

## AMIBIARSON IN THE TREATMENT OF CHRONIC INTESTINAL AMOEBIASIS

By R. N. CHOPRA, C.I.E., M.A., M.D. (Cantab.)  
LIEUTENANT-COLONEL, I.M.S.

B. SEN, B.Sc., M.B.  
and

G. SEN, M.B., D.T.M.

(From the Department of Pharmacology, School of Tropical Medicine, Calcutta)

CHRONIC amoebiasis is one of those diseases which are difficult to treat and which is frequently encountered by medical practitioners in the tropics. A long-standing infection with *E. histolytica* is the cause of much sickness and incapacity in India, specially among the European community. The presence of this organism in the system, however scanty, devitalizes the patient considerably and renders him susceptible to other infections; it is responsible for producing a variety of neurasthenic conditions met with in tropical climates.

Emetine is undoubtedly a very effective drug in acute amoebic dysentery, but when the disease passes into the chronic stage it is practically useless. The reason is not far to seek. Emetine is a toxic drug and its prolonged administration in sufficient amounts to reach the parasites deeply seated in the tissues is attended with grave risks. The presence of associated bacillary dysentery, especially of the Flexner type, also interferes with the action of this alkaloid by bringing about a marked acid reaction of the contents of the gut. A number of oxyquinoline derivatives, e.g., yatren, chinoform, vioform, etc., were supposed to possess

high amoebicidal properties, but recent investigations show they do not cure this condition. Rivanol, bismuth subnitrate, etc., have been tried with no better results. Acton and Chopra (1933) treated a large number of cases of chronic amoebiasis with the bismuthous iodide compound of the total alkaloids of *Holarrhena antidysenterica*, in doses of ten grains twice a day by the mouth for ten to twenty consecutive days, and they succeeded in curing 73 per cent in a series of 78 cases. To ensure a supply of the properly matured and properly dried bark for the manufacture of the alkaloids is, however, difficult and the number of failures with alkaloids obtained from the bark of indifferent quality is very large.

During recent years some organic compounds of arsenic have been introduced for the treatment of chronic intestinal amoebiasis. Of these stovarsol and treparsol were the most popular for some time, but further experience has shown that their curative action is not very powerful. A compound named carbarsone (4-carbamino phenyl-arsenic acid) was recently introduced by Messrs. Lilly and Co. of Indianapolis (U. S. A.) and has proved very efficacious. It belongs to the original series of organic arsenicals prepared and tested by Ehrlich and Berthem but which on account of its comparatively feeble trypanocidal properties was put on one side. Reed and his co-workers (1932) tried it in a small series of cases and found it very effective and non-toxic. Carbarsone is a white and crystalline solid without odour or taste and is stable in air, containing 28 to 85 per cent of arsenic in an anhydrous condition. Experimentally it is less toxic than stovarsol and possesses more powerful amoebicidal properties, its therapeutic index being about eight times as favourable as stovarsol. The drug is sold in 'pulvules' of 0.25 gramme each. The senior author tried carbarsone in two series of patients in the Carmichael Hospital for Tropical Diseases with very gratifying results (Chopra, Sen and Sen, 1933, and Chopra and Sen, 1934). The patients were mostly sufferers from chronic intestinal amoebiasis and the majority of them had had repeated attacks of dysentery. The drug was administered in doses of 0.25 gramme twice daily for 10 to 15 consecutive days. Out of 31 patients in the first series 23 (74.2 per cent) were cured, in 4 cases (12.9 per cent) the drug failed and in the remaining 4 (12.9 per cent) the result was indeterminate. In the second series the percentage of cure was a little higher; out of 22 cases, 17 were cured (77.3 per cent), 2 failed (9.1 per cent) and in the remaining 3 the result was indeterminate (13.63 per cent).

Encouraged by the satisfactory results obtained, the Bengal Chemical and Pharmaceutical Works, Limited, of Calcutta, have prepared a compound named Amibiarsol, the

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### Summary

A case of hydronephrosis is described due to an abnormally low attachment of the renal fascia to the ureter. This had resulted in constriction and kinking of the ureter with a complete 'block'. The kidney showed a hydronephrotic type of atrophy. Histological studies showed that the direct and primary effect of this pelvic distension on the kidney was a dilatation of the collecting tubules and ducts of Bellini, while the renal atrophy was more related to the vascular distribution.

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chemical composition of which is said to be very similar to that of carbarsone. The effectiveness of this drug against chronic intestinal amoebiasis was carefully tested on a series of cases in the Carmichael Hospital for Tropical Diseases. Most of these patients had *E. histolytica* in the stools in cystic form and suffered from general rather than intestinal symptoms. A few of them were admitted into the hospital for diseases other than amoebiasis, but examination of their stools showed a fair number of vegetative or cystic forms of *E. histolytica*. Amibiarsone was administered by mouth in exactly the same way as carbarsone, 0.25 gramme being given twice daily in gelatine capsules for 10 to 15 consecutive days. The patients were kept on ordinary diet and the bowels were kept open with daily administration of a saline purgative every morning while the drug was being administered. If

there was any evidence of a concomitant bacterial infection a course of autovaccine was also administered. The criterion of cure applied in this series of cases was six or more negative examinations of the stools on different days after cessation of all treatment. It has already been pointed out that this criterion for cure does not indicate that a real cure has been effected, but from experience extending over many years in this country we have found that six negative examinations indicate in the majority of cases a favourable prognosis, if not a definite cure. The difficulty of keeping the patient in the hospital when the acute symptoms are once relieved is very great and it was for this reason that this standard of cure had to be accepted. Whenever possible patients were kept under observation longer, and more examinations were made. The results of the investigation are analysed and given below:—

TABLE

No.	Race, sex, and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
1	H., M., 31	3 years; emetine 12 injections.	Scanty <i>E. h.</i> veg.	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
2	A.-I., F., 9	3 months; carbarsone 3 months ago without success.	<i>E. h.</i> (veg. and cyst), <i>E. nana</i> .	I. Amibiarsone 0.125 gm., b.d., for 10 days. II. 6 injections of autovaccine ( <i>B. pseudo-carolinus</i> from stool).	Do.	Do.
3	A.-I, M., 18	6 months	<i>E. h.</i> (veg. and cyst), <i>E. nana</i> .	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 7 exams.	Do.
4	H., M., 29	....	Scanty <i>E. h.</i> veg., hookworm ova, <i>Streptococcus faecalis</i> , <i>B. asiaticus</i> .	Amibiarsone 0.25 gm., b.d., for 7 days.	....	Left on risk bond on the 7th day of treatment. (Indeterminate). Cured.
5	H., M., 50	1 year	Scanty <i>E. h.</i> veg., hookworm ova.	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 7 exams.	Cured.
6	H., M., 28	2 years	Scanty <i>E. h.</i> veg. and cyst, <i>I. butschlii</i> cysts, <i>E. nana</i> veg. and cysts, <i>Streptococcus faecalis</i> .	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Do.
7	H., M., 30	Present attack 2 years. Dysentery 12 years ago. Emetine 21 injections.	<i>E. h.</i> veg., cellular exudates.	Amibiarsone 0.25 gm., b.d., for 20 days.	<i>E. h.</i> cysts, C-L crystals.	Failed.
8	M., M., 38	Originally admitted for diabetes.	<i>E. h.</i> cysts, <i>E. nana</i> cysts, hookworm ova, malignant tertian malaria.	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
9	H., F., 16	4 months	Very scanty <i>E. h.</i> veg., ascaris and trichuris ova.	Do.	Do.	Do.
10	I.-Ch., F., 45	Originally admitted for filariasis. Dysentery in childhood.	<i>E. h.</i> veg. and cyst, blastocystis, trichuris ova.	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 5 exams.	Indeterminate.

TABLE—contd.

No.	Race, sex, and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
11	M., M., 37	Admitted originally for lupus erythematosus.	Scanty <i>E. h.</i> cysts, hookworm ova.	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 6 exams.	Cured (negative from the 8th day of treatment)
12	M., F., 36	Originally admitted for chyluria.	Scanty <i>E. h.</i> cysts	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
13	H., M., 12	Admitted originally for asthma.	<i>E. h.</i> cysts, giardia cysts, <i>I. butschlii</i> , hookworm ova, ascaris ova, trichuris ova.	I. Amibiarsone 0.25 gm., b.d., for 10 days. II. Autovaccine (from sputum) 6 injections.	Negative 9 exams.	Cured (negative from the 8th day).
14	H., M., 16	1 year ..	<i>E. h.</i> cysts, giardia cysts, hookworm ova.	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured (negative from the 8th day of treatment).
15	H., F., 13	2 years ..	<i>E. h.</i> cysts, <i>I. butschlii</i> , <i>E. nana</i> , trichuris ova, tænia ova.	Do.	Do.	Cured (negative from the 8th day). Cured.
16	H., F., 20	Originally admitted for anæmia, suffered from dysentery 4 years ago.	<i>E. h.</i> cysts, <i>B. lactis ærogenes</i> .	Do.	Do.	Cured.
17	H., F., 39	22 years ..	<i>E. h.</i> cysts, <i>B. pseudocarinatus</i> , hookworm ova, <i>A. metalcaligenes</i> .	I. Amibiarsone 0.25 gm., b.d., for 10 days. II. 6 injections of autovaccine ( <i>B. pseudocarinatus</i> ).	I. Negative 6 exams. II. Giardia cysts.	Do.
18	H., M., 30	6 months for the present; suffered from amoebic dysentery 12 years ago.	<i>E. h.</i> cysts, hookworm ova.	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Do.
19	H., M., 35	7 years ..	<i>E. h.</i> cysts, hookworm ova, giardia cysts.	Do.	Do.	Do.
20	M., F., 16	Originally admitted for contracture of hand (hysteric).	<i>E. h.</i> cysts, hookworm and trichuris ova, <i>B. fæcalis alkaligenes</i> .	Do.	Do.	Do.
21	H., F., 11	1 year ..	<i>E. h.</i> (veg.), giardia cysts, <i>B. fæcalis alkaligenes</i> , <i>B. pyocyaneus</i> , <i>B. paratyphosus</i> (?).	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 7 exams.	Do.
22	M., M., 55	3 years, dysentery 15 years ago.	<i>E. h.</i> (veg.)	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Do.
23	H., M., 29	12 years emetine. Cabarsone (Lilly) Gavano Autovaccine Kurchi	<i>E. h.</i> cysts, <i>B. pyocyaneus</i> .	I. Amibiarsone 0.25 gm., b.d., for 10 days. II. Amibiarsone 0.25 gm., b.d., for 5 days after an interval of 5 days.	Degenerated <i>E. h.</i> cysts. Negative 6 exams.	Do.
24	H., M., 32	6 months ..	<i>E. h.</i> cysts, hookworm ova.	Amibiarsone 0.25 gm., b.d., for 10 days.	Do.	Do.
25	M., M., 21	Originally admitted for filariasis.	<i>E. h.</i> cysts, hookworm and trichuris ova, <i>B. lactis ærogenes</i> , urine culture staphylococci.	Amibiarsone 0.25 gm., b.d., for 15 days.	Negative 7 exams.	Do.

TABLE—contd.

No.	Race, sex, and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
26	H., F., 45	Originally admitted for dermatitis.	<i>E. h.</i> cysts, <i>B. pseudo-carolinus</i> , <i>B. lactis aerogenes</i> .	Amibiaron 0.25 gm., b.d., for 15 days.	Negative 4 exams.	Indeterminate.
27	E., F., 9	1 month ..	Scanty <i>E. h.</i> (veg.), <i>B. pseudo-carolinus</i> .	I. Amibiaron 0.125 gm., b.d., for 10 days. II. 6 injections of autovaccine ( <i>B. pseudo-carolinus</i> ).	Do.	Do.
28	H., M., 20	6 months ..	<i>E. h.</i> (veg.) + +, C.-L. crystals + +, atypical flexner.	I. Amibiaron 0.25 gm., b.d., for 10 days. II. 6 injections of autovaccine.	I. Scanty <i>E. h.</i> (veg.), C.-L. crystals. II. After the course of vaccine <i>E. h.</i> (veg.), C.-L. crystals. ....	Failed.
29	H., M., 30	Originally admitted for malaria.	<i>E. h.</i> (veg. and cyst), <i>E. nana</i> (veg. and cyst), blastocystis + +, hookworm and ascaris ova and strongyloides larvæ.	Amibiaron 0.25 gm., b.d., for 10 days.	....	Pt. left on the 6th day of treatment. Indeterminate.
30	E., M., 32	Since childhood; worse recently.	<i>E. h.</i> (veg. and cyst) +, <i>E. nana</i> (veg. and cyst) +, blastocyst +, <i>B. faecalis alkaligenes</i> .	I. Amibiaron 0.25 gm., b.d., for 10 days. II. 6 injections of autovaccine.	Negative 4 exams.	Indeterminate.
31	M., F., 38	5 years ..	<i>E. h.</i> (veg.), scanty <i>E. nana</i> (veg. and cyst), + +.	Amibiaron 0.25 gm., b.d., for 10 days.	<i>E. h.</i> (veg.) + C.-L. crystals +	Failed.
32	A.-I., M., 3	....	<i>E. h.</i> (veg. and cyst) +.	Do.	Negative 2 exams.	Indeterminate.
33	Jew, F., 46	1 month for the present, dysentery 5 years ago.	<i>E. h.</i> (veg.) +	Do.	Negative 6 exams.	Cured.
34	H., M., 7	Originally admitted for hæmophilia.	Scanty <i>E. h.</i> (veg.), oxyuris and trichuris ova.	Do.	Negative 7 exams.	Do.
35	A.-I., M., 21	Originally admitted for malaria.	<i>E. h.</i> (veg.) +.	Do.	Negative 4 exams.	Indeterminate.
36	M., M., 25	1 year ...	Scanty <i>E. h.</i> (veg.), hookworm ova, <i>B. pseudo-asiaticus</i> .	I. Amibiaron 0.25 gm., b.d., for 10 days. II. Amibiaron 0.25 gm., b.d., for 5 days.	Scanty <i>E. h.</i> veg. Negative 3 exams.	I. Failed. II. Indeterminate.
37	H., M., 24	Originally admitted for elephantiasis leg. Dysentery 12 years back.	Scanty <i>E. h.</i> (veg. and cyst), hookworm ova.	Amibiaron 0.25 gm., b.d., for 10 days.	Negative 6 exams.	Cured.
38	M., M., 40	5 years emetine	<i>E. h.</i> (veg.) + +, cellular exudates + + +.	I. Amibiaron 0.25 gm., b.d., for 10 days. II. Amibiaron 0.25 gm., b.d., for 5 days more.	I. Scanty <i>E. h.</i> (veg.). II. Negative 2 exams.	Failed. Indeterminate.

TABLE—concl'd.

No.	Race, sex, and age	Duration and previous treatment	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	REMARKS
39	A.-I., F., 57	Originally admitted for erythema.	Scanty <i>E. h.</i> (veg.)	Amibiarsone 0.25 gm., b.d., for 10 days.	Negative 4 exams.	Indeterminate.
40	H., M., 28	Originally admitted for malaria.	<i>E. h.</i> (veg.) +, chlo-mastix +.	Do.	Scanty <i>E. h.</i> cyst	Failed.

## Abbreviations:—

<i>E. h.</i>	= Vegetative stage of <i>Entamoeba histolytica</i> .
H. M.	= Hindu male.
H. F.	= Hindu female.
M. M.	= Mohammedan male.
M. F.	= Mohammedan female.
E. M.	= European male.

E. F.	= European female.
A.-I. M.	= Anglo-Indian male.
A.-I. F.	= Anglo-Indian female.
I. Ch. F.	= Indian Christian female.

Out of 40 patients 25 (62.5 per cent) were cured, in 5 patients (12.5 per cent) the drug failed and in 10 (25 per cent) the results were indeterminate. These last, although they left the hospital before the usual six examinations of the stools were completed, showed considerable improvement in their general condition. A perusal of the table shows that most of the cases showed the parasite in the cystic stage. The separate cure rates in vegetative and cystic infections are given below and it will be seen that the drug is more effective on the cysts than on the vegetative forms.

		Cures	Failures	Indeterminate	Total
Vegetative	..	7 (41%)	4 (24%)	6 (35%)	17
Cystic	..	18 (78%)	nil	5 (22%)	23

The proportion of probable cures to failures in this series is 5:1 as compared with 5.75:1 and 3.16:1 obtained by us with carbarsone and kurchi bismuth iodide respectively in a similar series of chronic cases. It may be noted here that case no. 7 showed the protozoa in the cystic stage after the treatment was over although the parasites were present in the vegetative form before treatment was started.

Cases nos. 36 and 38 failed with a ten days' course, but the results were indeterminate after a fifteen days' course of treatment.

The most usually noted untoward symptoms met with in this series during treatment with amibiarsone were in connection with the gastrointestinal and nervous systems. There may be slight pain in the epigastric region or flatulence when the drug is being administered. Slight headache and insomnia were observed in a few

cases. All symptoms however disappeared on the cessation of treatment and the patient felt better and his symptoms were relieved as the treatment advanced.

## Summary and conclusions

1. Amibiarsone is an organic compound of arsenic prepared by the Bengal Chemical and Pharmaceutical Works, Limited, Calcutta, on the same lines as the compound of the Ehrlich series, carbarsone of Lilly and Company. Its chemical composition is said to be similar to this compound.

2. It possesses amoebicidal properties and is administered in gelatine capsules in doses of 0.25 gramme twice daily for 10 to 15 days. In a series of 40 cases 63 per cent were cured, in 20 per cent the drug failed and 17 per cent were indeterminate. The proportion of probable cures to failures in this series was 5:1 as compared with 5.75:1 and 3.16:1 with carbarsone and kurchi bismuth iodide respectively.

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