FURTHER EXPERIENCE OF THE SPECIFIC CURATIVE ACTION IN AMOEBIC DISEASE OF HYPODERMIC INJECTIONS OF SOLUBLE SALTS OF EMETINE.

BY

LEONARD ROGERS, M.D., F.R.C.P., I.M.S.,

PROFESSOR OF PATHOLOGY, CALCUTTA.

IN the BRITISH MEDICAL JOURNAL of June 22nd* last I recorded cases illustrative of acute and chronic amoebic dysentery and acute hepatitis respectively in patients who were unable to take ipecacuanha by the mouth, but were rapidly cured by subcutaneous injections of soluble salts of emetine, without the production of vomiting or marked nausea, which are such serious drawbacks to the use of full doses of ipecacuanha by the mouth. During the two months which have elapsed since that note was written I have had frequent opportunities of using the new treatment in suitable cases, thanks mainly to the kindness of my I.M.S. colleagues in the different Calcutta hospitals, to whom I tender my best thanks. The results have been more than confirmatory of my first very favourable impressions, and leave no possible doubt as to the great practical importance of the discovery. Some of them are, indeed, so surprising that they must be seen to be fully appreciated, as words can convey but a feeble impression of the rapidity and completeness of the recoveries effected in very grave cases. In dealing with the more extensive material now available it will be well to classify the cases into different clinical groups.

I.—Extremely Acute Amoebic Dysentery with Marked Thickening and Tenderness of the Bowel and High Leucocytosis.

The most serious form of amoebic dysentery is a primary attack, or an acute exacerbation of a chronic one, in which parts of the large bowel can be felt through the abdominal wall as very tender, greatly thickened, rounded or sausage-shaped masses, showing that the whole thickness of the gut is involved, including the peritoneal coat, and nearly always accompanied by an extreme leucocytosis of from 30,000 to 50,000 per cubic millimetre. The prognosis in these cases is exceedingly grave, as gangrene, perforative peritonitis, or post colic abscess are frequent fatal complications. I find I have earlier notes of 13 such cases with leucocyte counts of from 25,000 to 49,250, 7 of which proved fatal within a few days, 4 were taken away in a dying condition by their relatives, and only 2, or 15 per cent. recovered, in spite of ipecacuanha having been given in quantities of 30 to 60 grains or more a day. The fact is that sufficient ipecacuanha cannot be administered quickly enough by the mouth to save more than a very small percentage of such cases. The following are examples of this class treated by emetine salts hypodermically.

CASE I.

Native male, aged 33, admitted to my ward for cholera with a history of having passed fifteen stools in the last twelve hours, the last containing blood. Specific gravity of blood 1059, blood pressure 112. On examining the stools no cholera organisms were found either microscopically or on culture, but very numerous small amoebae were present. The abdomen was distended and the caecum could be felt as a greatly thickened mass, extending into the hypogastrium and very tender to the touch, while the sigmoid showed less marked, but similar,

	First Day.	Second Day.	Third Day.	Fourth Day.
Number of stools—				
Day	9	3	2	1
Night	1	2	1	1
Emetine hydrobromide ...	1 gr.	1½ gr.	1 gr.	Ip. 40 r.
Mucus	Much	Nil	Nil	Nil
Blood	Much	Nil	Nil	Nil
Amoebae	Numerous	Nil	—	—
Leucocytes	30,050	22,500	12,250	9,250
Ratio to red	1 to 206	1 to 308	1 to 409	1 to 651
Polynuclears	90.8	84.4	72.4	52.8

* In the former paper, for "Docker, I.M.S.," read "Docker, A.M.S."

changes. He gave a history of three previous attacks of dysentery, the last being one month ago. Hypodermic injections of emetine hydrobromide were at once begun, and the progress of the case, together with the leucocyte counts, can be seen at a glance at the accompanying table.

The blood and mucus and the amoebae had disappeared from the stools in twenty-four hours, and by the fourth day the whole of the thickening and tenderness of the caecum and sigmoid, as well as the leucocytosis, had vanished, and the patient was convalescent. Further progress was uneventful, and he was discharged cured eleven days after his admission.

CASE II.

Native male, aged 24, admitted to my ward for cholera in the collapse stage at 7 p.m. with a specific gravity of 1064 and a blood pressure of only 50 mm. He was given four pints of hypertonic saline intravenously on admission, and required two subcutaneous ones of one pint each during the night. On the following morning he had recovered well from the collapse, but the stools showed thick blood and mucus, and microscopically very numerous young amoebae were present, together with cholera vibrios, the latter being obtained in pure culture, proving a mixed infection to be present. The descending colon and sigmoid flexure were greatly thickened and tender. At 1 p.m. he passed a stool containing a number of black shreddy sloughs, such as Ewart found to be a sure sign of fatal gangrenous dysentery, together with some white ones containing amoebae. Emetine treatment was at once begun, with the result shown in the following table:

	First Day.	Second Day.	Third Day.	Fourth Day.	Fifth Day.
Number of stools—					
Day	—	9	4	3	1
Night	15	0	2	3	0
Emetine HBr	Nil	1½ gr.	1 gr.	1 gr.	Ip. 40 gr.
Mucus	Choleraic	Much	Nil	Nil	Nil
Blood	Choleraic	Much	Nil	Nil	Nil
Amoebae	—	Numerous	Nil	—	—
Leucocytes	—	32,500	12,000	—	8,750
Ratio to red	—	1 to 171	1 to 457	—	1 to 538
Polynuclears	—	89.8	73.2	—	63.8

By the fourth day all tenderness and thickening of the large bowel, as well as the leucocytosis, had disappeared, and the patient was convalescent, being discharged cured at the end of seven days in hospital, and was seen two weeks later quite free from all dysenteric symptoms. He had thus been cured of sloughing amoebic dysentery coincident with a fairly severe attack of cholera.

Cases I and II are very good examples of the acutest form of amoebic dysentery in which the disease was cut short, and both great thickening of the bowel and an extreme degree of leucocytosis cleared up within three or four days, very great improvement having been apparent within twenty-four to forty-eight hours, under treatment with from 1 to 1½ grains of emetine hydrobromide daily, an equivalent of 90 to 135 grains of ipecacuanha. The chances of the recovery of either of them under ipecacuanha treatment by the mouth would have been very small. In the next case, although emetine failed to save the patient's life, yet even more convincing evidence of the specific action of the drug was obtained.

CASE III.—Fatal Gangrenous Amoebic Dysentery, in which the Amoebic Infection was Destroyed within Sixty Hours by Emetine Injections.

Native male, aged 45, and a confirmed opium eater, taking about 30 grains a day, admitted for dysentery of twelve days' duration, having had another attack a month before. Passing about twenty very foul stools a day with blood and mucus containing numerous amoebae. Abdomen somewhat distended and marked thickening and acute tenderness of the large bowel from the caecum to the splenic flexure, but most marked in the right iliac fossa, and a high degree of leucocytosis. Progress:

	First Day.	Second Day.	Third Day.
Number of stools—			
Day	4	11	2
Night	15	4	—
Emetine hydrobromide ...	1½ gr.	2 gr.	Nil
Mucus	Much	Less	Trace
Blood	Much	Less	Nil
Amoebae	Numerous	Numerous	Nil
Leucocytes	22,250	16,000	14,250
Ratio to red	1 to 263	—	—
Polynuclears	88.4	81.6	82.0

Three $\frac{1}{2}$ -grain doses of emetine were given the first day and he appeared to be rather better in the evening. The next morning he was passing more frequent stools again, so two 1-grain doses were given hypodermically, each equal to 90 grains of ipecacuanha, without any apparent depression and no nausea or vomiting. The washings of the stools of the first twenty-four hours showed a cupful of large raw-meat-like sloughs, and those of the second twenty-four hours were similar, but smaller and less blood-stained. The second night, after the two 1-grain doses of emetine, he had only four small stools containing a very little thin mucus faintly streaked with blood, while the morning stool was watery brown faecal, with only a minute trace of white mucus and quite free from amoebae. In spite, however, of large doses of opium, he had been unable to get any sleep, and suffered much from the great restlessness of opium eaters, being worn-out, cold, and clammy. The tenderness and thickening of the large bowel had disappeared except in the right iliac fossa, where they were as marked as before, so I recognized that local peritonitis, with either a post-caecal abscess or gangrene, must be present, for which nothing more could be done, and he died on the evening of the same day. A *post-mortem* examination was obtained, which revealed most extensive amoebic ulceration affecting the whole length of the large intestine, although the rectum was but slightly involved. The caput coli was gangrenous, with little but the peritoneal coat remaining, while inflammatory recent lymph on the surface bound it loosely to the ileum. A prolonged microscopical examination of scrapings of the ulcers in various parts of the bowel failed to reveal a single living amoeba, and sections through the walls of some of the more recent ulcers stained with haematoxylin showed not a single parasite, although they are ordinarily quite easily demonstrated by either of these methods. Thus, in spite of the terrible acuteness and extent of the lesions, every single amoeba appears to have been killed by the $\frac{3}{4}$ grains of emetine injected subcutaneously during the two and a half days he was in hospital, and thus the failure to save this opium-eating patient furnished the most conclusive evidence of the specific nature of the new method of treatment, and fully explained the apparently miraculous recoveries recorded in Cases I and II.

II.—Moderately Acute Amoebic Dysentery Rapidly Cured by Emetine.

Case iv and v are typical of acute amoebic dysentery, such as usually yield to full doses of ipecacuanha in time, but which are much more rapidly and certainly cured by the new treatment, and with far less suffering to the patient. For this common class the new method will be a great boon.

CASE IV.

A native female, aged 28, admitted for acute dysentery of fifteen days' duration and passing such numerous stools of pure blood and mucus that the bed-pan had to be kept constantly by her. Tenderness and thickening of the caecum extending into the hypogastrium, and restlessness were present. Numerous amoebae were found in the stools. After three days' treatment with ipecacuanha by the mouth the symptoms and great frequency of the stools and local signs remained the same, and I was asked to treat her with emetine. Two $\frac{1}{2}$ -grain doses were given the first day, and the next morning the stools were much less frequent and contained faecal matter, while her general condition had much improved. Two more $\frac{1}{2}$ -grain doses were given that day, and during the following night, that is from thirty-six to forty-eight hours after the first dose, not a single stool was passed, nor did she have any more dysenteric motions during the subsequent eight days before she was discharged cured. The thickening and tenderness of the caecum also rapidly disappeared.

CASE V.

A native male, aged 30, admitted for acute dysentery of fifteen days' duration, with pain in the abdomen, but no marked thickening of the bowel, and passing ten to twelve stools of blood and mucus daily, containing numerous active amoebae. After two days' treatment with ipecacuanha in 25-grain doses no improvement was apparent and the stools contained much blood, so emetine was injected in $\frac{1}{2}$ -grain doses twice daily for three days. By the end of that time the stools had been reduced to four soft yellow faecal ones a day, with no blood or mucus and free from amoebae, while the abdominal pain had disappeared. The leucocytes had also fallen from 12,750 to 6,250, and steady convalescence ensued.

III.—Chronic Amoebic Dysentery Rapidly Cured by Emetine.

The patient with dysentery of three and a half years' duration, recorded in my first paper as rapidly cured by emetine, has continued free from all dysenteric symptoms. One further case belonging to this class may here be mentioned.

CASE VI.—Chronic Amoebic Dysentery of Six Months' Duration Rapidly Cured by Emetine.

A Eurasian, aged 25, was admitted to my ward with a history of having passed four or five stools, containing blood and mucus, daily for six months. He had slight tenderness over the caecum, but no thickening could be felt. Leucocytes 12,000 per c.mm.

Stools of pure blood and mucus were being passed, containing very numerous active amoebae, as many as six or eight being seen in some fields of the microscope. Half a grain of emetine was injected once a day for three days, after which ipecacuanha 20 grains was given every evening. Twenty-four hours after the first dose of emetine the stools were free from blood or mucus and no amoebae could be found. No further signs of dysentery ensued during the seven days he was in hospital, and I saw him three weeks later, when he was still keeping quite well.

IV.—Acute Hepatitis Threatening Liver Abscess Formation Cured by Emetine.

The remarkable effects of ipecacuanha in preventing liver abscess by curing both acute and chronic hepatitis, which was demonstrated by me in 1907, has been repeatedly confirmed by other workers, including a recent paper in the *Journal of the London School of Tropical Medicine*. In my first note on the emetine treatment I recorded an example of the rapid action of the new method in a patient who could not take ipecacuanha by the mouth, and two further cases are now added.

CASE VII.

A native male, aged 17, admitted with very acute hepatitis with marked enlargement and extreme tenderness of the lower border of the liver. An evening rise of temperature to 101° F. had persisted for ten days, in spite of 30 grains of ipecacuanha daily during the last four evenings. Two $\frac{1}{2}$ -grain injections of emetine were now given, and within eight hours of the first dose the tenderness had remarkably decreased, and on the following day the temperature became normal and remained so for four days. It then rose again in the evenings, and x rays showed a shadow suggestive of liver abscess. A needle was passed into the lower part of the right pleura and a little purulent lymph was drawn off. Ipecacuanha was persisted with and the condition cleared up entirely without any further operative procedures being necessary. The beneficial effect of a single grain of emetine in the early acute stage of this case was very striking.

CASE VIII.

A European male, aged 29, was admitted for acute hepatitis with intermittent fever, and 20-grain doses of ipecacuanha were given every evening. As the fever and hepatic pain persisted for five days the liver was explored for pus under an anaesthetic, but with a negative result. Emetine hydrobromide was now injected daily in $\frac{1}{2}$ -grain doses, and the temperature at once fell to normal and the pain subsided. Ipecacuanha was reverted to after four days, but the improvement was less marked than under the emetine, so the daily $\frac{1}{2}$ -grain dose of the latter was recommenced, and at once rapid improvement set in, going on to complete convalescence after a few doses, and accompanied by a fall in the previously high leucocyte count.

V.—Amoebic Abscesses of the Liver and Spleen Cured by Aspiration and Emetine Injections.

As early as 1902 I showed that unopened amoebic abscesses of the liver are, in the great majority of cases, sterile as regards bacteria, and therefore suggested removing the pus by aspiration, and injecting soluble salts of quinine into the cavity to kill the amoebae in the wall of the abscess, in the place of the exhausting open operation with prolonged drainage. Later, I advised in addition the continued administration of full doses of ipecacuanha after any form of operation on such abscesses. This method is being used with increasing success in Calcutta at the present time, although it fails in some cases. The proof afforded in my recent paper that soluble salts of emetine rapidly kill the amoeba of dysentery when used in much higher dilutions than the quinine salts, clearly indicates the former drug as the more efficient one for the purpose just mentioned. Moreover, the evidence above recorded in this paper, to show that emetine can be given in sufficient doses to kill off rapidly all the amoebae in the greatly thickened wall of the large bowel in acute dysentery, made it highly probable that it would act equally well on the parasites in the walls of amoebic abscesses of the liver. The following remarkable case will show that this is actually the case.

CASE IX.—Acute Amoebic Dysentery with Multiple Liver Abscesses, in which all the Amoebae in the Litter were Killed by Subcutaneous Injections of Emetine.

A native male, aged 30, was admitted in a very low state for severe dysentery of two months' duration. I examined the stools and failed to find any amoebae, but as he was not improving $\frac{1}{2}$ -grain doses of emetine were injected twice on two consecutive days, making a total of 2 grains in all. The dysenteric stools decreased in number and much improved in character, but he remained in a low condition, and died twenty-six hours after the last injection. At the *post-mortem*

examination I found extensive ulcers of the amoebic type throughout the large bowel, but, with the exception of one extensive sloughing one in the caecum, their bases were clean and smooth and their edges overhanging, as if they had recently lost the usual tawny yellow gelatinous infiltration. The cause of death was found to be very numerous small recent amoebic abscesses of the liver from $\frac{1}{2}$ in. to 2 in. in diameter, scarcely a square inch of the cut surfaces being free from them. The pus from several of them proved sterile as regards bacteria on culture. I spent a long time examining scrapings from the walls of a number of the abscesses, but failed to find a single living amoeba, although in similar cases I had always been able to detect them with the greatest ease. On adding to the pus a little watery methyl-blue a few unstained granular degenerate amoeba-like cells were found, similar to amoebae which have been subjected for a short time to the action of a very dilute solution of emetine. These observations left no doubt in my mind that every amoeba in the liver had been killed by the emetine injected subcutaneously during life, as the body was fresh and the temperature very favourable for the preservation of the parasites. Moreover, sections of the walls of some of the smaller abscesses stained with haematoxylin also showed no amoebae, although they are readily demonstrated in this way when emetine has not been used in the treatment.

This case, taken with No. III above recorded, appear to me to afford strong evidence that emetine salts administered hypodermically in sufficient doses will kill all the amoebae in both the intestinal and liver abscess walls, and thus explains the extraordinary results recorded in this and my former paper, and affords good hope of even more uniform success in the treatment of the deadly and widespread amoebic infections when the new method is fully worked out and the most useful and safe doses ascertained. The following cases will serve to prove that emetine is also of great value in the treatment of amoebic abscesses of the liver and spleen, and is likely in the near future to save a large proportion of these unfortunate patients from the surgeon's knife.

CASE X.—*Epigastric Liver Abscess Cured by Aspiration and Emetine Injections after Failure of the Quinine Treatment.*

A native lad, aged 15, admitted for a liver abscess bulging in the epigastric region. Six ounces of liver pus were removed by aspiration, and 1 oz. of saline containing 10 grains of the soluble bihydrochloride of quinine injected into the cavity, and the puncture sealed with collodion. Intermittent fever continued and the abscess cavity refilled within four days. A second aspiration was now done, 8 oz. of liver pus being removed, and 1 grain of emetine hydrobromide, dissolved in 2 oz. of sterile salt solution, was injected into the cavity. The emetine salt was also injected subcutaneously in $\frac{1}{2}$ -grain doses every morning for four days, and again on the sixth day. In addition, 10 grains of ipecacuanha were given by the mouth every evening. After two days the temperature fell to normal and never again rose above 99° F. The abscess cavity steadily contracted and the tissues became firm, and he was discharged cured just under one month after the emetine injection, having been detained under observation to make sure that the abscess did not refill. This case is one which would, in all probability, have done well by the open operation, as the abscess was a comparatively small one, but the rapid subsidence of the fever, and cessation of formation of pus under the influence of emetine was very striking.

CASE XI.—*Right Lobe Liver Abscess Cured by Aspiration and Injection of Emetine.*

A native male, aged 30, admitted for liver abscess following dysentery six months before. On aspirating through a lower right intercostal space, 8 oz. of typical liver abscess pus were withdrawn and 1 grain of emetine hydrobromide dissolved in 2 oz. of sterile salt solution injected into the cavity and the puncture wound sealed with collodion. Half-grain doses of emetine were injected subcutaneously on each of the four following mornings and 25 grains of ipecacuanha given in the evenings, my supply of emetine being then very limited. The temperature rapidly fell to normal, but on three occasions during the next thirteen days it reached 100° F. in the evening. At the end of this time the liver was normal in size and there were no signs of further collection of pus, but to make quite sure a second exploration under an anaesthetic was now performed, with a negative result, and subsequent convalescence was only interrupted by a mild attack of benign tertian malaria.

In addition to the above cases, a third, very similar to No. XI, has done equally well, but it is yet too early to be certain of his permanent cure. On the other hand, in two others the pus obtained at the time of aspiration and injection of emetine was found on culture to contain large numbers of staphylococci, and consequently the abscesses had to be opened and drained, with ultimate recovery. I have previously pointed out, in connexion with my method of treating amoebic liver abscesses by aspiration and injection into the cavities of soluble quinine salts, that such a plan should only be persisted with if the pus is free from marked secondary bacterial infection, as is the case in 85 per cent. in my experience.

Amoebic Liver Abscesses Cured by Aspiration and Subcutaneous Injections of Emetine.

In two other cases, one of which is still under observation, liver abscess pus was evacuated by aspiration and emetine injected subcutaneously, but not into the abscess cavity. In one the emetine injections were given for acute hepatitis, which greatly improved, but, as leucocytosis persisted, the liver was explored and several ounces of pus withdrawn, after which steady convalescence ensued and the leucocytosis disappeared. In the other the emetine injections were commenced two days after the aspiration of liver pus, with an equally happy result. A single aspiration so exceptionally cures such cases that these two successive recoveries are in all probability due to the action of the subcutaneous injections of emetine in destroying the amoebae in the walls of the liver abscesses, so it may eventually prove unnecessary to inject the drug into the cavities; although in view of the harmlessness of the procedure, and the certainty that it will kill the parasites in the superficial parts of the lining membrane, it is advisable to do so in the present state of our knowledge.

CASE XII.—*Amoebic Abscess of the Spleen Cured by Aspiration and Emetine Injections.*

A native male, aged 32, admitted with enlargement of the spleen to 2 in. below the left costal margin and a tender prominence of the lower ribs, with redness of the skin over it. On exploration 8 oz. of thick reddish pus and blood, closely resembling that of amoebic liver abscesses, were withdrawn. Three days later there was evidence of refilling of the cavity, so a second aspiration of 4 oz. was performed, and this time 1 grain of emetine hydrobromide in 2 oz. of water was injected. I examined the pus microscopically, and found amoebae to be present, while it was sterile on culture for bacteria. On each of the next two days half a grain of emetine was injected subcutaneously, but the temperature once more rose, and six days after the second aspiration there was again slight bulging. A third aspiration was now done, but only a little pus and much blood was obtained, and a grain of emetine hydrobromide was again injected into the cavity, and two more $\frac{1}{2}$ -grain doses given subcutaneously. The temperature finally fell to normal two days later, and the abscess did not again refill, but complete recovery ensued.

This case is of great interest, both on account of the rarity of amoebic abscess of the spleen and because of its successful treatment by the new method; for when opened they are liable to heal very slowly and to leave obstinate sinuses. It was for this reason that a repetition of the emetine injection into the cavity was carried out, with the fortunate results recorded.

Taken as a whole, the cases above detailed of amoebic abscesses of the liver and spleen treated by emetine injections are full of promise. If further experience should confirm them a new era will be commenced in the treatment of this very serious and fatal disease, for the causative parasite can be destroyed by injections of emetine salts into the abscess cavities, after very thorough evacuation of their contents by aspiration, and subcutaneous injections of the same drug will kill the organisms in the deeper layers of the abscess wall through the blood stream (as well as in any latent amoebic ulcers in the large bowel which may have produced the liver trouble), and thus the necessity of resorting to the much more serious and exhausting open operation and prolonged drainage, with the almost inevitable secondary bacterial infection of the wound in damp hot climates, may be largely done away with, greatly to the comfort and benefit of the patients.

The Disappearance of Leucocytosis as Evidence of the Cure of an Amoebic Abscess of the Liver.

When using the above method it is often difficult to decide if the abscess is completely cured, or if some pus has again accumulated, necessitating a further aspiration. Here leucocyte counts are of great value, for I have frequently found that if an original actual or relative leucocytosis has not disappeared within about a fortnight after an aspiration, pus will usually be again found on exploring; while if the original increase in the white corpuscles has vanished, the abscess is really cured, and further aspirations are negative, although usually harmless.

Dosage.

Either the hydrochloride or the hydrobromide of emetine are equally useful, the former being the more soluble, while the latter requires about 2 c.cm. of sterile water or saline to dissolve it. At first I chiefly used $\frac{1}{2}$ -grain

doses, but now very seldom employ less than half a grain at a time, and often give as much as two-thirds, the equivalent of 60 grains of ipecacuanha, and have twice injected 1-grain doses subcutaneously without any vomiting or depression, but such a quantity is only required in extremely acute amoebic dysentery. The salts can be safely boiled for a very short time, but it is better to dissolve them in sterile saline, or to boil the solution first and then add the emetine salt. I have arranged with Messrs. Burroughs and Wellcome to put up the drugs, both as tablets and already dissolved in sealed ampoules, while Messrs. Parke, Davis are also supplying them in the latter form.

The Value of Emetine Treatment in the Differential Diagnosis of Amoebic from other Varieties of Dysentery.

The extraordinary rapidity with which very marked improvement follows the subcutaneous injections of $\frac{1}{2}$ -grain doses of emetine is of the greatest diagnostic importance, for cases of bacillary dysentery and other non-amoebic causes of the presence of blood and mucus in the stools are not, in my present experience, materially affected by the drug, although it has done no harm in them. Thus, in a case of chronic bacillary dysentery complicating kala-azar, emetine injections had no effect, and the disease steadily progressed to a fatal termination. Again, I was asked to treat with emetine a case of suspected amoebic dysentery with six to seven stools of blood and mucus daily. On examination the patient pointed to the caecal region as the seat of pain, and clinically I also thought the case to be probably amoebic, so injected $\frac{1}{2}$ -grain doses of emetine hydrobromide daily for three days, without the slightest effect on the number or character of the stools. I twice examined the stools for amoebae, with negative results, while cultures failed to separate any bacilli which would clump with either Shiga or Flexner serum. The rectum was then examined, and cancer detected high up. The failure of adequate subcutaneous doses of emetine to produce marked improvement within two or three days is, then, very strong evidence that the disease is not of amoebic origin. This specific action of emetine salts in amoebic disease alone is of the greatest interest and importance. Ever since I was the first to recognize the frequent occurrence of amoebic dysentery in India and to demonstrate that living amoebae are always present in scrapings of the walls of large tropical liver abscesses, I have never doubted the pathogenic action of these parasites. In my experience, whenever active amoebae of the *histolytica* type, including the variety described by Noc and shown by Grieg to be the common one in India, have been found in dysenteric stools (and I have almost invariably found this form only), the disease has eventually proved amenable to full doses of ipecacuanha, if not too acute or far advanced. Still, facilities and time for the microscopic examination of the stools of the large number of dysentery cases which often have to be dealt with in the tropics, are seldom available, so a simple and harmless clinical method of differentiating amoebic from other forms, such as is now furnished by the emetine treatment, is clearly of the greatest practical importance, and will also lead to the early adoption of suitable treatment in those cases, which prove not to be amoebic in nature. Moreover, it will allow of more rapid advances in our knowledge of the distribution of the two great classes of dysenteries than can be furnished by the very limited number of workers available for bacteriological researches on this subject in the tropics. We may, perhaps, also hope to hear no more doubts as to the existence of amoebic dysentery as a separate entity, such as were expressed in a recent editorial in a leading Indian medical journal.

Conclusion.

We have, then, in my method of the subcutaneous injection of soluble salts of emetine a specific treatment of amoebic hepatitis and amoebic dysentery, which is so rapidly beneficial in the latter as to be also of great diagnostic value between that and other causes of the passage of blood and mucus in the stools. Yet, strange to say, this remarkable remedy—probably the most active specific in the whole range of medicine, not excluding quinine and salvarsan—has for long been thrown away by those who pinned their faith in ipecacuanha sine emetina.

GRANULE-SHEDDING IN TRYPANOSOMA GAMBIENSE.

BY LIEUTENANT H. S. RANKEN, R.A.M.C.,
SUDAN SLEEPING SICKNESS COMMISSION, YEI, LADO ENCLAVE.

THE "infective granule" in trypanosomiasis has been described by Major W. B. Fry, R.A.M.C.¹ Major Fry kindly demonstrated to me the presence of these bodies in experimental trypanosomiasis in animals, and I have continued investigations on similar lines here. As I am unaware of observations having been made on the "granule" of *Trypanosoma gambiense* in human trypanosomiasis, the following notes may be of interest.

Blood and gland puncture wet preparations from cases of sleeping sickness have been examined by the dark ground method, and the results confirmed by vital staining.

"Granules" are present in the trypanosomes—usually three or four in number. They are small, circular, highly refractile bodies, obviously within the trypanosome, and constantly swinging backwards and forwards in its long axis, the wriggling or lashing of the host causing these movements. When the energy of the trypanosome diminishes, it may be observed that the granules do not swing to and fro synchronously with its movements but perceptibly later; apparently there is an interval for the transmission of a wave, the granules lying more or less free within the envelope of the trypanosome. This activity of the granules gradually increases in the wet preparation, and is further exaggerated if the trypanosome becomes anchored by the posterior pole and exhibits lashing movements of the body and flagellum; the granules are then seen to be perpetually dancing in every direction within the body, sometimes impinging on the cell membrane and rebounding from it. I do not suggest that the trypanosome is actually trying to discharge the granule by its movements, but the process appears very purposeful, and the granules seem as if they were anxious to get free. Finally the granule succeeds in its efforts and shoots out into the surrounding medium; it has been noticed that, before being shed, the granule in many instances approaches the surface, and may actually bulge out the covering membrane.

In older preparations the trypanosomes begin to show signs of fatigue and later of degeneration; this may be due to change of temperature, but is probably the effect of the powerful light to which they are exposed. They move sluggishly and sometimes become swollen and bloated. At the same time the granules exhibit changes, both in number and size. Instead of what may be regarded as the normal three or four granules of *T. gambiense* there may be five or six; frequently one or two are larger than the others, and sometimes there are very small granules in pairs closely apposed and connected in some way, as they move in unison and the transmitted wave affects them together. (The questions arise: Is this multiplicity due to fission? and is it only the larger granules that are concerned with a reproductive process?) At this stage granules may still be extruded, but when the trypanosome becomes even less active, extrusion is very uncommon. A later stage is reached when a trypanosome loses its natural form, swells up and becomes almost circular, while still showing one or two granules which it is unable to extrude. On the other hand, a trypanosome may be seen normal in form but quite inert and not containing any granules; it would seem, however, to be exceedingly rare for a trypanosome to discharge all its granules.

The occurrence of granule shedding is quite distinct, but is, I believe, relatively uncommon in normal circumstances. It is exceedingly easy to be deceived, as in these preparations there are countless dancing bodies—haemoconia and leucocyte granules, which impinge on the trypanosome, and are flung away by its lashing movements; also it is possible for these particles to adhere temporarily to the envelope of the trypanosome, and be detached at any time by some forcible movement. The objection may be raised, How can one ever be sure of extrusion of a "granule" if this fallacy be admitted? This, however, can be met by pointing out that, if particles should adhere to the trypanosome, they cannot swing to and fro in its long axis. Again, the larger granules have been seen to escape from a mori-