

venoms of the Indian cobras (*Naja naja* and *Naja tripudians*) and of the Egyptian cobra (*Naja haji*) are all equally effective in this respect.

We have already stated that the analgesic properties of cobra venom reside in the neurotoxin principle. The other active principles such as hæmolysins, hæmorrhagins, and cytolysins are also present in the venom and produce their effects when injected. Recent work has shown that there is a possibility of isolating and separating these active principles on account of differences in their biochemical reactions. Chopra and Roy (1936) have shown that the hæmolytic principle can be separated by passing the venom solution through a Seitz filter. The cytolysin and other principles can also be separated out by heat as they coagulate at different temperatures. The separation of these active principles and a study of their pharmacological action will be interesting and may give us therapeutic remedies of importance.

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YATREN IN INFECTION WITH INDIAN STRAINS OF *E. HISTOLYTICA* (CHRONIC INTESTINAL AMŒBIASIS)

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YATREN 105 is prepared by Bayer-Meister Lucius and is 7-iodo-8 hydroxy-quinoline-5 sulphonic acid. It is a finely crystalline powder,

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pale yellow in colour; it easily absorbs moisture and therefore must be kept dry. It has 36.2 per cent of sodium carbonate added to increase its solubility. It has no odour; it has a solubility of 4 to 5 per cent in water. When dissolved it is said to become iodine-oxy-quinoline sulphate of sodium with liberation of CO₂.

Yatren is also known by the names of loretin and quinoxyl. In Japan a brand of locally-prepared iodine-oxy-quinoline sulphate of sodium has been used with success. Chardyl is a Belgian preparation comparable to yatren.

Yatren has been considered by some authorities to be almost as good a specific for amoebic dysentery as quinine is for malaria. It is also said to be effective in bacillary dysentery. The claims regarding its efficacy in intestinal amoebiasis while strongly pressed by some workers have not been substantiated by others. Mühlens and Menk (Knowles and others, 1928) were the first to use yatren in eight resistant cases of chronic intestinal amoebiasis with remarkable clinical improvement. They gave it by the mouth in the form of keratine-coated pills in doses of 1.0 gm. three times a day, supplemented with rectal injections of 2.5 per cent solution when ulceration was present. A further course of three to seven days was given after a week's interval and later one more if necessary. A number of other workers have tried the drug and have found it to be an effective remedy in both acute and chronic forms of intestinal amoebiasis. According to Akashi (Chopra, 1936) yatren at first killed the *E. histolytica* present in the lumen of the intestines and then gradually attacked those in the superficial layers of the intestinal wall. Emetine, on other hand, did not act on the amoeba in the lumen of the gut, but killed them in the intestinal tissue. A combination of the two drugs was therefore recommended, emetine being first given in the acute stages followed by yatren in the later stages. Dalmeyer (Knowles and others, 1928) found yatren unfailingly successful, both in acute and chronic amoebic dysentery, and a number of other workers in Europe have come to a similar conclusion.

On the other hand, the other group of investigators have not found the drug to be so efficacious. Megaw and Knowles tried it in the Carmichael Hospital for Tropical Diseases on Indian strains of *E. histolytica* with variable results. The dosage recommended, *i.e.*, 1.0 gm. three times a day, produced diarrhoea which was troublesome to the patient although there was no tenesmus. Knowles and others (1928) were of opinion that unless diarrhoea was produced the results of treatment were poor. In fact according to him the drug acted by producing irritating to him the mucous membrane of the colon. In a series of 23 cases he treated, the ratio of probable cures to failures worked out to 1:1.3 when yatren was given by the mouth and in six

intractable cases which had a combined treatment with yatren by the mouth and per rectum simultaneously, the ratio was 1:1.5.

The opinion regarding this drug has been so favourable of late years that the senior author thought it worth while to try it again in a series of 50 cases in the Carmichael Hospital for Tropical Diseases to see its effects in infections with Indian strains of *E. histolytica* and in this paper we give the result of our trials. Carbarsonone undoubtedly has given uniformly good results in our hands, but there are cases which are resistant to this drug. Besides this, carbarsonone is contra-indicated when (1) albuminuria is present, (2) when the liver is damaged, and (3) in some forms of dermatitis. Yatren, if as effective, would be useful in these cases.

The patients in this series were admitted into the Carmichael Hospital for Tropical Diseases under the senior author. Most of them had *E. histolytica* in the stools and suffered from general, rather than intestinal, symptoms. A few were admitted for diseases other than amoebiasis, but examination of their stools showed a fair number of vegetative or cystic forms of *E. histolytica*. Yatren was administered by the mouth in the form of pillets, 4 pillets (1.0 gm.) being given twice daily for 10 days but where *E. histolytica* were still found in the stools the treatment was prolonged for 15 days. The doses recommended by the German workers, *i.e.*, 1.0 gm. (4 pillets) three times a day, could not be given in Indian patients because these produced severe diarrhoea. Where definite ulcers were revealed by sigmoidoscopic examination, a 2 per cent solution of the drug was also used as a bowel wash. The total quantity administered by the mouth amounted to 20 to 30 gm. in the course.

The patients were kept on ordinary diet and for the first one or two days the bowels had to be kept open with a dose of a saline purgative in the morning but from the third day, in most of the cases, a painless diarrhoea ensued. If there was any evidence of a concomitant bacterial infection, a course of auto-vaccine 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 does not indicate that a real cure has been effected, but from experience 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 patients 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

TABLE I

No.	Sex and age	Duration in months	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	Result	REMARKS
1	F., 32	..	<i>E. h.</i> (cyst) scanty, <i>Trichomonas hominis</i> . W. R. slightly positive.	Yatren 2 pillets, four times a day for 10 days.	Negative 6 exams.	Cured	A case of hypo-thyroidism. No abdominal symptoms.
2	M., 26	4 × 12	<i>E. h.</i> (cyst) scanty ..	Yatren 4 pillets, b.d., for 10 days.	Do.	Do.	
3	M., 32	..	<i>E. h.</i> (veg. and cyst)	Do.	Do.	Do.	A case of psoriasis. No abdominal symptoms.
4	M., 10	6	<i>E. h.</i> (veg.) ..	Yatren 2 pillets, b.d., for 10 days.	Do.	Do.	
5	M., 45	12	Do. ..	Yatren 4 pillets, b.d., for 10 days.	Do.	Do.	
6	F., 2	1½	<i>E. h.</i> (veg.) very scanty. <i>Bact. ærogenes</i> .	Yatren ½ a pillet, b.d., for 10 days.	Do.	Do.	
7	M., 22	..	<i>E. h.</i> (cyst) scanty, hookworm ova.	Yatren 4 pillets, b.d., for 10 days.	Negative 1 exam.	Indeterminate.	
8	F., 4	..	<i>E. h.</i> (veg. and cyst), <i>Bact. asiaticus</i> , <i>Bact. mobilis</i> , <i>Bact. pseudo-asiaticus</i> , <i>Bact. metalcaligenes</i> .	Yatren 1 pillet, b.d., for 15 days.	Negative 6 exams.	Cured	
9	M., 10	8	<i>E. h.</i> (veg.) scanty, <i>Trichomonas hominis</i> , <i>Bact. para-asiaticus</i> , <i>Bact. ærogenes</i> , hookworm ova.	Yatren 3 pillets, b.d., for 10 days.	Do.	Do.	A case of kala-azar with irregular bowels.
10	M., 30	12	<i>E. h.</i> (veg. and cyst), microfilaria in blood.	Yatren 4 pillets, b.d., for 10 days.	Do.	Do.	
11	M., 40	..	<i>E. h.</i> (cyst) scanty, <i>E. nana</i> (cyst), hookworm ova.	Do.	No stool exam. done.	Indeterminate.	
12	M., 20	1 × 12	<i>E. h.</i> (veg. and cyst) scanty, <i>Bact. ærogenes</i> , ascaris ova.	Do.	Negative 6 exams.	Cured	
13	M., 34	2	<i>E. h.</i> (veg. and cyst) very scanty, <i>Blastocystis hominis</i> scanty, M. T. rings in blood.	1. Yatren 4 pillets, b.d., for 5 days. 2. Yatren 3 pillets, b.d., for 5 days.	Do.	Do.	
14	M., 29	..	<i>E. h.</i> (veg.) scanty, <i>Bact. ærogenes</i> , ascaris ova. Mid-stream urine shows <i>Staphylococcus aureus</i> on culture. Microfilaria in blood.	Yatren 4 pillets, b.d., for 10 days.	Do.	Do.	A case of filariasis. No definite abdominal symptoms.
15	M., 34	1½ × 12	<i>E. h.</i> (veg.) scanty, C.-L. crystals scanty, <i>Bact. douglasi</i> .	Do.	<i>E. h.</i> (cyst) scanty. C.-L. crystals scanty.	Failed	
16	M., 25	4	<i>E. h.</i> (veg.) +, cellular exudate +, microfilaria in blood.	Yatren bowel wash for 10 days.	No stool exam. done.	Indeterminate.	Marked clinical improvement. Ba. meal shows colitis.
17	M., 30	..	Protozoa negative. C.-L. crystals. <i>Bact. pseudo-carolinus</i> .	Do.	Do.	Do.	
18	M., 25	..	<i>E. h.</i> (veg. and cyst) scanty, <i>I. butschlii</i> (veg. and cyst), Chilomastix, <i>Trichomonas hominis</i> , hookworm and trichuris ova. Microfilaria in blood. Marked anæmia, hyp-acidity.	Yatren 4 pillets, b.d., for 10 days.	Negative 6 exams. <i>Trichomonas hominis</i> .	Cured	
19	M., 54	..	<i>E. h.</i> (cyst) +, <i>E. coli</i> (cyst) +, <i>E. nana</i> (cyst) +.	Yatren 4 pillets, b.d., for 10 days.	Negative 3 exams.	Indeterminate.	

TABLE I—contd.

No.	Sex and age	Duration in months	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	Result	REMARKS
20	M., 42	18 × 12	<i>E. h.</i> (veg.) scanty. <i>Lambli</i> <i>intestinalis</i> (cyst).	Yatren 4 pillets, b.d., for 15 days.	Negative 6 exams.	Cured	
21	M., 32	..	<i>E. h.</i> (veg.) +, <i>Bact. asiaticus mobilis</i> . Microfilaria in blood.	Do.	<i>E. h.</i> (veg.) very scanty.	Failed	
22	M., 45	2½ × 12	<i>E. h.</i> (veg.) scanty, <i>Trichomonas hominis</i> scanty, <i>E. nana</i> (veg. and cyst), trichuris ova, <i>Bact. pseudo-carolinus</i> .	1. Yatren 4 pillets, b.d., for 10 days. 2. Six injections of autovaccine (<i>Bact. pseudo-carolinus</i>).	<i>E. h.</i> (veg.).	Do.	
23	M., 40	2 × 12	Degenerated <i>E. h.</i> (veg.), <i>Bact. pseudo-carolinus</i> .	Yatren 4 pillets, b.d., for 15 days.	Negative 5 exams.	Indeterminate.	
24	M., 34	..	<i>E. h.</i> (veg.) scanty, <i>Bact. pseudo-carolinus</i> .	1. Yatren 4 pillets, b.d., for 10 days. 2. Six injections of autovaccine (<i>Bact. pseudo-carolinus</i>).	<i>E. h.</i> (veg.)	Failed	
25	M., 17	7/30	C.-L. crystals ..	Yatren 4 pillets, b.d., for 11 days.	No stool exam. done.	Indeterminate.	Relief of the acute symptoms.
26	M., 27	2 × 12	<i>E. h.</i> (cyst) very scanty, <i>Lambli</i> <i>intestinalis</i> (cyst), <i>E. nana</i> (cyst) +, <i>Bact. asiaticus</i> .	Yatren bowel wash	Negative 6 exams.	Do.	Amibiarsone given orally. Ulcers partially healed up. Improvement in the general condition.
27	M., 14	1	<i>E. h.</i> (veg. and cyst)	Yatren 4 pillets, b.d., for 15 days.	Negative 5 exams.	Do.	
28	M., 14	4	<i>E. h.</i> (veg.) +, C.-L. crystals, <i>Bact. metalcaligenes</i> .	Yatren 4 pillets, b.d., for 15 days.	Negative 9 exams.	Cured	
29	M., 3	3/30	<i>E. h.</i> (veg. and cyst) +, hookworm and ascaris ova.	Yatren 4 pillets, b.d., for 10 days.	Degenerated cyst of <i>E. h.</i>	Indeterminate.	
30	F., 55	1 × 12	<i>E. h.</i> (veg. and cyst) +, hookworm and ascaris ova. <i>Bact. alkaligenes</i> , <i>Ps. pyocyaneus</i> .	Yatren 4 pillets, b.d., for 15 days.	Negative 5 exams.	Do.	
31	M., 29	1 × 12	<i>E. h.</i> (cyst) +, hookworm ova. Microfilaria in blood.	Yatren 4 pillets, b.d., for 14 days.	Negative 6 exams.	Cured	
32	M., 5	1 × 12	<i>E. h.</i> (veg.) +, cellular exudate +, enterococci +, <i>Bact. aërogenes</i> .	Yatren 1 pillet, t.d.s., for 10 days.	Negative 6 exams. Giardia cysts.	Do.	
33	M., 50	1	<i>E. h.</i> (veg.) scanty, <i>Bact. aërogenes</i> .	Yatren 4 pillets, b.d., for 15 days.	1. Neg. to <i>E. h.</i> 6 exams. 2. <i>Bact. asiaticus</i> .	Do.	Emetine outside.
34	F., 40	1 × 12	<i>E. h.</i> (veg. and cyst) scanty, <i>E. nana</i> (cyst) scanty, <i>enteromonas</i> , <i>Bact. alkaligenes</i> .	Yatren 4 pillets, b.d., for 15 days.	Negative 6 exams.	Do.	
35	M., 29	1 × 12	<i>E. h.</i> (veg.) +, <i>E. nana</i> cysts scanty.	Yatren 4 pillets, b.d., for 10 days.	Do.	Do.	
36	M., 39	6	<i>E. h.</i> (cyst) scanty, <i>E. coli</i> (cyst) scanty.	Yatren 4 pillets, b.d., for 15 days.	Do.	Do.	
37	M., 23	2 × 12	<i>E. h.</i> (cyst) scanty, <i>E. nana</i> cysts, <i>I. butschlii</i> (veg. and cyst).	Do.	<i>E. h.</i> cyst very scanty.	Failed	
38	F., 44	2½ × 12	<i>E. h.</i> (veg.) scanty, <i>Bact. asiaticus</i> .	1. Yatren 4 pillets, b.d., for 10 days. 2. Autovaccine (<i>Bact. asiaticus</i>).	<i>E. h.</i> (veg.) scanty.	Do.	

TABLE I—concl'd.

No.	Sex and age	Duration in months	Laboratory findings before treatment	Treatment	Laboratory findings after treatment	Result	REMARKS
39	M., 25	2 × 12	<i>E. h.</i> (veg.) scanty, <i>Ps. pyocyanæ</i> , streptococci, hookworm and trichuris ova, M. T. rings in blood.	1. Yatren bowel wash. 2. Autovaccine (streptococcus).	Negative 6 exams.	Given carbar- sone orally.	
40	M., 28	6 × 12	No protozoa	Yatren 1 pillet, t.d.s., for 7 days.	No stool exam. done.	Indeter- minate.	No improve- ment.
41	M., 35	3/30	<i>E. h.</i> (cyst) +	1. Yatren 4 pillets, b.d., for a day. 2. Yatren 2 pillets, b.d., for 1 day. 3. Yatren 4 pillets, b.d., for 3 days.	Do.	Do.	Left hospital before completion of treat- ment.
42	M., 41	..	<i>E. h.</i> (cyst) +. Urine: Staphylococcus.	Yatren 4 pillets, b.d., for 10 days.	<i>E. h.</i> (veg. and cyst).	Failed	Admitted for lymphan- gitis.
43	F., 24	10	<i>E. h.</i> (cyst) +, C.-L. crystals, <i>Bact. pseudo-carolinus</i> .	Yatren 4 pillets, b.d., for 10 days.	Negative 6 exams.	Cured	Emetine outside.
44	M., 30	1½	<i>E. h.</i> (cyst) scanty. <i>Lamblia intestinalis</i> (cyst) scanty.	Do.	Negative 7 exams.	Do.	
45	M., 35	1½ × 12	<i>E. h.</i> (veg. and cyst) +, trichuris ova, micro- filaria in blood.	Do.	Negative 6 exams.	Do.	
46	M., 19	..	<i>E. h.</i> (cyst) scanty, hookworm ova.	1. Yatren 2 pillets, t.d.s., for 1 day. 2. Yatren 2 pillets, b.d., for 7 days. 3. Yatren 4 pillets, b.d., for 6 days.	Do.	Do.	Admitted for spleno- megaly.
47	M., 26	7	<i>E. h.</i> (cyst) +, <i>Bact. arogenes</i> , microfilaria in blood.	Yatren 4 pillets, b.d., for 10 days.	Negative 6 exams.	Failed	
48	F., 34	5/30	<i>E. h.</i> (veg.) +	Do.	Do.	Do.	
49	M., 20	..	<i>E. h.</i> (cyst) +, hook- worm ova, tricho- <i>strongyloids</i> .	Do.	Do.	Do.	
50	M., 35	..	No protozoa	Yatren 4 pillets, b.d., for 3 days.	No stool exam. done.	Indeter- minate.	

examinations were made. The results of the investigation are analysed and given below.

Out of 50 patients 28 (56 per cent) were cured, and in 16 (32 per cent) the results were indeterminate, as the patients left the hospital before the total number of six examinations required could be completed. Some of these indeterminate cases showed considerable clinical improvement in their general condition. Entamœbæ were found in the stools of six patients after treatment and in these the treatment had definitely failed.

A perusal of the table shows that the majority 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 appears to be somewhat more effective when cysts were found in the stools than when vegetative forms were found.

The proportion of probable cures to failures in this series is 4.6:1 as compared with 5.75:1 and 3.16:1 obtained by Chopra, Sen and Sen

(1933) and by Acton and Chopra (1929) with carbar-sone and kurchi bismuth iodide, respect-
ively, in a similar series of chronic cases. It may be noted here that case 15 showed the protozoa in the cystic stage after the treatment was over, although the parasites were present in

TABLE II.

<i>E. histolytica</i>	Cured, per cent	Indeterminate (with favourable prognosis), per cent	Failed, per cent
Cystic form	62.9	29.6	7.5
Vegetative form	57.9	15.9	26.2

the vegetative form before treatment was started. The stool of case 17 was negative to *E. histolytica*, but radiographic examination revealed a condition of chronic ulcerative colitis.

In this case yatren bowel wash produced considerable clinical improvement. Examination of the stool of case 26 showed *E. histolytica* in the cystic stage and ulcers were found on rectal examination. In this patient yatren was not administered by mouth, but was used as a rectal wash. No change, either in the symptoms or in the ulcers, was observed.

No untoward symptoms were met with in this series during treatment with yatren. The diarrhoea which ensued after the second day of treatment continued till the course of treatment was over and was not troublesome in the majority of cases. This looseness of the bowels appears to be beneficial inasmuch as it keeps the ulcers free from irritation by the intestinal contents and helps in eliminating the toxins. Yatren is absorbed from the intestines and is excreted by the kidneys in the urine which gives a positive oxy-quinoline test, i.e., green colour with ferric chloride. It is absolutely non-irritant to the kidney and therefore can be given where albuminuria is present. It is also well borne when the liver is diseased and therefore in both these conditions, as well as in those in which there is a tendency to dermatitis, it can replace carbarsone with advantage.

Conclusions

From the small series of patients we have treated, we are justified in drawing the following conclusions :—

(1) Yatren possesses well-marked amœbicidal properties in doses of 1.0 gm. twice daily for 10 to 15 days in infections with Indian strains of *E. histolytica*. It is worthy of trial in cases of acute and chronic intestinal amœbiasis in this country.

(2) No untoward symptoms were noticed except mild painless diarrhoea which started on the second or third day of treatment and went on till the treatment was completed.

(3) Yatren is specially indicated in those patients who suffer from pathologic conditions of the liver and the kidneys and in certain forms of dermatitis where carbarsone is contra-indicated.

We are grateful to the Haverro Trading Company for supplying us the drug for this trial free of cost.

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*CYANIDE POISONING AND ITS TREATMENT WITH ANTIDOTES

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Introductory

HYDROCYANIC ACID is one of the earliest of poisons known. It is said to have been used by the ancients in the form of an infusion of peach leaves or kernels or of the seeds of other fruits in which the acid might be liberated. Scheele was the first to isolate the acid from the familiar prussian blue. He not only established its correct chemical identity but also tested some of its pharmacological properties on himself. Bohm and Schrader, following Scheele's method, demonstrated its presence in bitter almonds and in cherry and peach leaves. Throughout the nineteenth century, and more particularly during the last quarter, numerous contributions were made with regard to the effects of the poison on all forms of living matter—from the bacteria and unicellular organisms to the more highly-developed species of the mammalian kingdom. Within the last 20 years, the study of the cyanide problem has gained an added impetus due mainly to the brilliant researches on tissue respiration and cellular oxidation-reduction phenomena by Warburg (1923) and Keilin (1927). The discovery of some of the new antidotes to combat cyanide intoxication has further opened up an extremely interesting field of study into some of the peculiar biochemical defence mechanisms of the body. The introduction of some of these antidotes in clinical practice promises to offer a successful means of combating a desperate condition for which no satisfactory means were available only four years ago.

Incidence of cyanide poisoning

In recent years, accidental, occupational, and industrial cyanide poisonings have occurred with increasing frequency and hence the subject has attracted the attention of toxicologists and clinicians. Accidental poisonings result chiefly from fumigation and in chemical and photographic laboratories. There are also occasional cases of poisoning from the ingestion of bitter almonds. The escaping vapour in certain

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