: *E. nana, E. coli, D. fragilis.*	History of abdominal pains described as "gas pains" for past 5 years associated with tired feelings. For past 2 days has had severe cramps with 5–6 stools per day.	Small ulcerations throughout rectum.	70	*E. hist.* trophozoites. Other parasites.	Not done	Neg.	Before Rx: Normal limits. 5, 9, 12th days of Rx: Normal limits.	No amebae after 2 days.	Vomited once. No nausea or abdominal cramps.	5 mo.	Neg.	Neg.	Neg.	78	Neg.	No symptoms.
5	25	Amebic dysentery.	Bloody diarrhea and abdominal cramps for 9 mos. 2 to 12 stools	Rectal ulcerations severe, most numerous on Inf. valve.	75	*E. hist.* trophozoites.	Not done	Neg.	1, 5, 12th days Rx: Normal limits.	No amebae after 4 days. No symptoms after 3rd day.	Vomited twice. No abdominal cramps or other symptoms.	1 mo. 2 mo. 3 mo.	Neg. Neg. Neg.		Neg. Neg.			Rechecked as outpatient only. No proctoscopic examination. No symptoms.

		per day. Cramps relieved by "passing gas." Diarrhea worse after liquor.															
6	23	Carrier of *E. hist.* Other intestinal parasites: *N. americanus*, *S. stercoralis*, *T. trichiuris*, *A. lumbricoides*.	No symptoms. Denied any history of previous abdominal pains or diarrhea.	Normal findings	75	*E. hist.* cysts.	Positive for *E. hist.*	Neg.	Before and after Rx: Normal limits.	No amebae after 3rd day.	None	4 mo.	Neg.	Neg.	Neg.	84	Neg.	No symptoms.

TABLE 1—*Continued*

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
7	56	Amebic dysentery.	Onset 2 weeks prior to admission of 6–10 stools per day with blood noted on one occasion, but denies abdominal cramps. Had dysentery in 1910 with similar symptoms. Was treated by "injections."	Rectal ulcerations severe, with almost entire rectum involved. Direct smear showed enormous number of *E. hist.* trophozoites.	75	*E. hist.* trophozoites.	Pos.	Neg.	Before Rx: Normal limits. 3, 6, 10th days of Rx: Normal limits.	No amebae seen by direct smear after 4 days. Culture for amebae negative following 6th day. Symptoms relieved on 3rd day.	None	3. mo.	Neg.	Neg.	Neg.	84	Neg.	No symptoms.

* 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.

etc. It is still the drug of choice in the management of extra-intestinal amebiasis.

Since emetine has a powerful amebacidal action it is surprising that more attention has not been given to the possibilities of developing this drug in a form for oral use. A few attempts have been made to cover the drug with salol, or a keratin coating, in order to resist the action of the digestive juices and permit release of the drug lower in the bowel, or combining the salt with other drugs in an attempt to lessen the emetic properties. The currently available forms such as emetine bismuth iodide, emetine antimony iodide, etc., still cause salivation, nausea, and vomiting, and on the whole have not been successful.

In July, 1943, a small quantity of emetine hydrochloride in "enteric-sealed" tablets[1] was obtained. The tablets were designed to release their contents from 3 to 4 hours after ingestion and thus allow the drug to be freed in the lower bowel and avoid the irritating effects on the stomach.

PROCEDURE AND MATERIAL

This study is a report of the investigation of the first 20 patients in which the "enteric-sealed" oral preparation of emetine hydrochloride had been used for the treatment of intestinal amebiasis. Included in this group of patients are Latin Americans, British West Indians, and North Americans, of both sexes, and of age groups from 2 to 56 years. Each patient was proven to harbor *Endameba histolytica* before treatment was instituted, and all were under the complete care, as hospital patients, of the senior author (B. S.) during the course of treatment. The following routine was established:

(1) Daily stool examinations by one of us (C. J. or B. S.) for amebae. Smears following saline purges and culture methods were not used for these, but were used in the re-examination studies. Practically all cases, however, harbored other intestinal parasites, and were given purges and anthelminthies following the emetine treatment. The opportunity of using these stool specimens in searching for amebae, was not neglected.

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

(3) Daily urinalysis.

(4) Daily blood pressure reading.

(5) Complete blood count every third day.

(6) Electrocardiogram every third day, except on infants.

(7) Proctoscopic examination before and after treatment.

(8) Accurate count of number of stools passed per day.

(9) All individuals were examined on daily rounds for any signs of toxicity and closely questioned for any symptoms of vomiting, diarrhea, abdominal pains, malaise, or neuritides.

At the time this investigation began, no specific data were at hand relative to the amount of emetine absorption which might occur from the intestine. The therapeutic and the toxic dosage of the oral preparation were unknown.

[1] Emetine hydrochloride "Enseals" (Enteric-Sealed Tablets, Lilly). Each tablet containing ½ grain of the alkaloid.

TABLE 2

2 grains daily for 8 days—total 18 grains

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
8	25	Amebic dysentery, chronic. Other intestinal parasites: *E. coli*.	Periodic attacks of diarrhea and colicky abdominal pains for 1 year. Has lost 10 lbs. in weight in past 6 months.	Normal findings.	75	*E. hist.* cysts. *E. coli* cysts.	Not done.	Neg.	Before and after Rx: Normal limits.	Negative for amebae in 3 days.	Vomited 3 times with slight temporary increase in no. of stools. No abdominal cramps. One pill passed in stool.	1 mo. 2 mo.	Neg. Neg.		Neg. Neg.			Rechecked as outpatient only. No attacks of diarrhea or cramps since treatment.
9	25	Amebic dysentery.	Periodic attacks of diarrhea for past 3 years. Sometimes constipated, has steadily lost weight.	Large ulcerations of rectum. Direct smear positive. 1 day after Rx: no evidence of ulcers.	80	*E. hist.* trophozoites.	Not done.	Neg.	1, 5th day of Rx: Sinus arrythmia, otherwise normal. 2 days after Rx: Sinus arrythmia, other	No amebae after 4 days. No further symptoms after 3rd day.	Vomited once. Lost 3½ lbs. during Rx.	Not obtained						

			Relieved by paregoric, but not stopped. Usually has 5 stools per day. The last attack has lasted for 15 days.						wise normal.				?				
10	13	Amebic dysentery. Secondary anemia, severe. Sicklemia, mild. Other intestinal parasites: *N. americanus*, *A. lumbricoides*, *T. trichiuris*, *S. stercoralis*, *E. coli*, *G. lamblia*.	Has had a bloody diarrhea for past 6 months. Father states child has shown a progressive listlessness and apathy and seems to be losing weight.	Entire rectum and sigmoid covered with enormous masses of *T. trichiuris* worms. No amebic ulcerations noted.	40	*E. hist.* trophozoites. Other parasites.	Not done.	Neg.	1, 5th day of Rx: Sinus tachycardia other wise normal. 2 days after Rx: Sinus tachycardia otherwise normal.	No amebae after 4 days. Diarrhea stopped after 5th day.	None. Severe trichiuris infestation. Sed. rate 74.	3 mo.	Neg.	Neg.	Neg.	72	Trichiuris worms seen in rectum.	Marked improvement in blood picture and general health. No symptoms since treatment.

TABLE 2—*Continued*

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
11	19	Amebic dysentery, chronic. Anemia, secondary.	No symptoms other than gradual weight loss for past 3 years.	Normal	70	*E. hist.* trophozoites.	Not done.	Neg.	1, 5th day. Normal limits. 2 days after Rx: Normal limits.	No amebae after 4 days.	None	1 mo.	Neg.		Neg.			Rechecked as outpatient only.
12	41	Amebic dysentery. Other intestinal parasites: *N. americanus*, *S. stercoralis*, *T. trichiuris*.	Abrupt onset one month ago of 7–10 loose liquid stools per day, associated with marked tenesmus.	Rectal ulceration severe. Direct smear positive.	80	*E. hist.* trophozoites. Other parasites.	Not done.	Neg.	First Rx: Normal limits. (3, 6th day) Second Rx: 1, 4th day; Normal limits.	Symptoms subsided in 3 days. No amebae after 3 days.	None Cysts of *E. hist.* found 6 days after 1st Rx. Retreated.	6 days	*E. hist.* cysts.		*E. hist.*		2 days after 1st Rx: Ulcerations gone but several reddish areas present. Direct smears negative. 4 days later normal appearing mucosa.	Given retreatment of 2 grains daily for 6 days. No *E. hist.* after 4 days. Rechecked again in 1 month, and found positive for *E. hist.*, but denied any symptoms. Proctoscopic negative. Hb. 84%. Given re-treatment of 2 grains daily for 8 days.

13	14	Amebic dysentery. Other intestinal parasite: *E. coli*. Anemia, secondary.	Onset 2 mos. ago of diarrhea and abdominal cramps. Seen twice before and diagnosed as Gastro-enteritis.	Mucosa pale. No lesions.	70	*E. hist.* trophozoites. Other parasites.	Positive for *E. hist.*	Neg.	Before Rx: Normal limits. 2, 5th day; Normal limits.	No amebae after 3 days.	None	1 mo.	Ne)	Neg.	*E. hist.*	78	Normal	No symptoms since original Rx. Gained 5 lbs. in weight—felt well. Given retreatment of 2 grains daily for 6 days. No toxic symptoms. No amebae after 4 days.

TABLE 3

Larger doses

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HGB % GM	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	ameba culture	HB % sahli	Proctoscopic	
14	45	Amebic dysentery. Secondary anemia, severe. Pansinusitis, acute. Other intestinal parasites: *N. americanus, S. Stercoralis.*	Acute diarrhea and abdominal pains for past 8 days. Has 6-8 liquid stools daily. No vomiting.	Several discrete ulcerations sprinkled throughout rectum and sigmoid. Mucosa pale.	40	*E. hist:* trophozoites. Other parasites.	Not done	Neg.	Before Rx: Normal limits. 3, 6th day. Normal	No amebae after 10 days.	*Treatment:* 1 gr. daily for 7 days, then 2 gr. daily for 4 days: 15 grains in 11 days. Diarrhea persisted. Large amount of inflammatory exudate in stool, culture negative. Given sulfaquanidine, with relief of diarrhea.	6 mo.	Neg.	Neg.	Neg.	82	Normal	No symptoms since original Rx. Marked improvement of anemia.
15	20	Carrier of *E. hist.* Other intestinal para	No symptoms. Parasites found on routine	Neg.	80	*E. hist.* cysts. Other parasites.	Not done	Neg.	2, 7th day of Rx: Normal limits.	No amebae after 3 days.	*Treatment:* 1 gr. daily for 9 days, then 2 gr. daily for	4 mo.	Neg.	Neg.	Neg.	90	Normal	No symptoms since treatment.

		sites: *N. americanus, S. stercoralis C. mesnili, E. coli.*	stool examination.								3 days: 15 grains in 12 days. None							
16	30	Amebic dysentery. Other intestinal parasites: *A. lumbricoides.* Secondary anemia, severe. Pregnancy.	Onset 17 days previous of 4-8 stools per day, associated abdominal pain. Had similar episode "long time ago" for 3 or 4 days.	Scattered discrete pinhead ulcerations throughout rectum, below sup. valve.	42	*E. hist.* trophozoites. Other parasites.	Positive for *E. hist.*	Neg.	1, 5, 9, 12, 15, 19th days of Rx: Normal limits.	*E. hist.* trophozoitee present in stools throughout course of Rx.	*Treatment:* 1 gr. daily for 15 then 2 gr. daily for 4 days: 23 grains in 19 days. Vomited once. Proctoscopic normal at 17th day of Rx. Symptoms subsided in 4 days.	3 mo.	Pos. *E. hist.*			54	Rectal ulcers present.	Has felt well since original Rx. Is 5 months pregnant. Given retreatment of 2 grains daily for 8 days. No toxic symptoms. No *E. hist.* by smear or culture after 5 days.

TABLE 4

Infants and children

CASE NO.	AGE	DIAGNOSIS	SYMPTOMS	PROCTOSCOPIC	HB % SAHLI	STOOL EXAMINATION			E.C.G.	IMMEDIATE RESULT	TOXIC SYMPTOMS AND COMMENT	RE-EXAMINATION						COMMENT
						Direct smear	Ameba culture	Bacteria culture				Time since Rx	Direct smear	Saline purge	Ameba culture	HB % sahli	Proctoscopic	
17	9½	Amebic dysentery. Other intestinal parasite: *T. trichiuris.*	Onset 2 weeks ago of 4-10 day but with no abdominal cramps. Never noticed blood in stools.	Normal	80	*E. hist.* trophozoites. Other parasites.	Positive for *E. hist.*	Neg.	Before Rx: Sinus arrythmia. 1, 5th day of Rx: No change	No amebae after 3 days	*Treatment:* ½ grain twice daily for 6 days: (4 grains total). Vomited once.		Not obtained					
18	11	Carrier of *E. hist.* Other intestinal parasites: *N. americanus, E. coli, E. nana, G. lamblia, T. trichiuris, S. stercoralis, A. lumbricoides, T. hominis.* Secondary anemia.	Absolutely denies any symptoms!	Negative	65	*E. hist.* cysts only. Other parasites.	Not done	Neg.	Before Rx: Sinus arrythmia. Normal limits. 7, 10th days of Rx: No change.	No. *E. hist.* after 4 days. Remained positive for *E. coli* cysts.	*Treatment:* ½ grain twice daily for 12 days (total 8 grains). None.	3 mo.	Neg.	Neg.	Neg.	78	Normal	No symptoms

19	$1\frac{2}{12}$	Amebic dysentery. Other intestinal parasite: *G. lamblia*	Bloody diarrhea of 5 week duration associated with occasional rectal prolapse. Poor appetite, irritable and has lost weight.	Not done	70	*E. hist.* trophozoites. Other parasites.	Positive for *E. hist.*	Neg.	Not done	No amebae after 4 days.	*Treatment:* ½ grain daily for 9 days (total 3 grains). Given sulfaquanidine at same time for six days. No toxic symptoms. Bloody diarrhea ceased after 3 days. No further prolapse.	3 mo.	Pos. *E. hist.*		*E. hist.*	54	Not done	Appetite for past month poor. "Occasional" diarrhea. Given retreatment of ¾ grain daily for 15 days (total 10 grains). Recheck in 5 mos. showed *E. coli, C. mesnili, G. lamblia,* but no *E. histolytica.*
20	$1\frac{6}{11}$	Amebic dysentery, chronic. Other intestinal parasites: *E. coli, E. intestinalis, C. mesnili, G. lamblia, T. hominis.* Secondary anemia.	Onset one week ago of diarrhea, associated with mild fever. Has had 3 similar episodes in the past year. Appetite remains good.	Not done	60	*E. hist.* trophozoites. Other parasites.	Not done	Neg.	Not done	No amebae after 4 days.	*Treatment:* ½ grain daily for 9 days, (total 3 grs.) None.	2 mo.	Neg.	Neg.	Neg.	72	Not done	No symptoms

Analysis of results following 1 grain daily for 12 days

Inasmuch as one grain a day for 12 days had been used at Gorgas Hospital as the maximal dose in the parenteral method of administration, a similar amount was given by mouth in the first 7 cases. (See table 1). The patients received 1 tablet of ⅓ grain of emetine hydrochloride, orally, three times a day for 12 days.

No serious toxic effects were noted in these patients. The pulse rates, blood pressures, urinalyses, blood counts, electrocardiograms, all remained within normal limits. The blood picture in cases with anemia usually improved. One patient vomited once, and another vomited twice. The vomiting was abrupt and sudden, not accompanied by nausea or abdominal cramps. The drug was continued without any increase in this symptom. These isolated vomiting spells were unexplained until it was noted that one of the tablets in a bottle had lost part of its covering. No further vomiting occurred after discarding broken tablets.

A mild, non-bloody diarrhea of 3 to 5 stools per day occurred in a few cases, but no tenesmus or abdominal cramps were noted. One patient's (2) stools became entirely negative for amebae after 2 days of treatment but showed trophozoites and cysts nine days after the completion of treatment, and before being discharged from the hospital. This was the only immediate failure on this dosage. He was successfully given another course of one grain per day for 12 days, at an interval of 13 days from the original treatment. The stools became negative for amebae in 2 days. Re-examination in one month, and six months, showed no *Endameba histolytica*.

Analysis of results following 2 grains daily for 6 days

Encouraged by these results the drug dosage was doubled and the number of days halved. This dosage was used in 6 cases (see table 2). The patients thus received 2 tablets of ⅓ grain each, three times a day, for 6 days. No serious toxic reactions were noted in this series. Vomiting occurred in two cases (8), (9). Neither complained of abdominal cramps or nausea. There was one immediate failure in this series (12). *Endameba histolytica* cysts were found 6 days after completion of treatment, and he was immediately given a second course of the drug, which was successful, and no toxic symptoms were manifested. There was one delayed failure (13) in which *E. histolytica* was found by culture one month after treatment. There had been no symptoms in the interim and the patient had gained 5 pounds. When another similar course of emetine was given the parasites disappeared in 4 days.

Analysis of results following larger doses

Three cases were given varying dosages. (See table 3.) Case 16 was the only case in the entire series of twenty whose stools remained persistently positive for *E. histolytica* trophozoites. This patient was given 1 grain per day for 15 days, then 2 grains daily for 4 days, or a total of 23 grains, in 19 days, after which healing of the rectal lesions occurred, and there was complete relief of symptoms. She requested discharge for personal reasons but returned 3 months later. At this time amebic rectal ulcerations were again found and she was given treatment

of 2 grains daily for 8 days. The stools became negative by smear and culture in 5 days, and the rectal ulcerations disappeared.

Analysis of results in infants and children

There were 4 infants and children in this series (see table 4). These were given much smaller doses than adults. There was one delayed failure in this group. This child (19), with severe amebic dysentery, was given 1 tablet ($\frac{1}{3}$ grain) daily for 9 days, a total of 3 grains. Complete relief of symptoms was obtained, but a re-examination in 3 months demonstrated *E. histolytica* trophozoites. He was then given 2 tablets a day ($\frac{2}{3}$ grain), for 15 days, a total of 10 grains, without manifesting toxic symptoms.

Results of re-examinations of patients

We were able to re-examine 18 of the 20 cases in from one to seven months following the original treatment. Three of these were examined as outpatients, and only stool examinations were done, using direct smear and culture methods. The remaining 15 cases were re-admitted as hospital patients and subjected to complete studies. Three direct smears from each of several normally passed stools were first studied. If these were negative, a saline purged stool was obtained, and three smears from each of several specimens of this stool were carefully examined microscopically. Daily cultures, at least one of which was from the saline purged stool, were taken on St. Johns medium as described in Craig (15). All patients except the infants, had a proctoscopic examination. Any case in which either cysts or trophozoites of *Endameba histolytica* were found, was considered a failure, disregarding the presence or absence of symptoms, or the time since the original treatment.

It is interesting to note that although 5 of these 20 patients were not cured from a parasitological standpoint, 4 of them became symptom-free, and remained so, since the original treatment. One case (19) had a history of "occasional diarrhea, poor appetite" for one month prior to admission for re-examination, which was done 3 months following the original treatment.

DISCUSSION

The present series of cases is small but some preliminary conclusions can be drawn from the results obtained. Oral emetine therapy (with "enteric-sealed" tablets) for intestinal amebiasis deserves further study. Reed (16) states that "emetine is a powerful, dangerous, and valuable remedy whose complete action is not known." The results obtained in our preliminary study indicate that when used as described in this series, it is not dangerous. When given parenterally, or in a form which permits rapid absorption from the stomach or upper intestinal tract, it may be a toxic substance. In our patients, when the drug was given in such a form that it theoretically reached the distal portion of the small intestine or the colon before being liberated, no serious toxic reactions were noted.

The presence of the alkaloid in the upper intestinal tract is usually attended by nausea and vomiting. A few of the patients in this series experienced vomiting. This symptom occurred only once or twice during the course of treatment. It

was probably caused by the use of chipped tablets, which allowed the emetine to be released in the stomach or upper intestinal tract. The mild diarrhea which appeared in some cases during the treatment was not considered as an indication for withdrawing the drug.

SUMMARY

In a preliminary study of 20 cases of intestinal amebiasis due to *Endameba histolytica*, including both acute and chronic forms, treated with emetine hydrochloride enteric-sealed tablets orally, encouraging results were obtained in 15 patients in a short period of time. These patients have been observed over periods of time ranging from one to seven months. None of the usual serious toxic reactions associated with the parenteral administration of emetine were noted. Results were judged on the basis of clinical improvement, healing of the bowel as observed by proctoscopic examination, and the disappearance of the amebae in microscopic studies and cultures of the stools. No recommendations as to the optimum dosage for the treatment of intestinal amebiasis with the oral emetine preparation used in this study can be given at this time. Further evaluation of this preparation is now in progress.

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