THESIS on

AMŒBIC DYSENTERY

BY

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AMOEBIC DYSENTERY

History.

The name of the disease "Dysentery" was apparently suggested by the great Hippocrates and it was evidently different in his mind to diarrhoea.

Later Celsus describes ulcers, from which blood flows, in the interior of the intestines and that this blood is mixed with the faeces and mucus.

In 1859 Lambl described intestinal amoebae, but the first recognition of amoebic dysentery, as a separate disease, dated from Losch's paper in 1875, in which he states that he discovered a large number of amoebae in the faeces of a patient suffering from chronic dysentery, some four years and he gives an accurate description of these protozoa naming the parasite Amoeba Coli. It is fairly clear now that what he described was not the Entamoeba Coli, which is harmless, but the Entamoeba histolytica, the true dysentery germ. Ulceration of the bowel and typical flask shaped abscesses were found post mortem in the above case and this fact favours such views.

It was Kartulis who at Koch's instigation set himself to work out the rôle of amoebae which were found present in faeces in cases during the Cholera epidemic of 1883 in Alexandria, and in 1887 he demonstrated the amoebae in a liver abscess. In 1891 he demonstrated the causal relationship between amoebae and dysentery in young cats whom he inoculated per rectum with dysenteric material. Sir William Osler too discovered amoebae in a liver abscess in America.

Hlava of Prague 1887, Councilman and Lafleur 1891, Kovacs 1892, Kruse and Pasquale 1893, Rogers 1901, all established the connection of the amoeba with dysentery and liver abscess. Kruse and Pasquale suggested that there might be more than one

kind of amoeba - one harmful, the other harmless and Schaudinn about 1903 established the fact. The non-pathogenic he called Entamoeba Coli, the pathogenic, Entamoeba histolytica.

In 1907 Vierick described a further amoeba which he called Entamoeba tetrag and Elmassian one he called Entamoeba minuta. These latterly have been shown t be stages of the Entamoeba histolytica.

To Vedder ~~was~~ is due the discovery of the amoebicidal properties of EMETIN a to Rogers is due the credit of applying the treatment of Emetin in cases of amoe dysentery with such success.

Etiology.

Dysentery is a disease of the Tropics and Subtropics. It extends widely over Africa, Asia, America, the Malay and Phillipine Islands, South Europe inclu ing the Balkan States and Gallipoli. Also cases and even epidemics have been r ported in more northern latitudes in France, Germany, the British Isles, Sweden and Iceland. It has been found too that sometimes the individuals affected hav never left their northern homes. The infection in these cases in all probabili has been conveyed by "Carriers".

The Amoeba histolytica, the specific cause of this disease, is introduced the human body in the form of cysts, which are found abundantly in water contam ed with the faeces from a dysenteric patient. This water may be used for eith drinking purposes or for the washing of vegetables which are eaten uncooked, as lettuce and tomatoes. The cyst wall is dissolved in the gastric or intestinal secretions, the nuclei are liberated and grow into young amoebae, which ~~They~~ invade tissues of the large bowel establishing themselves in the submucosa.

It has also been proved by later knowledge that food contaminated by the faeces of flies and man to man contagion are further sources of infection.

Persons who have apparently recovered from an attack of amoebic dysentery may have entamoebae of the "minuta" type, multiplying in the intestine without there being any active invasion of the tissues.

These entamoebae are constantly encysting and the individual may be passing enormous numbers of the infective encysted forms in the stools. Such people are termed "Convalescent Carriers" by Walker and Sellards, and they are a danger to themselves in being liable to relapse and to other people by distributing broadcast the infective cysts.

Walker & Sellards ~~They~~ also describe what they call a "contact carrier" a type of individual who is found to be infected with "minuta" generations without ever having suffered from amoebic dysentery.

From experiments carried out by Arkwright, Yorke, Priestley and Gilmore February to March 1916 on fifty dysentery convalescents three to six months after the onset of their illness nine were still excreting E. histolytica and two were still excreting B. dysenteriae (Shija). These eleven men were therefore potential sources for the outbreak of fresh epidemics.

The adult Entamoeba histolytica is from 25-30μ, is fairly active in its movements, with the protrusion of pseudopodia - the ectoplasm ~~is~~ can generally be distinguished from the endoplasm. ~~This sometimes though may be lost.~~ The Endoplasm is not distinctly vacuolated, is fairly homogeneous, and may contain red blood corpuscles. The nucleus measures 7-10μ and is not seen well in an unstained specimen. The limiting membrane of the nucleus is difficult to define, it is so very thin. The

granules of chromatin, ~~uniform~~ uniform, more or less in size, are arranged peripherally and are somewhat scanty. At the centre a granule, the karyosome, with a clear area limited around by granules can be seen. Between this and the periphery there is a lining network of fibres continued from the lining membrane. The nucleus is generally eccentrically placed. This active amoeboid stage is found microscopically in the mucus passed per rectum in acute amoeboid dysentery.

The stage which is described as the Entamoeba minuta is found in the soft diarrhoeal stool in an attack. The amoeba measures only about 12-16 μ. It has no definite ectoplasm, the endoplasm contains vacuoles, the nucleus is small but rich in chromatin - and it has no definite karyosome arrangement. The final stage or the encysted form - the Entamoeba tetragena - is most easily discovered in the solid faeces between dysenteric attacks during convalescence. The cyst contains four nuclei. Its average diameter is 12-14 μ and it is round or oval in shape. The wall is not very defined but the chromidial bodies are clear. In addition there is a large vacuole in the cytoplasm, which disappears with further development of the cyst and nuclei. The latter appear ring shaped. The protoplasm is finely granular - the nuclei may be arranged in pairs - Chromatin is peripheral and the karyosome definite.

Adult Entamoeba histolytica

Pathology.

On the young amoebae reaching the large bowel they pass in to the crypts in the mucus membrane or the immediate tissues around i.e. the spaces between the crypts containing the blood and lymphatic vessels. The invasion causes thrombosis, haemorrhage (first seen to the naked eye as red slightly raised spots) degeneration of tissue and sloughing. The ulcer appears on the surface of the swelling where these changes are taking place. The undermining laterally produces a flask shaped abscess. Several of these may merge into one big ulcerated surface - the mucous membrane itself being quite healthy a short distance from the lesion. The muscular coat usually remains the base of the ulcer, but it may become involved and even the subserous coat may become affected. The peritoneum is rarely reached, but when it is, perforation or peritonitis may supervene. The bowel involved is almost entirely the caecum, large intestines and rectum. Kuenen in Java reported that he had found the small intestine affected. When healing takes place the necrosed tissue is cast off, adhesion of the edges of the undermined mucosa occurs ~~takes place~~, the epithelium spreads over the whole lesion and a thin scar results. When the disease is chronic there is a tendency for the bowel wall to hypertrophy and if the ulceration has been very intense partial stricture may occur.

Symptoms.

In simple acute dysentery, the onset is somewhat sudden, with pain in the abdomen of a colicky nature soon followed by discomfort and bearing down at the anus. There may be vomiting. Diarrhoea sets in quickly. At first the stools may be natural contents of the bowel. This however rapidly changes to a watery yellow mucoid admixture accompanied by a slight tinging of the mucus (which may

be purulent) with blood, or it may be almost pure blood that is passed. From 12 to 30 stools of an odour fairly typical, may be passed during the twenty four hours - in fact they ~~are~~ may be so numerous that it is difficult to persuade a patient away from the commode. Fever is only slight if present, 100° or so, and it is irregular in its course. Exhaustion occurs in different degrees - emaciation and dryness of skin are present and the victim wears a "worried look".

In some cases the onset is not so sudden, but begins with an ordinary diarrhoea, which soon however develops into the ordinary dysenteric symptoms. If there is no improvement at this stage the pain, straining, and constant defaecation produce sleeplessness. Vomiting may set in - the pulse rate rises to 100 or 120 - the abdomen becomes retracted and tender over the course of the colon and with an increasing exhaustion the heart may become flabby, the pulse rate rises, temperature falls and patient succumbs. In a favourable case, after a few days, the stools change - blood is less - sloughs of mucous membrane with mucus are passed - faeces tend to become more solid and finally gain a normal character with the passage of some mucus. This latter however clears up in time. In Gangrenous Dysentery the symptoms are more rapid and acute. The stools quickly become bloody, greenish, blackish or brownish, very offensive and sloughs appear as thick stringy masses. Peritonitis or perforation may supervene.

In the chronic forms, there has usually been a previous acute attack, which yields to treatment for a time and then relapses. When this occurs three or four times the case becomes chronic. Looseness of bowels with yellowish stools, mucus, and blood, alternating with constipation is usually met with. Momentary pain of a colicky nature is complained of over the sigmoid or caecum. Very slight causes such as

an indiscretion in diet, ~~in~~ taking unsuitable purgatives, or gettingwet and chilled bring about acute exacerbations.

In another type all the symptoms though present are very slight and the patient is able to "carry on". He however becomes thin and emaciated. An examination of the stools will clear up the real significance of these symptoms. In still another type, so called "latent", no definite signs are present but there is some abdominal discomfort and chronic indigestion with two or three loose stools a day. A history can generally be elicited of an acute attack of diarrhoea some time previously. Here again, on examination of the stools, the microscope will often prove the presence of the Entamoeba histolytica in some one of its forms.

Complications.

The commoner complications are hepatitis and liver abscess but infection by the amoeba of the lungs, spleen, brain, parotid gland, bladder, female generative organs, skin and bones have been reported. As has been before mentioned peritonitis and perforation may occur.

Sequelae.

Peritoneal adhesions follow a peritonitis and may give rise to an intestinal obstruction. Also the scars of the deep ulcerative surfaces may contract and produce stricture of the gut.

Anaemia and dilatation of the heart are not uncommon, hepatitis and abscess of the liver may occur - sometimes ~~often an~~ another acute attack of dysentery.

Diagnosis.

Clinical signs alone are not sufficient to distinguish between the different forms of dysentery, but Emetin treatment goes a long way in aiding diagnosis, as

on the administration

in Amoeba histolytica infection alone, rapid improvement generally occurs. On the other hand in the bacillary forms no improvement takes place. In mixed forms a partial improvement is seen. However the microscope is the only safe road to a sure diagnosis and Entamoeba histolytica its flagellae or cysts must be demonstrated in the faeces to prove the case one of amoebic dysentery. The real difficulty is in differentiating the Entamoebae histolytica from the Entamoeba Coli.

The diagnostic points are:-

"A" AMOEBOID STAGE

	Ent. Histolytica	Ent. Coli.
Size	25-30 μ	22-38 μ
Mobility	- Active for some time	Sluggish
Nucleus	- Thin membrane, with Chromatin.	Heavier in chromatin like a Signet Ring.
Contents	- Red blood corpuscles	Blood corpuscles rare.

"B" ENCYSTED STAGE

Size	11-14 μ	16-25 μ
Nuclei	- Four usually same size	Eight may vary in size.
Cyst Wall	- Thin.	Thick and double contour.

Prognosis.

If the case is diagnosed and treated in an early stage the results are decidedly good, but unfavourable in an advanced stage of ulceration, or, if there are signs of hepatic abscess.

However, much has been done, as has been proved during the Gallipoli Campaign, by the injection of Emetin. In the 17th General Hospital, Alexandria, up to October 1915, 300 cases of dysentery were admitted 70% of which proved by microscope to be amoebic. Of these 70% only 1% died and in these deaths bacillary infection was superadded.

Treatment.

It was Veddel in 1910, who found 1 in 100,000 Solution of Emetin (an alkaloid of Ipecacuanha) killed amoebae in Vitro.

Sir Leonard Rogers later applied this result to the treatment of Amoebic Dysentery in the human subject and obtained thereby brilliant results. He introduced it as a salt in the form of Emetin hydrochloride of which he injected a solution subcutaneously or intravenously into the human subject. A single lethal dose according to him is 15 grains and he has given Grs. I intravenously without ill effects. Allan found that a four grain dose produced nausea, Baermann and Heinemann found doses of 2 - 2½ grains led to weariness, loss of appetite, 5-6 grains dyspnoea, vascular paralysis, vomiting, thin stools, and a great slowing of pulse. From the above it is apparent that a dose of one grain given hypodermically is well within the margin of safety, and this is the dose that has been used daily either in one or two injections of half a grain night and morning, during a certain number of days according to the effect on the patient. During the time of my acting as a Medical Officer on a Hospital Ship plying between Gallipoli and Egypt the last three months of 1915, several hundreds of cases of dysentery came under my observation and as a matter of routine all my own and most of my colleagues' cases were injected with two thirds to one grain daily in one dose for the six or seven days the patients remained on board. These injections were given subcutaneously. Spirit and Iodine being used locally to disinfect the skin. In no case was nausea complained of, and no additional vascular depression noticed. Some deaths that occurred in Alexandria in one of the General Hospitals were supposed to be due to the cumulative effects of Emetin, but at a discussion that was held at the 21st General

Hospital, Alexandria the evidence brought forward was not at all convincing. However, the circulatory system must not be ignored during Emetin administration.

It is advisable to inject deeply into the loose tissue under the skin. If this is not done the process is more painful and sometimes a small tender lump that is somewhat persistent remains. No local septic infection was seen in any of the cases injected. The Emetin hydrochloride appears to act better the fresher it is and a new solution was made daily. With regard to the length of treatment: this naturally varies, depending on the progress of the case, i.e. as shown by an examination of the stools. In some individuals it acts after the third or fourth day like a charm, in others improvement is not noticed till after the fourth day. Again after great improvement has occurred for a few days, a relapse may follow and the cases seem somewhat refractory to Emetin. If however, it is steadily continued, with certain intervals, a cure results in the majority of cases.

On the other hand if a running diarrhoea remains and there is no evidence of amoebae in the stools on examination, the Emetin has done its work in killing the amoebae but an inflammatory condition of the gut exists. Sir Ronald Ross terms these cases post amoebic colitis. Daily injections of Emetin for from 6 to 8 days or even longer will almost certainly in cases of pure amoebic dysentery, when it is acute, be sufficient to either cure or improve. Anyhow it is advisable to give the patient a rest for four or five days after this course. Re-examine the stools and if necessary repeat ~~the course~~ the injections for a further four or five days. Some authorities advocate giving a second course of Emetin after a month's interval for precaution's sake, to prevent relapse on the one hand and a future hepatitis or liver abscess on the other. This I think should be most decidedly followed out.

The cure must be demonstrated by a microscopic examination not only after the attack is over but a month later. With the specific treatment of Emetin other treatment is often necessary.

The Emetin destroys the Amoebae in the submucosa but the cysts which have escaped with the secretions into the lumen of the intestines remain active and untouched by the alkaloid. These are prepared again to enter the bowel wall and continue their ravages supposing they receive no lethal dose of Emetin or have not been swept on and evacuated in the stools. To attack the cysts and undeveloped forms of the amoebae that lie in the lumen of the gut, Pulv. Ipecac. given by the mouth in doses of five grains every night may be substituted for the Emetin injection for a few days. Sometimes a small dose of Castor Oil or Calomel (gr. $\frac{1}{6}$ every hour for four to six doses) will assist in their evacuation. Sir R. Ross gives Pulv. Ipecac. by the mouth in small doses in the "running diarrhoea". Professor S. Kartulis recommends 2 c.c.m. of Acid Tannic Solution (20% strength in normal saline) subcutaneously injected. The Tannic Acid must be absolutely pure. He also gives rectal injections of Acid Tannic 4 pts., Iodiform 3 pts., Sod. Chlor. 6 pts., Arrowroot 25 pts., Aq. Destillata 1000 pts., used in two enemas in 24 hours. It is allowed to be retained for from 15 to 20 minutes. After three or four days treatment, only one injection is given per diem for a week and two or three times a week for two further weeks. This extra treatment is only adopted where the Emetin fails to complete a cure.

Low and Dobell reported (Lancet August 19th 1916) three cases that they treated successfully with Emetin Bismuth Iodide in three grain doses by the mouth once a day for twelve consecutive doses.

One case was of especial interest as Emetin in the usual form administered daily up to 13 grains had failed to get rid of the infection and only five doses of their new compound sterilised the patient.

Perhaps Ipecacuenha by the mouth might have acted in the same way.

Sandwith recommends, during Emetin treatment, "the simultaneous employment of Bismuth Subnitrate in large doses".

He gives 15 to 60 grains every four hours to an adult. To avoid constipation a saline mixture once or twice a week is advised.

General Treatment.

The patients should be confined to bed, the abdomen well covered by a flannel or wool binder. Hot poultices relieve pain and are comforting if the pain is severe. Hot hip baths are also useful when obtained. A dose of Castor Oil should be given at the onset. If there is any collapse a little Strychnine or Camphor injected hypodermically and hot water bottles should be placed around patient. If on the other hand pain is very severe and there is much tenesmus Inj. Morphia. Hypo. gr. $\frac{1}{6}$ may be given or a Starch and Opium enema (Tinct. Opii m.40 Starch Mucilage 1 oz.) is found to give relief. The diet should consist entirely of liquid and for the first 24 hours milk should be avoided. Albumen water, Whey, Chicken Broth, lemon or lime juice, barley water given in moderation at regular intervals will be found sufficient. The next day small quantities of milk in dilute fresh tea, slimy soups made with fresh butter as suggested by Kartulis and on board a Hospital Ship more especially Horlicks Malted Milk. It is easier to make more pleasant than the ordinary ship's milk and more appreciated by the patient. On the fourth day provided the tongue is not very dirty, milk, either

citrated or peptonised in moderate quantity may be tried. Bengers Food, Coco Macaroni or Arrowroot in fresh butter and Custard may be taken. This diet ca continued up to the end of the week. After this it may be gradually improved by giving pure milk, light boiled eggs, biscuits, finely minced chicken, mashe or sieved potato and milk puddings, before going on to an ordinary light diges diet, which latter must be maintained for six months. Alcohol in all forms should be avoided ~~together with~~ also beef, spices, pickles, coarse vegetables or fr

In post. dysenteric Colitis Salol in Grs. 10 dose three times a day for a few days and for a further time in Grs. 5 doses - or Bismuth Salicylas in Grs. 15 doses are useful. In collapse Saline infusions, Adrenalin M.X of 1% soluti every four hours - Strychnine injections, or Pituitary may be given. Constipa tion is prevented by giving paraffin in regular doses as necessary or Castor O two teaspoonfuls for a dose when something more drastic is required.

In the case of mixed bacillary and amoebic infection A.D. Serum 40 cc. fol ed next day by 20 cc. together with Emetin injections has been followed by some good results but not uniformly so.

Enemata of Sulphate of Quinine 1-2000 to 1-500 followed by Starch and Opiu are useful in acute tenesmus also irrigation with Permanganate of Potash Solution every second or third day followed by Nitrate of Silver grs. 30 to three pints relieve tenesmus. Eusol half strength in normal Saline has also been found useful in easing pain.

Surgical Treatment.

Appendicostomy has been performed and a catheter tied in the appendix. The has then been irrigated daily. This has been tried but I have not heard it

spoken of with enthusiasm in acute cases, in fact it is condemned by some surgeons.

In the chronic type it has been more successful.

My observations on the effect of Emetin treatment of dysentery have been recorded from cases sent from Gallipoli to Alexandria by the Hospital Ship "Lanfranc" on which I was one of the Medical Officers. As a rule the patients before arriving on board had received two or more doses of Emetin not amounting though to more than half a grain per diem and sometimes not even that regularly administered. This had been the dose suggested by the authorities but as to how many times a day or for how long were matters left to the individual Medical Officer. There was no bacteriologist aboard and the amount of work to be done in the short time the patients remained on the ship didn't permit of microscopical faecal examination. After some experience it was possible by clinical signs to make a fair diagnosis by the effect of Emetin on the patient. The different forms of dysentery to be distinguished were the amoebic, the bacillary, or both these together, and the diagnosis made clinically after a few days administration of Emetin though crude was fairly correct as proved later.

It was my custom at first to give every case of dysentery after a special note of the circulatory system a subcutaneous injection of Emetin grains half twice a day, but owing to pressure of work the dose was gradually increased to <u>one grain once a day only</u>. This was continued during the rest of my experience without as far as could be seen any ill result. The patients remained on board for about a week on an average. To make sure of a diagnosis was only possible when hospital was reached but when no improvement was seen after four grains of Emetin had been

injected it was pretty safe to assume the case wasn't a pure amoebic dysentery and injections were stopped for other treatment until it could be microscopically proved to be the contrary. In many definitely diagnosed amoebic cases recurrence of symptoms occurred during convalescence on the way home from Egypt to England, a matter of eleven days. Some came on board with looseness and perhaps a little blood occasionally (was passed p.r.) or (they) were quite free from symptoms and signs, but later in three or four days, had a relapse. In these cases a further course of Emetin one grain per diem rarely failed to give good results after (the) second or third day - the injections being kept up till six grains had been given.

The Conclusions come to were:-

I. That the dose of one grain of Emetin subcutaneously injected once a day produced no ill results.

II. That many cases yielded to treatment after receiving 3 or 4 grains and were relieved of all distressing symptoms by the end of the voyage. These were undoubtedly pure amoebic cases.

III. That others were greatly improved, blood having disappeared in the stools, mucus lessened, pain and the tenesmus relieved and the number of motions though still high very much diminished.

IV. That others again showed no improvement whatsoever after four grains were injected. These were probably the cases of bacillary infection.

V. That a second course of Emetin should be given one month after an attack, whether there are amoebae, cysts, or flagellae to be seen in the stools or not, to prevent further relapses, hepatitis, liver abscess, and last but not least to prevent a possible "Carrier" infecting a new district.

CASES admitted to H.M.H.S. "Lanfranc".

1. GERRARD, Pte., admitted from C. Beach Suvla with a diagnosis of Dysentery of four days duration. He had had ½ grain of Emetin twice only. The motions of which there were 9 or 10 per diem contained much mucus and blood ~~and~~ also there was abdominal pain and tenesmus.

One grain of Emetin was given daily. After four grains had been injected there was great improvement. Motions were reduced to five p.d. and all blood had disappeared. Continuing the injections for another three days i.e. after the patient had received seven grains in all, the number of actions was reduced to two per diem and though there was some mucus still, the stools were becoming more formed and were coloured.

This patient left the ship for a Cairo Hospital and was lost sight of.

2. McINTYRE, L/Cpl. had had Dysentery diagnosed by a Medical Officer in the R.A.M.C. at C. Beach, Suvla. It was of three days duration. Numberless stools were passed per diem containing much blood and mucus. Tenesmus was also a prominent symptom. One grain of Emetin had been injected ashore. A further six grains were injected on the ship and he left the ship very much improved. He had five stools a day, all blood had disappeared, "slime" less and tenesmus less acute. This case was also sent up to Cairo and couldn't be traced.

3. RIPPON, Pte. admitted at Suvla with a four days illness diagnosed Dysentery. A large amount of blood and mucus were being passed and the motions were constant. He had had two grains of Emetin injected ashore. Another four grains were given on

board but there was no improvement shown in any way so the Emetin was stopped and the patient was treated with doses of Sodii Sulphas and Acid Sulph dil every two hours. Enemas of Starch and Opium given with ten grains of Dover's powder administered by mouth at night. Some slight improvement was shown.

This case was removed to a hospital at Alexandria and proved to be, by the bacteriologist, one of bacillary infection and no amoebae were found.

4. McKINNON, Pte. admitted on the fourth day with usual symptoms of dysentery. He had had one and a half grains of Emetin ashore.

One grain of Emetin was given daily for six days, an improvement was shown and after having had constant motions with much blood, slime and pain he left the ship having three loose motions a day with no trace of blood but some mucus. The pain had disappeared from abdomen and tenesmus had become decidedly less. The motions were showing a yellow colour. This proved later to be a case of Amoeboid Dysentery.

A.W.W. Capt. was sent home from Alexandria, (the voyage taking 11 days) convalescing from an attack of Amoebic Dysentery.

He had still some "looseness of the bowels" and passed mucus with his motions. Bismuth and Salol were tried but failed to stop this condition. Four grains of Emetin were injected in four days and after the third dose only one action was passed per diem and the mucus with this was very much reduced. This good result continued for the rest of the voyage.

G.J.J. Capt. admitted from C. Beach, Suvla with jaundice. He had had two attacks of diarrhoea, starting the first one, three months ago. He became much jaundiced two weeks previously. This however had all improved but he was left

with alternate attacks of constipation and diarrhoea the latter being accompanied by blood and mucus. He had also indefinite colicky pains in the left inguinal region. After $\frac{2}{3}$ grains of Emetin had been injected once a day for three days the blood and mucus cleared up and the motion though loose was inclined to be formed and yellow in colour. After a further two days there was a relapse and the Emetin in one grain doses per diem was repeated for two days while the patient was on board and the motions became more normal again. He was removed to a hospital in Alexandria and Amoebae in the stools were demonstrated.