THE EFFECTS OF AMOEBIC DYSENTERY AS ENCOUNTERED IN BRITISH TROOPS FROM 1942 TO 1946.

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Recent experiences in the Tropical Theatres of War have brought forward the problem of Amoebic Dysentery, a disease of considerable latency prone to relapse and to a chronic course during which it becomes extremely refractory to treatment.

It is proposed to describe the disease as it was observed in Bengal in 1942 and 1943 and later to discuss cases of Amoebic Dysentery treated in the United Kingdom in 1945 and 1946.

The importance of the disease is enhanced by the fact that manifest cases may form only a small proportion of the persons infected at any one time. Silverman and Leslie[1] describing Amoebic Dysentery in the United States say "In new Orleans alone it has been estimated that the protozoon is harboured by close to 15% of the general population. Most of these cases are symptomatically below the clinical threshold". Statistics compiled following the last War also emphasise the latency of the infection. Stitt[2] makes the following statements:- "Of nearly 7,000 troops and civilians, without any history of bowel trouble, examined in the Eastern Mediterranean Area or invalided from that region, 10.5% were found infected". The evidence of latent infection can well be surmised in an area such as Bengal and it is scarcely surprising that many British troops acquired Amoebic Dysentery there.

The first collection of cases to be described were almost all fresh infections arising among British troops in Bengal in 1942. At this time, one first became acquainted with the disease and observations were made on a large scale.

The second series of cases was treated in Bengal in 1943 and chronic cases only will be discussed. The refractory character of the Amoebic Type of infection was now giving rise to concern and increasing numbers of chronic cases were encountered. The incapacitating effects of Chronic Amoebiasis, the attempts at cure and the results of therapy will be discussed.

Thirdly, a few cases treated in the United Kingdom in 1945 and 1946 as the result of recent advances in therapy will be described.

Discussion of the views of various writers on Amoebiasis will be carried out and the conclusions from the three Groups of cases treated over a period of four years will also be discussed.

Finally, the main points of importance will be briefly summarised.

THE FIRST GROUP OF CASES.

Amoebic Dysentery will now be described as it was encountered in a British General Hospital in Calcutta between May, 1942, and December, 1942, a period of eight months inclusive. At this time the condition was met with on a scale not hitherto experienced among British Troops in this region. The influx of fresh troops into the area from the United Kingdom and the arrival of cases from the Burma Retreat were the main factors causing an increasing number of patients.

The large number of cases of Amoebiasis can be gauged from the fact that about twenty beds were reserved for Dysentery cases in the Hospital at the beginning of 1942 while in August, 1942, a two hundred bedded Hospital was required for patients with Dysentery alone and the beds were always full.

Analysis of Cases of Dysentery.

The total number of cases of Dysentery of all types treated from May to December, 1942, was 1,672 and an analysis of the relative incidence of the types of Dysentery is of interest.

Type of Dysentery.	Number of Cases.	Percentage of Cases.	
Amoebic Dysentery	815	49%	(Includes 1% Amoebic Hepatitis)
Bacillary Dysentery	562	34%	
Clinical Dysentery	256	15%	
Mixed Bacillary and Amoebic Infections	39	2%	
TOTAL	1672	100%	

Even if it is postulated that the majority of cases of Clinical Dysentery were, in fact, mild cases of Bacillary Dysentery, it will be seen that Amoebic Dysentery was more common than Bacillary Dysentery. Amoebic Dysentery, with its far greater tendency to relapse, was therefore a problem of some magnitude.

The relative proportions of Amoebic and Bacillary Dysentery are of interest when compared with work cited by Manson Bahr[3] in the text book "The Dysenteric Disorders". J. Cunningham (1923) found that "86% of the Dysentery in the jails of Bengal was Bacillary". Acton and Knowles found in 1920-1923 "that in Calcutta, Bacillary Dysentery was at least five times as common as Amoebic".

Diagnosis of Amoebic Dysentery was of a high standard in this series of cases and was made on the finding of Vegetative Entamoeba Histolytica in the stools in every case.

Aetiology.

This was studied from the point of view of length of Service in India and Seasonal Incidence.

It was found that of 200 cases, 64% had served for six months or less in India. The disease was therefore a fresh infection of recent arrivals in the Tropics in the majority of cases. This is explained partly by the fact that large numbers of troops in the Area had only spent a short period in India. It is without doubt also an indication of the liability to infection of troops who have not yet acquired the knowledge of avoiding food and drink from doubtful sources.

With regard to the Seasonal Incidence, there was a marked rise at the time of the Monsoon, i.e. approximately early in July to the beginning of September with a subsequent tailing off from the end of the Monsoon to the cooler months. Flies would seem to be an unlikely vector during the torrential rain of the Monsoon and a water borne spread at this time is the apparent cause of the high incidence. Bacillary Dysentery, the monthly figures for which are also stated, showed a similar maximum rise during the Monsoon Season. Infected water was therefore the most likely source of both types of Dysentery.

Cases of Dysentery treated in 1942 and January, 1943.

Type of Dysentery	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.
* Amoebic Dysentery.	7	23	150	149	112	154	107	102	47
Bacillary Dysentery.	17	33	100	139	48	66	68	91	52

* Amoebic Hepatitis not included in this Table.

Clinical Features of the Cases.

The average case of Amoebic Dysentery was admitted to Hospital with a history of diarrhoea with blood and mucus of a few days to a few weeks' duration. Abdominal pain was generally present.

The patient was usually ambulant on admission and the condition did not impress one as being particularly serious initially. It was only later that the chronic nature of the complaint became apparent.

Mortality.

Deaths were few in this series. There were four fatal cases during the period and of these one was due to Amoebic Dysentery only while the remaining three were mixed Bacillary and Amoebic infections. The fatal cases were all admitted in a serious condition.

Out of 854 cases of Amoebic and mixed Bacillary and Amoebic infections, the Mortality therefore amounted to 0.5%.

Therapy.

The treatment in current use in 1942 consisted of 12 injections, each of gr. 1, of Emetine Hydrochloride. A period of four days rest was given after the eighth injection of Emetine and a course of Carbarsone, gms. 0.25 b.d., was given commencing on the second day of rest and continuing for ten days.

Test of Cure.

This consisted in the examination of the stool on six successive days for E.H. or E.H. cysts with negative findings.

Investigation on the Evaluation of Carbarsone.

Carbarsone was found to be particularly effective against the cystic form of E.H. At first it was given only when E.H. cysts were found in the stools but later it was instituted as a routine measure.

The following investigation exhibited the value of the drug:-

126 cases of Amoebic Dysentery were treated with Emetine injections and Carrier Tests of the Stool for E.H. were made.

93 cases = 74% remained free of E.H. cysts.

33 cases = 26% passed E.H. cysts in the stool.

The cases still passing cystic forms of Entamoeba Histolytica received treatment with Carbarsone, gms. 0.25 b.d., for ten days and all became cyst free.

Carbarsone retention enemata (2%) were found to be of value in a few subsequent cyst passers who continued to pass cysts following the administration of Oral Carbarsone.

Chronic Cases.

The few cases encountered at this time were treated by a second course of Emetine injections with Chiniofon Retention Enemata.

Kurchi Bismuth Iodide was sometimes used as an interim measure during the period between courses of injections. It had a symptomatic use in checking diarrhoea but in no case were the stools found to be free from Entamoeba Histolytica following the exhibition of this drug.

Comment on the First Series of Cases.

Over 800 cases of Amoebic Dysentery were treated in this series and it has been pointed out that we were dealing mainly with a fresh infection acquired by individuals who had recently arrived in the Area. They did not present the picture of chronic invalidism that was later to become so apparent. Some of the cases had acquired Protozoal Dysentery during the Retreat from Burma but again they were almost entirely "fresh infections".

In view of the subsequent incidence of Chronic Refractory cases arising in this Theatre of War the number of cases of Amoebic Dysentery, 815 cases in addition to 39 mixed infections, and the high recurrence of Amoebic Dysentery as compared with Bacillary Dysentery are worthy of note. The period of eight months was a comparatively short one.

The peak incidence of the disease during the monsoon months of June to September is marked and, in spite of the importance of the fly as a vector, is strongly in favour of a water borne spread during the Monsoon.

Lawrence and Bennett[4] have given "A Study of Diarrhoea occurring at Army Air Force H.Q., Calcutta, India" among American Troops. They stressed the need for careful stool examination in view of the fact that 52.5% of 198 cases of diarrhoea reporting sick in the Monsoon period were found to be suffering from Amoebic or Bacillary Dysentery or both. The water supply to the camp was found satisfactory although, of course, there was no check on drinks purchased outside the camp. Effective fly control helped to check the disease. Their article describes an increase of diarrhoea at the time of the Monsoon since in July cases of diarrhoea were almost double those of any previous month. Their observations in 1944 therefore agree with ours made in 1942.

Results of Therapy.

Assessment of therapy is difficult since for operational reasons the patients were only retained until six stool examinations had been made. Many "relapses" were admitted to other Hospitals and the period of eight months is too short to exclude "relapses" in a disease which remains clinically quiescent for notoriously long periods.

Between May and December, 1942, inclusive, 5% of the cases originally treated in the Hospital were again admitted suffering from Amoebic Dysentery. It has been pointed out in the above paragraph that this was a minimal figure and that the actual "relapse rate" must have been much larger. The figure foreshadowed the incidence of chronic cases later encountered and was an unsatisfactorily high "relapse rate" within a short period.

The reasons for the adoption of treatment by Emetine injections and Carbarsone alone should be given at this stage. Firstly, it had been the standard treatment previously in vogue in the Area when cases of Amoebic Dysentery among British Troops were much fewer and a high rate of recurrence might not seem so impressive. Secondly, it has been pointed out that Amoebic Dysentery presented itself as a mild disease with a low mortality. The rapidly induced phase of quiescence following the exhibition of Emetine injections and Carbarsone lead to a dangerous sense of false security. It would hardly have seemed justifiable to give treatments involving long periods of absence from duty in a condition that appeared so mild and so quick in its response to Emetine Hydrochloride. Thirdly, the Hospital was full to overflowing and work for the Medical Staff was very heavy. Emetine injections were easy to administer in comparison with Emetine Bismuth Iodide and Retention Enemata and entailed a shorter period of Hospitalisation. The Hospital was so full at times that cases had to be evacuated hundreds of miles for completion of treatment when a few initial Emetine injections had controlled the diarrhoea. It has been previously shown that the return of the Army from Burma and the influx of new troops from the United Kingdom were the causes of the crowding of the Hospitals and that the position was further aggravated by the high incidence of Amoebic as compared with Bacillary Dysentery. Fourthly, and most important of all, Amoebicidal drugs apart from Emetine Hydrochloride and Carbarsone were in

extremely short supply. Routine treatment of cases with Emetine Bismuth Iodide and Chiniofon was impossible. Emetine Bismuth Iodide became available at a later date for selected chronic cases in special centres only.

Treatment was therefore carried out as fully as possible under the circumstances. When the poor results of therapy employed in 1942 became apparent, the Medical Authorities revised the course of treatment for Amoebic Dysentery and Emetine Bismuth Iodide was obtained when required for chronic cases.

It should be noted that the course of treatment for Amoebic Dysentery in Civil Practice in India often consists of six Emetine injections only. The production of chronic illness and carrier states with dissemination of the disease is bound to occur when such inadequate courses are employed.

The value of Carbarsone is a feature which emerges from the point of view of therapy. This drug appeared to have an undoubted effect on the cystic stage of Entamoeba Histolytica and I feel convinced that the inclusion of Carbarsone in every course of treatment for Amoebic Dysentery is justifiable. The result of the Carbarsone investigation is probably rather optimistic in view of the limited period of surveillance possible.

Kurchi Bismuth Iodide appeared to be of no value as an Amoebicidal agent although it afforded symptomatic relief from diarrhoea in some cases. It is considered that the use of this drug should be abandoned.

THE SECOND GROUP OF CASES.

The second series of cases was studied in Calcutta in a General Hospital between May, 1943, and November, 1943, with particular reference to Chronic Amoebiasis. The sufferer from Chronic Amoebic Dysentery was now more frequently encountered. Second and third attacks of Protozoal Dysentery were common. The Hospital was made into a Centre for the treatment of Chronic Amoebiasis.

The definition of Chronic Amoebic Dysentery for the purpose of this investigation was an active Amoebiasis of the colon in a patient who had previously received four courses of Emetine injections for Amoebic Dysentery.

The finding of Vegetative Entamoeba Histolytica in the stool or of Amoebic ulcers on Sigmoidoscopy was held to constitute active Amoebiasis of the colon.

The cases forming the material for this investigation were fifty in number. Special facilities had been made for their treatment with Oral Emetine Bismuth Iodide in addition to Chiniofon Retention Enemata. Each case was suffering from Chronic Amoebic Dysentery as defined above.

In describing these cases it is noteworthy that the criterion of four previous courses of treatment is a very strict one indicating a very marked degree of chronicity.

Aetiology.

The period of Service in India and the question of relapse or repeated attacks are of particular interest.

I The Period of Service in India.

Twenty cases taken at random from the series averaged two years' Service in India. Only one case had more than three years' Service in India. Chronicity was therefore developed within a relatively short period. It had moreover occurred in cases originally treated in 1941 and 1942.

II The Question of Relapse or Repeated Attacks.

The query arises as to whether (a) the cases acquired repeated infection when the bowel had healed or whether (b) Chronic Amoebic ulceration resulted in repeated attacks of diarrhoea, remaining only apparently quiescent after courses of Emetine injections.

The latter view is favoured for the following reasons:-

1. Some cases of Amoebic Dysentery in the series would become completely free from ulcers on Sigmoidoscopy three weeks after the commencement of treatment. Six stools would be negative. Nevertheless, 12% of the series, while fulfilling the above criterion of cure, again produced Entamoeba Histolytica in the stool during one month's period of observation in the Hospital. The apparent cure of the disease if observed over an inadequate period is thus illustrated.

2. Some cases had never been free from Amoebic Dysentery since the original attack and were relieved only by Emetine injections.

e.g. Case 9 acquired Amoebic infection in Assam eleven months before admission.

He spent six weeks only with his Unit since the original onset, the remainder of the time being spent in Hospital. While in Hospital, he received six courses of Emetine injections, ½ gr. 72 in all, supplemented by Stovarsol. He lost five and a half stones in weight.

There were several similar cases and it seems probable that the other cases, who were temporarily free from symptoms following repeated therapy, were also harbouring persistent Amoebic infection.

3. The known fact of the return of symptoms of Amoebic Dysentery following repatriation to the United Kingdom, where reinfection can practically be ruled out, indicates the intermittent nature of symptoms due to a latent chronic infection.

4. A case was later observed where twelve Emetine injections had been given for Amoebic Dysentery with relief of symptoms and six negative stool findings. He later died of Aplastic Anaemia and Autopsy showed large active Amoebic ulcers throughout the colon.

Symptoms.

Intermittent Diarrhoea was invariable. All cases had loose motions, with or without blood and mucus, ranging from five to ten a day.

Abdominal pain was complained of by 72% of the cases. It was usually colicky in nature. The site of the pain was as follows:-

Caecum and Ascending Colon	20%
Descending Colon and Pelvic Colon	26%
Generalised Pain	26%
No Pain	28%

Loss of weight was a frequent complaint. In 25 cases a history of an average loss of weight of twenty five pounds was given. Lassitude was almost invariable.

The average duration of symptoms since the first attack of Amoebic Dysentery was ten months.

The average number of treated attacks, as recrudescences, of Amoebic Dysentery was four.

The average total quantity of Emetine given by injection since the original attack was gr. 40. Many cases had also received Sulphapyridine, Stovarsol and Kurchi as supplementary measures.

Signs.

All the cases exhibited laxness of the skin, confirming the history of loss of weight.

Mental apathy occurred but the patients were not neurotic and cooperated well.

No marked case of Anaemia was seen.

The caecum and the descending colon were palpable and tender in about 50% of the cases.

Stool Examination.

96% of the cases were diagnosed as definitely suffering from Amoebic Dysentery by the finding of the Molile Vegetative Entamoeba Histolytica in the stool after repeated examinations.

4% were diagnosed on positive Sigmoidoscopic findings.

Sigmoidoscopy.

Sigmoidoscopy is of particular value in Chronic Amoebic Dysentery. While often of value in diagnosis, it is of special use in assessing progress of the lesions, which can be directly observed. It must be pointed out, however, that the stools may still be positive when large ulcers in the rectum and Sigmoid Colon have completely healed.

It was found that it was not necessary to pass the instrument for a distance of more than six inches in most cases. Passage beyond this distance is apt to increase both the risk and the discomfort of the procedure.

The typical lesion seen in the chronic cases was the large Chronic Amoebic ulcer of irregular shape with a hyperaemic margin and a greyish yellow sloughing base. At other times small scattered haemorrhagic flecks were dotted over the mucous membrane. A further finding in some cases was a number of pitted depressions covered by mucous membrane. These represented the sites of previous healed ulceration.

It was interesting to observe directly the response of the lesions to therapy. Large ulcers were often seen to disappear completely following combined treatment. This was often achieved within a period of three weeks after the commencement of the course. In other cases ulcers of the same size would show no change at all following treatment. The specific action of Emetine on the Amoebic lesions in some cases and the complete failure to influence the lesions in others (Vegetative Entamoeba Histolytica could be recovered from the ulcers which did not disappear) leads to interesting speculation and is in favour of an inaccessibility of the Amoeba to attack. It will be discussed further when the question of secondary infection is considered.

All cases were sigmoidoscoped on admission and again after completion of treatment, an interval of approximately three weeks elapsing between the two examinations.

Twenty uncured cases following treatment were analysed. Of these 13, or 65%, displayed tenderness of the caecum while 7, or 35%, only, showed sigmoidoscopic lesions at this time. All cases continued to pass Entamoeba Histolytica in the stools.

The lowest Sigmoidoscopic levels at which ulcers were seen are of interest (20 cases).

Anterior Rectal Fold	-	35%
Left Rectal Fold	-	30%
Pelvi Rectal Spincter	-	5%
Sigmoid Colon	-	15%
No ulcers seen although stools positive	-	15%

Thus 85% of chronic cases with positive stools showed positive findings on Sigmoidoscopic examination.

A good long Proctoscope would have shown ulcers in 65%.

Treatment.

The treatment adopted was that recommended by Manson Bahr[3] in 1941. Emetine Bismuth Iodide gr. 2 was given each evening for 10 days in the form of an emulsion or powder. Phenobarbitone gr. 1 was given one hour before the Emetine Bismuth Iodide to prevent vomiting.

At the same time each patient received 6 oz. of a 2.5% Chiniofon Retention Enema each morning for 10 days. This was preceded by washing out the bowel with a Sodium Bicarbonate Solution. Most patients were successful in retaining the Chiniofon for six hours.

Side Effects of Emetine Bismuth Iodide.

Emetine Bismuth Iodide frequently produced nausea but vomiting was not unduly severe.

A careful record of the Pulse and Blood Pressure showed no significant change following treatment.

Emetine Bismuth Iodide therefore appears to possess the advantage of being a drug of very low toxicity and in view of the known toxic cardiac effects of Emetine Hydrochloride given by injections, this fact is worthy of note in the treatment of Chronic Amoebiasis.

Diet.

The Diet need not be described in detail. None of the patients were starved but roughage was avoided.

Test of Cure Applied.

Cases who had six negative stools after treatment with a negative Sigmoidoscopic examination and who developed no fresh symptoms or signs during a period of observation of one month were presumed cured after re-examination.

Results.

Cured Cases.			
After One Course	-	36%	Total 42%
After Two Courses	-	6%	

Failed Cases.			
After One Course	-	52%	Total 58%
After Two Courses	-	6%	

Comment on the Clinical Features of the Cases.

The Symptoms and Signs of Chronic Amoebic Dysentery may be summarised as lassitude, intermittent diarrhoea and loss of weight with abdominal pain and tenderness in the majority of cases.

While Sigmoidoscopic examination was helpful and showed lesions in 85% of the cases, it will be seen that the only reliable diagnostic measure is the finding of Vegatative Mobile Entamoeba Histolytica in the stool and this was achieved in 96% of the cases. Repeated examinations of fresh stools are of course necessary.. In the Hospital the Laboratory was adjacent to the Annexe. The patient put his name on a piece of paper and placed the paper with the bed pan in a fly proof cupboard in a room adjoining the Laboratory. The stool was immediately collected and examined, examination thus taking place within a few minutes of the passage of the stool.

Comment on Results of Treatment.

Fifty Chronic cases of Amoebic Dysentery, averaging four courses of Emetine injections over a period of ten months, were an indication of the unsatisfactory nature of the treatment of Amoebic Dysentery by this method.

The A.L.F.S.E.A. Technical Memorandum of 5th July, 1944, emphasised the necessity for more intensive treatment and more thorough standards of cure.

Emetine Bismuth Iodide was in extremely short supply and the arrival of the drug in limited quantities for the treatment of Chronic cases in our Centre was welcomed. The treatment carried out was that recommended by Sir Philip Manson Bahr in an article to the Lancet[5] and in his book "The Dysenteric Disorders"[3]. Manson Bahr in the former article quotes Carmichael Low and Dobell (1916-1918) and states that Emetine when injected does not come directly into contact with the precystic form of Entamoeba Histolytica because it is not excreted in the faeces. Emetine Bismuth Iodide is excreted in the faeces and acts on the cystic forms of Entamoeba Histolytica. Manson Bahr states that a total quantity of Emetine Bismuth Iodide gr. 20-30 should be given in doses of gr. 2-3 for ten nights and that a 2.5% Chinofon retention enema should be given concurrently every morning for ten days. He states "In a series of 361 so treated there was a relapse rate of 3.7% within a year: but this residuum was finally cleared of infection by a further course of the same treatment combined with portein shock therapy."

The course recommended by Manson Bahr was not tried in fresh infections in our Centre as Emetine Bismuth Iodide was not available in sufficient quantity. It was hoped that it would prove successful in Chronic Amoebiasis. It has been shown that, while an advance on treatment by injections of Emetine Hydrochloride, 42% of the cases only were cured.

Manson Bahr[5] states that insoluable preparations of Emetine Bismuth Iodide and excessive quantities of Chiniofon with inadequate retention are common causes of failure. These factors do not apply in the series of Chronic cases.

58% of the Chronic cases in this series had to be returned to the United Kingdom as uncured and there was thus a need for still more intensive therapy in Chronic Amoebic Dysentery in the Far East.

The fact which emerges is the definite superiority of oral Emetine Bismuth Iodide over Emetine Hydrochloride injections in the treatment of Chronic Amoebiasis of the Colon.

The possible causes of failure in the 58% of cases of this series who failed to respond to treatment will be discussed later.

In conclusion, and to stress the invalidism and incapacity caused by the Chronic form of the disease, the period of absence from duty of twenty of these cases will be given. It was ten months within a period of two years' Service in India, surely a most urgent argument for the energetic treatment of this disease, however long the period employed in therapy may be.

TWO FATAL CASES TREATED IN 1943.

Two severe cases which do not belong to the Chronic Series will be described here. They belong to this period chronologically and are included with the object of describing concurrent bacterial infection in Amoebiasis, a condition which will be prominent in the third Group of cases and in the Discussion.

Case One - A.C. F.D.

History of occasional diarrhoea of one year's duration. Admitted 27.7.43. Stools examined repeatedly and on 29.7.43. Vegetative Entamoeba Histolytica was found with a Bacillary Exudate. No organism cultured.

Toxaemia increased despite Emetine injections and Sulphapyridine and the patient died on 2.8.43.

Post Mortem Examination.

About one pint of thin greyish pus in the pelvic cavity. Flakes of fibrino pus and a small collection of fluid between the coils of the bowel. Surface of large bowel covered with fibrin, intensely but patchily congested.

Perforation on lateral aspect of splenic flexure, about a quarter of an inch in diameter with liquid faecal contents escaping. Large intestine very friable and tore on the slightest manipulation. About six large areas were seen completely devoid of mucous membrane, completely encircling the bowel for a distance of four to five inches and covered by partially detached yellow sloughs.

Pathologist's Comment.

Death due to peritonitis due to perforation of the large bowel due to Bacillary Dysentery.

Amoebic Dysentery also present.

Case Two - C.Q.M.S. F.C.

Admitted 16.7.43. Diarrhoea for three days. Nausea and vomiting after food. Temperature 101°.

18.7.43. Stool showed Vegetative Entamoeba Histolytica.
19.7.43. Emetine injections commenced.
20.7.43. Irregular remittent pyrexia persisted. Onset of pain in the Right Iliac Fossa.
21.7.43. Condition deteriorated. Increasing abdominal distension. Patient died.

Post Mortem Examination. Performed by Major Parker, RAMC.

About two oz. of fluid in the peritoneal cavity. Peritoneal surface of the large bowel markedly and of the small bowel somewhat reddened. No evidence of perforation.

The large bowel was grossly dilated in the whole of its course and accounted for the distension. The Sigmoid Colon practically filled the pelvis. The Caecum was adherent laterally and anteriorly to the abdominal wall by a fibrous adhesion. The appendix was absent.

The wall of the large bowel showed inflammatory changes throughout its whole extent. Very large numbers of Amoebic ulcers were present in uniform concentration throughout the whole length. Many were over half an inch in diameter. Most were oval and lay parallel to the mucosal folds. The floors were covered with dark sloughs. The intervening mucosa showed some diffuse reddening only.

Pathologist's Comment.

Death was due to toxaemia from Acute Intestinal Amoebiasis.

Comment on the Two Cases.

In both cases there was evidence of secondary bacterial infection. In the first case the organism was thought probably to belong to the Bacillary Dysentery Group but there was no definite proof of this. The fact remains that secondary infection was responsible for the friable state and perforation of the bowel and the subsequent death of the patient.

The second patient exhibited marked toxaemia and the inflammatory changes throughout the bowel indicated bacterial invasion as Amoebic Dysentery per se produces a localised lesion.

THE THIRD GROUP OF CASES.

The final Group of cases to be described was collected in the United Kingdom in a Military Hospital in 1945 and 1946. The series is unfortunately small as the Hospital dealt with all types of cases and patients with Amoebic Dysentery were only occasionally encountered. The cases quoted were all chronic in type as the Chronic Disease is of particular interest in view of the preceding two groups of cases treated in India.

The care of fresh infections in 1942 and of chronic cases treated in 1943 having been described, the treatment of Chronic Amoebiasis in 1945 and 1946 in the light of the most modern methods of therapy warrants a full description. The record in the first two Groups has been one of a considerable percentage of failures and it has been shown that prolonged and thorough treatment is essential, particularly in the established chronic form of the disease.

The cases in this series were five in number. Three were chronic cases of Colonic Amoebiasis while the remaining two were suffering from Amoebic Hepatitis. The patients with Hepatic infection had both suffered from Chronic Colonic Amoebiasis and merit inclusion in the Group.

The course of treatment adopted was in accordance with the work of Lt.Col. W.H. Hargreaves[8]. This treatment was circulated in the Army in a Medical Memorandum and has given extremely encouraging results in the few of my cases treated in this manner to date. While working in a Military Hospital in England, Hargreaves gave Penicillin to an almost moribund case of Amoebic Dysentery at Major General Biggam's suggestion. The Penicillin was followed by the usual methods of treatment. Impressed by the results of treatment, he developed an initial course of 2,000,000 units of Penicillin and 80 gms. of Sulphasuxidine in all chronic cases of Amoebic Dysentery before proceeding with Amoebicidal drugs. It was found that the appearance of the bowel, as observed through the Sigmoidoscope, would often improve before any anti amoebic treatment was given. He treated 47 severe refractory cases and states "have rarely found more than one course of E.B.I. to be necessary to cure the Amoebic infection".

He concluded his article by saying "It has been found that an attack on invading Bacteria with Penicillin and Sulphasuxidine produces improvement in severe refractory cases of Chronic Amoebiasis and makes them more amenable to specific anti amoebic treatment".

Hargreaves' period of "follow up" as his cases were observed in the United Kingdom and no line of evacuation was necessary, was thorough and makes his results all the more valuable.

Three cases of Chronic Colonic Amoebiasis were treated:-

Case One - Sgt. R. Aet 35.

The patient was admitted to Hospital for treatment of a Dermatological condition. On 24.1.46. he complained of colic and loose motions with the presence of Macroscopic blood which occurred on 25.1.46.

He gave a previous history of three treated attacks of Amoebic Dysentery in October, 1944, March, 1945, and September, 1945. He received Emetine injections and Yatren Retention Enemata on each occasion.

On examination the patient was obviously underweight. No abdominal tenderness was present and the liver and colon were not palpable.

The stool showed Vegatative Entamoeba Histolytica on 28.1.46. Sigmoidoscopy on that date showed numerous large irregular ulcers, each 2 to 5 m.ms. in diameter. The margins of the ulcers were red and congested while their bases were covered with a yellow slough. A culture was taken on a Blood Agar medium from the ulcers and showed no pathogenic organisms. Culture on a Desoxycholate medium was negative.

On 29.1.46. a course of Penicillin, 100,000 units as an initial dose and then 33,000 units 3-hourly, was commenced by intramuscular injection, and was continued until 2,000,000 units had been given. A course of Sulphasuxidine, gms. 5 four hourly, was given, the total quantity being gms. 80. On 2.2.46. the patient felt much better and was having one loose motion a day only.

On 5.2.46. a course of Emetine Bismuth Iodide, gr. 3 each evening for 12 days, was commenced and the patient concurrently received a 2.5% Yatren Retention Enema each morning for 12 days. This was followed by Carbarsone, gms. 0.25 b.d. for twelve days.

Proctoscopy on 20.2.46. showed no ulceration of the rectum, the condition having completely cleared from that region. At this time the patient was having two loose motions, without blood, each day.

Condition on Completion of Treatment.

The patient was passing one formed motion a day only. His appetite was good and he had no complaint of abdominal pain. He had gained 2½ lbs. in weight. No abdominal tenderness was present. Six stools were negative for Entamoeba Histolytica and a proctoscopy had shown no ulceration.

The patient was discharged from Hospital and is being kept under observation. He has agreed to report back to the Hospital at monthly intervals for further examination.

Case Two - Pte. U. Aet 31.

The patient was transferred to the Military Hospital on 9.1.46. from an E.M.S. Hospital where he had been admitted on 26.11.45. and treated as a Post Dysenteric colitis.

He stated that the motions had been loose since 24.11.45. and that he had noticed blood in them. Apart from this he had no symptoms.

He gave a history of three previous attacks of Amoebic Dysentery and two attacks of Bacillary Dysentery in India and Burma. He was treated with Emetine injections and Carbarsone for each attack and received Yatren Retention Enemata for the second attack. During the first attack he was among the cases described in the original group of cases treated in Bengal in 1942.

On 9.1.46. he was found to be well nourished and the liver and colon were not palpable or tender. Stool examinations were negative.

On 21.1.46. a Sigmoidoscopy was carried out. The rectum was tender and the mucous membrane was indurated and diffusely congested. It presented marked irregularity of the surface. Several irregular ulcers, 2 to 4 m.ms. in diameter and with yellow sloughing bases and hyperaemic margins, were visualised. The swab taken from the ulcers showed no E.H.

On 23.1.46. Proctoscopy was carried out and a specimen taken from an ulcer was examined immediately. Vegetative Entamoeba Histolytica was present. A culture taken on a Blood Agar plate showed numerous Haemolytic Streptococci. No organsisms of the Bacillary Dysentery Group were grown on a Desoxycholate Medium.

Penicillin, Sulphasuxidine, Emetine Bismuth Iodide, Yatren and Carbarsone were administered as in the previous case. Diarrhoea had almost ceased by the end of the Penicillin and Sulphasuxidine course.

Condition on Completion of Treatment.

A fortnight after completion of treatment the patient was examined. He was passing one formed motion only in 24 hours and no blood was present. He had no complaints at all and was gaining weight.

No abdominal tenderness was present and the colon was not palpable. Six stools were examined for Entamoeba Histolytica and all were negative. Proctoscopy at the time of completion of treatment showed a little pitting of the mucous membrane due to healed ulceration only.

He was discharged to Civil Life and is reporting his future progress by post.

Case Three - Bdr. B. Aet 26.

The patient had been a Prisoner of War in Japanese hands in Malaya for three years.

He was transferred to the Military Hospital on 18.11.45. He gave a history of intermittent looseness of the motions since July, 1942. Blood and mucus were originally present in the stools at the onset.

He had received four prolonged courses of treatment for Amoebic Dysentery since the onset and stated that gr. 151 of Emetine had been administered by injection at various times. He had also been treated with Yatren and Quinoxyl Retention Enemata on several occasions and Carbarsone was administered in addition. Records were scanty but the patient stated that his stool had always been positive on examination for Entamoeba Histolytica in spite of treatment.

He received some of the Emetine injections while on transit through India and suffered from a sudden onset of breathlessness which was attributed to the action of Emetine on the heart.

Condition when first seen.

On 18.11.45. he still complained of breathlessness. He was passing 8 to 9 loose stools every day and complained of pain below the right costal margin and of colicky pain in the left iliac fossa.

On examination his general condition was fair and he was well nourished, having gained weight rapidly since his release.

The liver was palpable two finger breadths below the costal margin and was tender. The descending colon was palpable and tender.

The pulse rate was 92 and the B.P. was 120/80. No Cardiac Murmurs were present on auscultation.

The ankle jerks were absent owing to Beri Beri.

Stool examination showed the vegetative form of Entamoeba Histolytica.

Sigmoidoscopy showed large deep chronic ulcers with haemorrhagic edges over the rectal wall. The mucous membrane between the ulcers appeared congested and inflamed.

Blood examination. Total White Cells 7,450. Neutrophil Polymorphs 66%, Lymphocytes 20%, Monocytes 11%, Eosinophils 3%.

Treatment. A course of Penicillin 2,000,000 units and Sulphasuxidine gms. 80 was followed by a course of Emetine Bismuth Iodide, Yatren and Carbarsone as in the previous cases.

An Electrocardiogram having shown no abnormality, it was considered justifiable to give full doses of Emetine.

On 16.12.45., the treatment having been completed, he was having two motions a day only and the abdominal pain had disappeared. He had gained 10 lbs. in weight since admission. The liver was still palpable and tender and the pelvic colon was thickened and tender. Sigmoidoscopy showed a perfectly normal appearance, the ulcers having disappeared. The stool, however, showed fairly numerous vegatative and cystic forms of Entamoeba Histolytica.

It was thus evident that the first course of treatment had failed, the rectal ulcers having cleared up while ulceration obviously persisted higher in the bowel.

A second course of Penicillin, Sulphasuxidine, Emetine Bismuth Iodide, Yatren and Carbarsone was commenced on 16.1.46. and completed on 17.2.46.

Condition following treatment.

A fortnight after the completion of treatment, the patient was passing two to three motions a day. The stools were occasionally loose. He complained of slight occasional pain in the R. subcostal region only.

On examination his weight was 12 st. 4¾ lbs., representing a gain of one stone since admission. Slight tenderness was present in the hepatic region but the liver was no longer enlarged. The colon was not tender or palpable.

Proctoscopy showed no ulceration of the rectal mucous membrane and six stools were negative for Entamoeba Histolytica.

He was discharged to Civil Life and is being kept under supervision. He has agreed to report back for observation of his progress.

Two Cases of Amoebic Hepatitis will now be described:-

Case One - L/Cpl. L.

Admitted to Hospital 18.10.45. The patient was already in a low Category on account of Chronic Amoebiasis at the time of admission.

His symptoms commenced in 1942 in Egypt when he noticed irritation in the peri anal region with looseness of the motions.

He was treated almost continously from 1943 to 1945 for Amoebic Dysentery and Amoebic Hepatitis. During this time he received two courses of Emetine injections, Emetine Bismuth Iodide, Yatren Retention Enemata and Carbarsone Tablets. He was discharged from Hospital in 1945 as cured and a Sigmoidoscopy performed prior to discharge was negative.

On admission on 18.10.45. he complained of a "jabbing pain" below the ribs on the right side of three months' duration. He also complained of persistent nausea and of colicky pain in the Right Iliac Fossa. He had had occasional diarrhoea, about five motions a day, for three months. On examination he exhibited marked loss of weight and the liver was enlarged to one finger breadth below the costal margin and tender. Tenderness was also present in the right intercostal spaces over the liver and in the caecal region. The peri anal region was red and excoriated.

The Total White Cell count was 11,600 and the Differential Count was Neutrophil Polymorphs 73%, Eosinophil Polymorphs 2%, Lymphocytes 20%, Monocytes 5%.

Screening of the Right Diaphragm showed an initial lag in the medial portion of the Right Cupola but final movement was full and free.

Six stools were examined and all were negative for Entamoeba Histolytica.

On Sigmoidoscopy the rectum was found to be stenosed while the mucous membrane was congested. There was no ulceration but several pits were present suggesting healed ulceration. A specimen was taken and Entamoeba Histolytica was not found.

Conclusion. In view of the enlarged tender liver, the sigmoidoscopic appearances, the slight elevation of the white count, the lag of the diaphragm on screening and the previous history a diagnosis of Amoebic Hepatitis was made. Post Dysenteric Colitis was also present.

Treatment. It was decided to commence treatment with a full course of Emetine injections as Amoebic Hepatitis is acknowledged to be particularly susceptible to the effects of Emetine Hydrochloride by injection.

No active evidence of Amoebiasis was found in the bowel but it was considered advisable to administer Penicillin and Sulphaguanidine in view of the inflamed condition of the rectum and peri anal region. Treatment was given as follows:-

21.10.45. Emetine Hydrochloride gr. 1 daily by injection for 12 days.
22.10.45. Course of Sulphaguanidine, total gms. 80.5.
23.10.45. Course of Penicillin, 100,000 units.stat. and 33,000 units three hourly intramuscularly. Total 2,000,000 units.
11.11.45. Emetine Bismuth Iodide gr. 3) Concurrently
Yatren 2.5% Retention Enema) for 12 days.
23.11.45. Carbarsone gms. 0.25 b.d. for 12 days.

14.12.45. Condition Following Treatment.

Still three stones below his normal weight in 1942. Pain in the hepatic region had completely disappeared. Appetite good and passing two stools a day only.

On examination the liver was not palpable and tenderness was no longer present in the hepatic and caecal regions.

The White Cell count was 8,450. Neutrophil Polymorphs 56%, Lymphocytes 36%, Monocytes 4%, Eosinophils 3%, Basophils 1%.

Five Stools were formed and Entamoeba Histolytica was not present.

A Sigmoidoscope was passed to 8 inches and the mucous membrane of the bowel was perfectly normal.

The patient was examined again on 26.1.46. and had gained one stone in weight. He complained of about one "loose" motion a week only. Occasional pain occurred below the right costal margin but the liver was not palpable or tender. He stated that he felt better than he had ever done since 1942.

Case Two - Gnr. D.

The patient was a Prisoner of War in Japanese hands and suffered from Beri Beri and Bacillary Dysentery while in captivity. In May, 1945, he was treated for Amoebic Dysentery while a Prisoner of War and stated that his liver was affected then.

On 2.11.45. he was admitted to Hospital complaining of pain below the right costal margin with fever. The liver was enlarged to three finger breadths and was very tender.

Three hourly blood slides showed no Malaria Parasites. Repeated stools showed no Entamoeba Histolytica cysts or ova.

A high Polymorphnuclear Leucocytosis was present. W.B.Cs. 21,000. Neutrophil Polymorphs 80%, Lymphocytes 17%, Monocytes 1%, Eosinophils 2%.

He failed to respond to a course of Anti Malarial treatment and pyrexia continued with rigors and profuse sweating.

Sigmoidoscopy showed scars of healed ulcers only.

A diagnosis of Amoebic Hepatitis was made and he was given a course of 12 Emetine Hydrochloride injections, each of gr. 1. The White Cell count fell to 16,400 with 73% of Neutrophil Polymorphs during the course and the liver became steadily smaller and less tender.

Pyrexia, however, continued throughout and a course of Penicillin, total 1,000,000 units, was administered between 13.11.45. and 17.11.45. During this course, the temperature fell to normal and did not rise again.

Emetine Bismuth Iodide with Yatren Retention Enemata and Carbarsone were then given as in the previous case.

Results of Treatment.

One month following the completion of treatment he had no complaints at all. He had gained one stone 2 lbs. in weight since his admission to Hospital.

The liver was just palpable and no tenderness was present.

The White Cell count was 9,950. Neutrophil Polymorphs 53.5%, Lymphocytes 42%, Monocytes 3.5%, Basophils 1%.

Comment on the Third Group of Cases.

The three cases of Chronic Colonic Amoebiasis in this series had a history of Amoebic Dysentery ranging from fifteen months to three and a half years. Case One and Case Two had received three courses of Emetine injections and Case Three had received gr. 150 of Emetine by injection.

All the cases were treated with a view to elimination of secondary infection by Penicillin and Sulphasuxidine before commencing Emetine Bismuth Iodide, Yatren and Carbarsone. As Hargreaves[8] has observed, the patients experienced improvement before Amoebicidal drugs were commenced. Haemolytic Streptococci were cultured from the Amoebic ulcers of Case Two but no secondary invader was cultured from Case One. No culture was taken prior to treatment in Case Three.

The three cases have shown very satisfactory progress to date. Rectal ulceration has healed completely although it has been shown in the second Group of cases that this is no certain criterion of cure. An even more satisfactory feature is the disappearance of Entamoeba Histolytica from the stool in every case. Complete symptomatic relief has resulted except in Case Three, a very refractory case requiring two courses of treatment to effect apparent cure.

The number of cases is very small as few cases of Amoebic Dysentery were treated in the Hospital. The period of surveillance is short and rather inconclusive. The cases will be further followed but it was impossible to retain them in the area for a longer period purely for surveillance as they were all due for Release from the Forces and wished to return to their homes where they will be under the care of the Out Patient Departments of their local Hospitals.

The cases of Amoebic Hepatitis are included as it is felt that secondary infection here also played a part.

The first case appeared to be suffering from a Post Dysenteric Colitis as evidenced by the stenosed and congested character of the rectum. The mucous membrane regained its normal appearance following Penicillin and Sulphaguanidine. When seen two months after the completion of treatment, he showed no evidence of Amoebiasis. The diarrhoea had been almost completely relieved and the colonic infection had previously been observed to have cleared up on sigmoidoscopic examination.

The second case was very acutely ill due to Amoebic Hepatitis, the pyrexia failing to respond to Emetine injections. The diminution in the size of the liver and the decreasing tenderness of the organ did not indicate an Amoebic Abscess. Penicillin was commenced as it was considered that a secondary bacterial invasion of the liver was present. The pyrexia subsided dramatically during the course. The patient recollected having had a number of boils before admission to Hospital and the Staphylococcus was thus a possible invader.

It is not suggested that secondary infection is common in Hepatic Amoebiasis but in these two chronic cases it was certainly considered to play an important part.

This Group is too small for any dogmatic assertions. It can merely be stated that the results of treatment inspired confidence. They compare favourably with the results obtained in the cases treated by Emetine Bismuth Iodide and Chiniofon alone in 1943. The initial improvement following Penicillin and Sulphasuxidine is striking. The cases quoted will be followed up for a further period to ascertain if relapse occurs. One feels that this method of treatment is sufficiently promising to be adopted enthusiastically in all cases of Chronic Amoebiasis encountered, in spite of the lengthy treatment period of five weeks or more. Case Three was the type of case where passage of Entamoeba Histolytica would have continued throughout with previous methods of treatment.

The role of Secondary Infection will be considered further in the Discussion. It is felt that it accounted for the complete lack of effect on Amoebic ulcers of the rectum as observed in some of the second Group of cases following Emetine Bismuth Iodide and Chiniofon only.

DISCUSSION.

The unsatisfactory standards of treatment for Amoebic Dysentery in common use in 1942 cannot be over estimated. The inadequacy of the therapy often employed is apparent to all who have followed cases through for a period of years.

The gravity of the disease in Bengal will be seen from the statistics quoting the incidence of Amoebic Dysentery as compared with Bacillary Dysentery among our troops. Amoebic Dysentery in the Monsoon Season was the second commonest disease in the General Hospital in which the Bengal work was done, ranking only below Malaria in numbers of cases and constituting a more potent cause of Chronic Invalidism. Interest was therefore centred on the results of treatment of the condition and therapy has become more thorough in consequence.

It has been pointed out that the Relapse Rate in the first Group of cases was striking but a low figure compared with the probable actual percentage of relapses following Emetine Hydrochloride injections. Appreciation of the problem of the relapsing case can be seen in the revision of treatment in the Army. A Technical Memorandum was issued in South East Asia Command in July, 1944, stating that all cases of Amoebic Dysentery should receive a course of Emetine Bismuth Iodide with Yatren or Chiniofon Retention Enemata and a course of Carbarsone. The need for adequate observation of cases following treatment was also emphasised.

Cases of Amoebic Dysentery occurring in Military Hospitals in the United Kingdom now receive a through course of treatment which will be described later. Chronic cases are treated by the method of Hargreaves[8]. Experience has shown that there is ample justification for prolonged methods of treatment initially, even in spite of the loss of duty entailed during treatment.

The second Group of cases were all Chronic Infections and warranted special study as chronicity had become such a problem in 1943. The poor results obtained were a stimulus to further interest in Chronic Amoebiasis.

The third Group of cases was unfortunately small as one was not working in a Hospital where cases of Chronic Amoebic Dysentery were specifically admitted.

Each Group of cases has been commented upon serially and it now remains to coordinate the findings with the work that has been done at various times upon Amoebic Dysentery. The chronic nature of the disease and the manner in which it appears to resist all treatment in certain individuals have been the most outstanding manifestations throughout the groups of cases. It is proposed, therefore, to devote the discussion largely to the potential incidence and effects of Chronic Amoebic Dysentery and to the reasons which cause certain cases to become chronic and to resist the established methods of treatment with Amoebicidal drugs.

The Potential Incidence of Chronic Amoebic Dysentery and the Effects of the Chronic Disease.

There is little doubt that a large number of cases of Chronic Amoebic Dysentery will be encountered among soldiers returning from Service in the Far East.

It has been pointed out that of over 800 cases of Amoebic Dysentery treated in 1942, 5% were readmitted to the same Hospital within a period of eight months. The fifty chronic cases treated in the second Group were a sequel of treatment undertaken in 1941 and 1942.

Stitt[2] has described the incidence of Amoebic Dysentery in repatriated troops following the last War:- "of 31,000 British troops returning to England from the Near East, the majority of whom had had Dysentery or other intestinal disturbances, 9.8% were found infected with Entamoeba Histolytica". Presumably most of these cases had received treatment prior to repatriation.

With regard to the future course of cases of Chronic Amoebic Dysentery, Silverman and Leslie[1] state that they have seen cases of uncomplicated Amoebic Colitis with histories of thirty years' standing. In the series of cases already described, cases have been encountered with histories of three to four years' duration. The recurrences of the disease and the consequent invalidism are apparent to any Physician who has studied the condition over a period of years. The inevitable conclusion is that short courses of treatment and brief periods of observation are useless and that the disease must be attacked energetically when it becomes first apparent. Treatment must be even more thorough for the chronic case.

The problem of Chronic Amoebiasis gave rise to considerable interest and concern in the United Kingdom during the War years. The majority of cases of this type were repatriated refractory cases from India and Burma. Such cases were discussed by Dr. A.R.D. Adams of the Liverpool School of Tropical Medicine and Lt.Col. Hargreaves at a meeting of the Royal Society of Tropical Medicine and Hygiene held on November 6th, 1944, (Reported in the Lancet)[6]. Dr. A.R.D. Adams stated that some of these cases had received 50 to 300 injections of Emetine and that some had resisted every remedy.

The end result of the refractory case is at best a state of Chronic Invalidism, a condition of progressive asthenia and weakness with recurrent attacks of troublesome diarrhoea rendering the individual incapable of sustained work. Death may occur from intercurrent infection, perforation of the bowel, amoebic liver abscess or cachexia.

Factors Promoting the Development of Chronic Amoebiasis.

Before the most recent methods of therapy can be reviewed, is is essential to establish the factors promoting chronicity and their relative importance. They will be considered under the following headings:-

(1) Inadequate treatment.
(2) "Emetine fastness".
(3) An abnormally virulent strain of Entamoeba Histolytica.
(4) Secondary Bacterial Invasion of Amoebic lesions with consequent failure of healing and failure to eradicate the Entamoeba Histolytica.
(5) The Site of the Amoebic lesion.
(6) Inadequate periods of observation following apparent cure.

(1) Inadequate Treatment.

Hargreaves[8] quotes Dobell's work published in 1917 by which it was fully proved that Emetine Hydrochloride given by subcutaneous injection (10-12 gr. or more) was successful in only about one third of the cases treated. The unsatisfactory results obtained in the cases treated in Calcutta in 1942 therefore occasions no surprise. This abbreviated course of treatment, which was later repeated again and again on relapsing cases with complete lack of success, must be regarded as very inadequate. The sequel is seen in the 50 chronic and refractory cases treated in 1943. These cases had received an average of four courses of Emetine injections in ten months.

A further danger of treatment by Emetine injections alone is the false security thus afforded. Cases often appear to experience cure for a considerable period and while a certain proportion are actually cured, a further large fraction will be apparently cured. The course therefore appears very effective to the observer who has become recently acquainted with the disease and one was wrongly impressed with its efficiency in 1942. It does undoubtedly cure a percentage of cases and one has seen cases who were completely cured on stool and sigmoidoscopic findings twelve months after one such abbreviated course. Nevertheless there is ample justification for giving a prolonged course of treatment to every fresh case of Amoebic Dysentery as chronic cases must be avoided.

The present course recommended in the Army for fresh cases consists of a few initial Emetine injections to control the diarrhoea. This is followed by Emetine Bismuth Iodide gr. 3 each evening for twelve days while a concurrent course of Yatren Retention Enemata is given each morning for the same period. A course of Carbarsone gms. 0.25 b.d., follows for twelve days. This course is a very thorough one. I have not collected any statistics from the use of it but it certainly gives the impression of being effective even if a few relapses do occur.

Treatment of the fifty chronic cases of Amoebic Dysentery in 1943 proved that Emetine Bismuth Iodide was of value but showed that further treatment was essential in addition to E.B.I. and Chiniofon.

To summarise, inadequate treatment has proved a common cause of Chronic Amoebic Dysentery. The use of a prolonged course of treatment in fresh infections is amply justified in spite of the lengthy nature of the treatment.

The treatment of Chronic Amoebic Dysentery will be discussed further in subsequent sections.

(2) Emetine Fastness.

The question of "Emetine fastness" now merits discussion. Dr. A.R.D. Adams at a Meeting of the Royal Society of Tropical Medicine and Hygiene[6] stated that the failure of cases of Chronic Amoebiasis to respond to treatment could be due to an abnormally virulent strain of Entamoeba or to "Emetine fastness" due to excessive Emetine dosage. He recommended for this reason that 3 to 6 preliminary Emetine injections only should be given to control the acute manifestations.

Dobell and Laidlaw[7] carried out in vitro experiments with Entamoeba Histolytica in subcultures with a view to determining the development of "Emetine fastness". They stated "These experiments also indicate that it is not easy, they suggest in fact that it is impossible, to obtain a strain of Entamoeba Histolytica which is resistant to Emetine". Hargreaves[8] has recently reviewed the position with regard to Emetine Resistance. He quotes further work of Dobell in 1945 in which all attempts to produce an Emetine resistant Entamoeba Histolytica by growing it in media containing Emetine proved negative. Hargreaves, from his own observations, also feels that Emetine Resistance is not a factor of importance. After discussing the work of Bonnin and Aretas (1938) and Halawani (1930) in favour of Emetine resistance and the work of Dobell (1945) disproving Emetine resistance, he concludes "Thus there is as yet no scientific evidence that Emetine Resistant strains of Entamoeba Histolytica exist or can be produced".

(3) The Virulence of Entamoeba Histolytica.

It might be postulated that the Entamoeba Histolytica encountered in India and Burma was of a particularly virulent strain and that large numbers of chronic cases were therefore encountered. It seems likely, however, that the high incidence of the disease in the area and the predominance of the Amoebic over the Bacillary type of Dysentery, in Bengal at least, were more important causes of the large residuum of chronic cases from this Theatre. Refractory cases of Chronic Amoebiasis have also been encountered from other Theatres of War and have proved equally hard to cure.

(4) Secondary Bacterial Invasion.

In my opinion, this is the subject of greatest importance from the therapeutic point of view.

The Amoebic lesion is not normally characterised by a pyogenic reaction when divorced from invading organisms. This is illustrated by the Amoebic Abscess of the liver, which consists of necrotic liver tissue only without pus cells.

Formation of true pus is only seen when secondary infection of the abscess cavity has occurred. Major J.C.S. Paterson, R.A.M.C., while working in the Pathological Laboratory, drew my attention to sections of the bowel in fatal cases of Amoebic Dysentery. Although Amoebae were seen throughout the bowel tissue, a Polymorph response was only observed at points where the mucosa had been breached, thus facilitating the entry of invading organisms from the bowel lumen.

Brigadier C. Naunton Morgan[9] wrote in 1944 with reference to Amoeboma, "In the early stages of the tumour formation the whole mass will melt away miraculously after Emetine treatment. When the Amoebic lesion has been present for a long period, however, the superadded result of chronic secondary infection, fibrosis and distortion of the colon will prevent the mass disappearing with anti amoebic treatment". The use of the phrase "chronic secondary infection" is of interest and the secondarily infected Amoeboma so described appears to resemble the recalcitrant Amoebic Ulcer.

The two fatal cases described with Post Mortem Reports in 1943 are examples of Amoebic Dysentery complicated by secondary infection of the colon. Bacterial invasion was the cause of death in the two cases and it is postulated that it is the cause of chronicity in many others. Silverman and Leslie[1] have reported two severe cases of "Ulceronecrotic Intestinal Amoebiasis" of great severity with perforation of the colon. Organisms of the Bacillary Dysentery group were the secondary invaders in each instance.

A certain amount of research on secondary infection has been carried out by various workers and the literature is well reviewed by Stitt[2] who describes the following[3] investigations:-

Vogel found a Gram Positive Streptococcus, differing immunologically from the Haemolytic Streptococcus, which was capable of producing intestinal lesions on inoculation into animals.

Nauss and Salinger (1935) found that kittens were not infected by a strain of Entamoeba Histolytica "unless a haemolytic culture of B. Coli was injected with it".

Cleveland and Sanders (1930) and Cleveland and Collier (1930) in experimenting on the bowel and liver of cats found that strains of Amoebae seemed to lose their virulence if cultured for a year or more. To quote Stitt, "However they demonstrated that it was the bacteria growing with the Amoebae that had lost virulence, for when the virulence of the bacteria was regained by liver passages, the amoebae that had apparently lost their pathogenicity were again capable of producing a high percentage of abscesses when inoculated with the bacteria".

In addition to pointing out ~~that~~ the importance of secondary infection, this investigation indicates the probability of the recrudescences of clinical attacks of Amoebic Dysentery being due to changes in the intestinal organisms. Reactivation of Amoebae of attenuated virulence may thus occur.

Napier[10] in his Principles and Practice of Tropical Medicine emphasises the importance of secondary infection when discussing the treatment of Chronic Amoebic Dysentery.

W.H. Hargreaves[6] at a Meeting of the Royal Society of Tropical Medicine and Hygiene stated his belief in the treatment of secondary infection of the bowel with Penicillin and Sulphasuxidine, Sulphasuxidine coping with the Penicillin resistant organisms.

W.H. Hargreaves[8] in an article to the Lancet stressed further the importance of the preliminary treatment of secondary invaders in Chronic Amoebiasis and quoted his excellent therapeutic results in support of this.

Willmore[6] stated in November, 1944, that he had used the combined treatment since 1926 and that he was now encountering chronic cases resistant to treatment. He found that treatment of concomitant bacterial infection often resulted in a subsequent favourable response to the Amoebicidal drugs.

In a letter to the Lancet, A.M.M. Payne[11] has quoted Acton and Knowles (Dysenteries of India Calcutta 1928) who stressed the importance of the Streptococcus in resistant cases. Payne took swabs through a Sigmoidoscope in four cases of Amoebic Dysentery. A Haemolytic Streptococcus was grown from two cases. Material was taken from rectal ulcers and inoculated on a Blood Agar plate in two cases from my third Group. Haemolytic Streptococci were grown from one case.

It would be a most profitable investigation to culture material from all Amoebic ulcers in Chronic Amoebiasis. Such material could be cultured on desoxycholate and Blood Agar media and the percentages of occurence of the various types of secondary bacteria could be assessed. Such an investigation would provide valuable information with regard to a therapeutic attack upon the organisms involved. Much of the research on this question to date has been done on experimental animals and has been corroborated by the therapeutic response in patients.

The bacteria described as secondary invaders have been the Bacillary Dysentery Group, the Streptococcus and B. Coli. The relative frequency of the occurrence of the former two organisms would be of interest.

Two of the three cases of Chronic Colonic Amoebiasis in my third Group showed a diffuse inflammation of the whole rectal mucous membrane between the ulcers. This undoubtedly signified secondary infection, and was proved to be due to a Haemolytic Streptococcus in one case. This small collection of cases has shown an encouraging response to treatment so far.

Dr. Walter L. Palmer[12] of Chicago states that Gonzalez and Vejar recently reported a case of fulminating Amoebic Dysentery complicated by a Hepatitis of Staphylococcal origin. The case was treated with Penicillin with good results.

The occurence of secondary infection in cases of Amoebic Hepatitis is probably uncommon unless such infection is introduced during aspiration of an abscess. It it thought that Gnr. D. in the third Group of cases had a secondary staphylococcal infection of the liver and that this was successfully treated by Penicillin in addition to Emetine. No direct bacteriological proof was obtained.

The work of D.H. MacKenzie[13] on Sulphasuxidine should be quoted in view of the use of this drug in the course recommended by Hargreaves. He investigated the use of Sulphasuxidine in operations on the Colon and Rectum and confirmed the decrease of Gram Negative organisms (colonies of B. Coli) after administration of a dose of gms. 20 daily for four days before an operation. The same effect could not be produced with Sulphaguanidine. Sulphathiazole was as effective as Sulphasuxidine but was, of course, more toxic and more apt to give rise to renal complications.

In conclusion, there is a most convincing body of work in favour of the fact that the Amoebic lesion fails to heal due to secondary infection of the bowel, leading to inaccessibility of the Entamoeba Histolytica to the action of the usual Amoebicidal drugs. In view of the probable nature of the secondary organisms, Penicillin and Sulphasuxidine, as used by Hargreaves, would appear to be the drugs of choice in the preliminary treatment of Chronic Amoebiasis.

(5) The Site of the Lesion.

It seems probable that the proximal part of the colon is often the last stronghold of the disease following treatment.

Of twenty cases in the second Group still uncured following Emetine Bismuth Iodide and Chiniofon, 13 = 65% exhibited tenderness of the caecum at the end of treatment while 7 = 35% only showed Sigmoidoscopic lesions at the end of treatment. All produced Entamoeba Histolytica in the stool at the end of treatment.

It is in the caecum and ascending colon that perforation of Amoebic ulcers commonly occurs and the largest and deepest ulcers are often found in this region Post Mortem.

The conclusion is that negative stool examinations are even more important than negative Sigmoidoscopic findings when assessing cure of a case.

(6) Inadequate Observation.

In view of the long periods of freedom from symptoms in uncured cases of Amoebic Dysentery, a long period of observation with adequate tests of cure is required following treatment.

In the first Group of cases treated in Calcutta, it will be seen that no proper "follow up" system was possible. The Hospital was overflowing and cases had to be discharged rapidly.

The chronic cases in the second Group were observed for one month after the end of treatment. This was all that Military necessity would allow as evacuation of the cases was essential to other Hospitals. The period served to detect several refractory cases which had passed the initial tests of cure satisfactorily but were still in fact uncured i.e. 12% of the total. In the fifty chronic cases, the average number of recrudescences was four in ten months, indicating a recurrence of symptoms every ten weeks.

It is therefore contended that each case of Amoebic Dysentery should be kept under surveillance for a period of three months at least following treatment.

The third Group of cases has not yet been observed for a sufficient period to ensure that no relapse will occur. They are being kept under observation.

The Use of Other Amoebicidal Agents apart from Emetine in Chronic Amoebic Dysentery and Arguments for the Continued Use of Emetine Bismuth Iodide.

Discouraging results have been obtained until recently in the treatment of Chronic Amoebic Dysentery in cases returning from the Tropics. The effectiveness of Emetine in such cases has therefore been questioned and efforts have been made to find a drug which might prove more potent.

Morton[14] has described the use of Diodoquine. His cases were of marked chronicity and had suffered from 3 to 9 relapses before treatment was started. The standard dose of the drug was 3.2 gr. t.d.s. for twenty days. Some cases received Emetine injections in addition while still others were given Emetine Bismuth Iodide with Yatren and Carbarsone plus Diodoquine. Approximately one third of the cases relapsed.

In conclusion Morton states that the drug is valuable in cases which have become "Emetine fast" due to inadequate therapy and that the drug has advantages in being non-toxic in therapeutic doses.

The results obtained in this report are not convincing in proving that Diodoquine is superior to Emetine Bismuth Iodide. It would be interesting, however, to try Diodoquine following a preliminary course of Penicillin and Sulphasuxidine. In this way comparison with Hargreaves' results would be made.

One still feels that Emetine Bismuth Iodide and Yatren are sufficiently powerful Amoebicidal agents if preceded by treatment to attack secondary bacterial invasion. Dobell, Gettings, Jepps and Stephens[15] treated 155 Amoebic Dysentery carriers with Emetine Bismuth Iodide in doses of gr. 3 daily for twelve days. They found that 142 cases (91.6%) were finally discharged as cured. This is a tribute to the efficacy of the drug. Dobell and Laidlaw[7] showed in 1926 that Emetine in Vitro was "a specifically lethal poison for Entamoeba Histolytica". It did not affect other Amoebae occurring in the bowel. They stated "Certain human beings when infected with Entamoeba Histolytica appear to be incurable with Emetine however administered and when given in considerable amounts for a long period". This statement has proved lamentably true during the War. The results of Hargreaves[8] and one's own limited experience are, however, very much in favour of a failure of Emetine to exert a specific effect because of concomitant bacterial invasion. It appears likely that Emetine Bismuth Iodide is still the most potent drug available in the treatment of Chronic Amoebic Dysentery if supplemented by Penicillin and Sulphasuxidine.

SUMMARY.

1. Amoebic Dysentery has constituted a considerable problem during the War.

2. Large numbers of British troops suffered from Amoebic Dysentery for the first time in 1942 in Bengal. Most of the patients were recent arrivals in India. 815 cases were treated in eight months in a Hospital in Calcutta in 1942.

3. The incidence of Amoebic Dysentery was greater than that of Bacillary Dysentery among British troops treated in Calcutta in 1942.

4. There was a marked rise in the incidence of Amoebic Dysentery at the time of the Monsoon, favouring a water borne spread. Bacillary Dysentery showed a similar rise in the Monsoon period.

5. The immediate mortality from fresh infections with Amoebic Dysentery was low.

6. Emetine Hydrochloride injections and Carbarsone were administered as routine treatment in 1942. The period of observation of cases following treatment was unduly short. The form of treatment and the short period of observation were dictated by conditions at the time.

Relapses occurred following this treatment and the proved relapse figure of 5% within eight months is a minimal one.

Carbarsone appeared to be of value in eradicating Entamoeba Histolytica cysts.

Kurchi Bismuth Iodide was valueless as an Amoebicidal agent and was of symptomatic use in relieving diarrhoea only.

7. Fifty chronic cases of Amoebiasis were treated in 1943 as the Hospital had become a Centre for the treatment of Chronic Amoebic Dysentery.

All the cases had recieved repeated courses of Emetine injections and it is postulated that they had experienced relief from this treatment but had never been cured. The unsatisfactory nature of treatment by Emetine injections and Carbarsone alone was thus displayed again.

8. Chronic Amoebic Dysentery leads to a state of invalidism with mental apathy, intermittent diarrhoea, weakness, gross loss of weight and abdominal pain.

9. Sigmoidoscopy is an excellent method of assessing progress in Chronic Amoebiasis but stool examinations are even more important in diagnosis. Thus 85% of cases in which the stools were positive showed Sigmoidoscopic lesions.

It was interesting to observe the disappearance of ulcers in three weeks in some cases of Chronic Amoebiasis while other ulcers showed no response following Emetine Bismuth Iodide and Chiniofon.

Sigmoidoscopy is a good test of cure but stool examination is even more reliable.

10. Emetine Bismuth Iodide was a drug of low toxicity in that the pulse and blood pressure were not affected following treatment.

11. Emetine Bismuth Iodide and Chiniofon alone cured only 42% of fifty chronic cases. This consitituted an advance in that the patients had not been cured by Emetine injections. The result was nevertheless disappointing.

12. 12% of the cases relapsed during observation over a period of one month, thus emphasising the importance of an adequate period of surveillance.

13. The lack of response to Emetine Bismuth Iodide and Chiniofon or Yatren was apparent to various workers when chronic refractory cases from the India and Burma Theatres returned to the United Kingdom.

14. Failure of previous methods of treatment give rise to speculation on the causes of chronicity.

15. Hargreaves[8] contended that secondary infection was responsible for the failure of Chronic Amoebiasis to respond to treatment by Amoebicidal drugs. He therefore advocated a preliminary course of Penicillin and Sulphasuxidine in all such cases.

A few cases were personally treated in this way in the United Kingdom. Three cases of Chronic Colonic Amoebiasis have progressed well to date and are still under observation. A Haemolytic Streptococcus was cultured from the Amoebic ulcers of one case.

16. Perusal of the researches of various workers corroborates the importance of secondary infection in Amoebic Dysentery. It is considered that this is the most important factor from the therapeutic point of view. Cultures from Amoebic ulcers on Desoxycholate and Veillon media from a large number of Chronic cases would enable the frequency of occurrence of some of the various secondary organisms to be assessed.

17. An adequate period of surveillance after treatment of Amoebic Dysentery is essential. Observation for three months at least is suggested as fifty chronic cases treated in 1943 averaged two and a half months between recurrences of symptoms.

18. After witnessing the effects of this disease for four years, one feels that no treatment, however prolonged, can be too thorough in the eradication of the infection.

Some of the material embodied in this Thesis was presented in 1943 at a Conference of Medical Specialists of the Eastern Army and in 1944 at a Conference of Medical Specialists of South East Asia Command.

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