

ON BACILLARY DYSENTERY - ITS DIAGNOSIS, SPREAD AND CONTROL.

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Introductory.

The work on which this thesis is based was done in Bangalore and Poona Southern India in both of which places bacillary dysentery is endemic. The period covered is roughly thirty three months viz: in Bangalore from January 1928 to January 1929 and Poona from February 1929 to September 1930. The laboratory work was carried out in the Military laboratories during these periods while I was officer in charge of these laboratories. The patients dealt with were mainly soldiers of the Army in India British and Indian and a smaller number of British women and children. In addition the carrier condition of a large number of the civilian (Indian) population employed in a menial capacity by the Army was investigated. It is, perhaps, necessary to define what is meant by bacillary dysentery. The definition adopted by the War Office Committee on Dysentery which was assembled during the Great War was "An infectious disease, with or without fever, tending to epidemic spread; characterised clinically by diarrhoea, usually accompanied by tenesmus and by the passage

of blood and mucus, with a purulent inflammatory exudate; the lesions affect the colon pre-eminently; but may extend to the lower part of the ileum.

In the milder forms of the disease the clinical symptoms may be those of simple diarrhoea."

These words accurately define the disease.

The disease is endemic in many part of the world especially in tropical and sub-tropical countries but it depends on no peculiarity of climate for there have been epidemics all over the world and on the high seas. In Europe it is an institutional disease being present in asylums (Gettings⁽¹⁾) (Harding⁽²⁾) and occasionally causing epidemics therein. While the advance of hygiene has caused its apparent disappearance in modern Europe yet Hurst⁽³⁾ and Glynn and others⁽⁴⁾ have shown that it is more common than is usually supposed.

It appears and spreads in any community where the rules of sanitation are inadequately observed.

This explains its occurrence in asylums and in armies in the field; in the former the dirty habits of the inmates are responsible, in the latter, circumstances imposed by Military necessity ^{often} ~~after~~ result in a relaxation of a strict sanitary regime.

The thesis is divided into three parts.

In the first part the laboratory methods employed

are described and the results tabulated and discussed. In the second part the results of the examination of civilians for a carrier condition are given and the method of spread of the disease is discussed. In the third part the means of prevention are considered.

Source of specimens. Specimens were received from Military hospitals British and Indian and family hospitals which were situated either in the same place as the laboratory or up to several hundred miles away.

In the former case the selection of the specimen for examination was made by the trained laboratory staff from whole stools sent direct to the laboratory, in the latter the personnel of the hospital selected the specimens and despatched them to the laboratory in accordance with instructions issued to them; these specimens despatched by post were not received until they were from 12-36 hours old.

There must be the closest possible contact between local hospitals and the laboratory for the best results to be obtained and it is necessary for the laboratory worker that the clinician and the subordinate personnel of the dysentery wards understand exactly what is required; the main points to be mutually arranged are

- (a) that there is the least possible delay between the passage of the stool and its receipt in the laboratory.
- (b) that adequate precautions are taken

where large numbers are being dealt with to ensure that correct names are attached to specimens.

- (c) that specimens continue to be sent from each patient until a provisional diagnosis is received from the laboratory.

It may here be mentioned that heating of bed-pans is unnecessary in Southern India. The clinician must be made to feel that his active cooperation is not wasted, the laboratory worker must therefore arrange

- (1) to let him have as early a diagnosis as possible consistent with reasonable accuracy
- (2) to have competent laboratory personnel always present to deal with specimens
- (3) to detain personnel bringing specimens from the wards to the laboratory for the shortest possible time.

Unless steps are taken to obviate it the menial personnel despatched from the local hospitals to the laboratory will waste a considerable time en route; this is dealt with by the despatches^y noting the time of despatch on the form which gives the details of the patient and the laboratory entering time of despatch and receipt in a day book in which particulars of all

specimens are entered up; the attention of the clinician can then be called to any undue delay.

METHOD OF EXAMINATION OF SPECIMENS.

On receipt in the laboratory a portion of blood-stained mucus is selected, washed in sterile saline, and plated on Litmus Lactose Bile Salt Agar (see Appendix). A similar specimen is emulsified in saline on a slide into a thin film, covered with a coverslip and ringed with vaseline. The reaction of the stool is tested with litmus paper and recorded.

The film is then examined under the microscope using $\frac{1''}{6}$ objective with the condenser in place and the diaphragm partially closed. In the great majority of cases a provisional diagnosis can be made at once and a report sent to the clinician on which his treatment can be based.

The reports will be in the following form

- (1) active forms of *Entamoeba histolytica* present.
- (2) Bacillary exudate present
- (3) the stool is dysenteric but the exudate is indefinite.

The first report does not come within the scope of the thesis.

The second report means that the dysentery is due to a bacillus and it is necessary to describe what is meant by a bacillary exudate. This exudate consists of large numbers of cells the chief of which are polymorph leucocytes in various stages of degeneration i.e. pus cells, red blood corpuscles and large phagocytic mononuclear cells. Seen under the microscope in the unstained specimens referred to above the polymorphs are rounded cells with a nucleus showing as green refractile dots, these dots are often three or four in number and have led to these cells being mistaken for cysts.

The red blood corpuscles appear as pale green and refractile cells just as red cells would appear in normal saline under the microscope, they do not tend to become aggregated together but are scattered evenly throughout the preparation.

The large mononuclear cells or macrophages are the largest cell in the exudate, round, pale with a large round nucleus which often shows vacuolation; these cells often contain ingested foreign bodies such as bacteria and some observers have stated that they are motile, while this is very probable I have never observed motility in these cells during several hundred examinations. The presence of such an exudate in the stool of a patient with the clinical symptoms of acute dysentery means that the dysentery

is bacillary in origin.

The exudate is said to be present in a variety of other conditions involving inflammation of the intestinal tract; Little and Bornshin⁽⁵⁾ state that exactly the same exudate was seen in three cases of typhoid fever which ended fatally without perforation and in two or three cases of cholera amongst Indians, in the latter cases they suggest that this was merely the waking up of a chronic bacillary dysentery infection.

I have seen a similar exudate in a patient suffering from inflammation of internal piles but in this case there was a history of previous dysentery and the exudate contained very few red blood cells. Of 91 cases diagnosed bacillary dysentery in 1929 because such an exudate was present in their stools while they had acute dysenteric symptoms 75 were afterwards diagnosed bacteriologically (76.9%)

The following table taken from the Report on the Health of the Army for the year 1929 shows the findings in different laboratories in India.

Laboratory	Cases with bacillary exudate	Percentage positive to B.dysenteriae.
Kohat	167	66.4
Rawalpindi	85	71.7
Lahore	164	67.6
Banma	80	80.0
Poona	91	76.9
Bangalore	82	68.0
Secunderabad	151	68.2
Quetta	203	35.9
Karachi	87	60.6
Meerut	126	37.3
Lucknow	40	85.0
Bareilly	75	94.6

While the same report states that bacteriological examination of 1616 cases showing an indefinite exudate yielded dysentery bacilli in 15.3 per cent.

My own results in Poona in 1929 show that in 61 cases showing an indefinite exudate 10 (16.4%) showed B. dysenteriae (9 Flexner 1 Shiga) on culture.

The presence, therefore, of a bacillary exudate in cases of clinical dysentery as a diagnostic feature of the bacillary variety, is supported strongly by bacteriological findings and the

results of treatment also amply justify such a diagnosis. The third report is of little help to the clinician and is unsatisfactory to the laboratory worker, it means nothing. It often indicates either that the patient has had the symptoms for some days in the case of bacillary dysentery or in the case of protozoal dysentery that there has been delay in forwarding the sample or that admixture of urine has destroyed the typical vegetative forms of the entamoeba.

In my experience a delay on examination of half an hour in a case of protozoal dysentery where urine is mixed with the stool is quite sufficient to render actively motile entamoebae immobile and unrecognisable. There are cases in which although the exudate is indefinite there is a distinct suspicion that it is bacillary and a more judicious selection of the specimen and further examination often reveals a part showing the typical exudate. In all cases where the exudate is indefinite a thorough search for vegetative forms of the *Entamoeba histolytica* is indicated. If this search fails and cultures do not help, the examination of material obtained by rectal swabbing may clear up the condition. The following is a typical case. An officer was admitted to hospital in Bangalore with dysenteric symptoms, he had a previous history of five attacks of dysentery none of which had been definitely diagnosed. His first two specimens showed an indefinite

exudate no amoebæ and cultures were later negative. Examination of material obtained by rectal swabbing showed vegetative forms of *Entamoeba histolytica*. An exudate, examined within 48 hours of the first onset of acute symptoms, which is indefinite and which has been selected by trained personnel is almost certainly not bacillary.

It may be argued that the expert clinician can, by naked eye inspection of the stools, say which cases are bacillary in origin and which are probably not. This is to a certain extent true and in the absence of facilities for microscopic examination might conceivably have to be acted upon, but it does not give that precision to treatment which microscopic examination does. After a large personal experience of both methods of examination I should feel very unhappy to have to treat cases of acute dysentery on a diagnosis not based on microscopic and cultural examinations.

Specimens received by post from hospitals at a distance from the laboratory consisted of portions of blood-stained mucus in 30% neutral glycerine in 0.6% saline. The glycerine must not be acid and its reaction must be tested frequently.

In addition a film of the exudate is made on a slide and sent to the laboratory to be stained and examined

for character of the exudate and films of mucus on cover slips are made fixed in Schaudinn's solution and sent in 70% alcohol to the laboratory.

These cover-slip preparations are stained by Haidenhain's iron haematoxylin method and examined for amoebae.

The films thus obtained were not nearly so satisfactory as fresh specimens and during the latter part of 1929 and early in 1930 personnel from hospitals at a distance were trained in the microscopic examination of these cases and the recognition of exudates and entamoebae and while these films continued to be sent greater reliance was placed, gradually, upon the local findings.

The specimens of mucus in glycerine and saline were plated on the Litmus lactose bile salt medium, the films of exudate on slides were stained by Lashman's stain and examined for the character of the exudate but the actual spreading and drying of the film and the staining of the cells in a background of mucus makes the specimens much less easy to interpret than a fresh specimen.

BACTERIOLOGICAL DIAGNOSIS.

Plates are examined after 24 hours in the incubator. The colonies of the dysentery bacilli have no very distinctive features on plates, they vary in size some being extremely small pinhead colonies resembling a streptococcal growth others being as large as the coliform group; as they do not ferment lactose the medium remains blue and the colonies appear as semi-transparent regular round colonies. It is impossible to distinguish by the appearances on the plate any difference between dysentery bacilli and several other non lactose fermenting organisms such as *B. morgan*, *B. schmitz*, streptococci etc. For this reason several colonies must be examined for motility and by Gram staining and from two to six colonies showing gram negative non motile bacilli are subcultured in to two peptone salt media tubes one of which contains 1% Glucose and the other 1% Mannite and an appropriate indicator (Andrades was used.)

It is recognised that, theoretically, it is fallacious to test the motility of bacilli from cultures on solid media but in practice it was seldom that one found an organism originally non motile showing motility later.

Plates with few or no suspicious colonies should be re-incubated for a further 24 hours and examined in the same way again when they frequently yield positive results.

The Glucose and Mannite tubes are examined after 24 hours and subcultures made from them into similar tubes containing lactose and dulcitol also into broth and into plain peptone salt for indol testing.

The following day, that is the third day after the original plate culture was made, these sugar fermentation tubes will indicate how the organism ought to be tested with specific antiserum; if Glucose alone shows fermentation and no indol is produced the organism in broth is put up with specific anti shiga serum and if it agglutinates the diagnosis is complete; if mannite also shows fermentation the organism is put up with polyvalent Flexner antiserum it may agglutinate in which case it may be called a *B. dysenteriae*^e flexner or it may not in which case it may be considered provisionally a flexner bacillus but not serologically proven and should be subcultured and replated and tested again at intervals; after three such tests if it still remains inagglutinable I have been in the habit of reporting the organism as "an organism with the morphological and biochemical characters of *B. dysenteriae flexner* but

unagglutinable with specific antiserum.

No gas is produced in any of the media used, by dysentery bacilli.

It will be seen that by this method it is three days from the receipt of the specimen before a definite bacteriological diagnosis is given; this has no serious disadvantages provided that a bacillary exudate has been found; the clinician will have commenced treatment on that finding. The time can be shortened by subculturing on broth or on an agar slope direct from the plate when the glucose and mannite tubes are inoculated and using these subcultures for agglutination purposes, by this means the serological results are available on the second day after receipt of the specimens.

This proved quite satisfactory in my hands.

The specific anti-sera used were for the first year prepared in the laboratory, after that they were obtained from the Enteric fever laboratory at Kasauli. Dreyer's macroscopic method of agglutination was used with $4\frac{1}{2}$ hours in the water bath at 55°c .

No trouble was experienced with B, dysenteriae shiga either in sugar fermentations or agglutinability; they were all true to type and generally agglutinated to the full titre of the anti-serum used.

On the other hand the Flexner group gave considerable trouble, many of them did not agglutinate with polyvalent flexner antiserum. Some agglutinated after a variable number of sub cultures. This failure to agglutinate may have meant that one was dealing with types not represented in the polyvalent anti-serum but most often meant that rough colonies were being used and re-plating and selection of smooth colonies for agglutination purposes frequently resulted in agglutination occurring.

Some of those which do not agglutinate were later found to be B. sonne; for this reason all lactose tubes were returned to the incubator and examined daily for ten days. B. sonne ferments lactose between the third and fifth day of incubation.

Another very much rarer group were met with which at first were considered to be inagglutinable flexners but which were found to ferment Dulcitate after two to seven days incubation; these were not regarded as true dysentery bacilli.

TABLE I.

Cases of Acute Dysentery examined.	Number showing Bacillary Exudate	Bacteriological Findings.		Total diagnosed Bacillary-bacteriologically or on appearance of exudate.	Protozoal i.e. Vegetative forms of E histolytica found	Laboratory findings Negative.
		B. Flexner.	B. Shiga. B. Sonne			
480	278 (57.9%)	199	21 11	351 (73.1%)	62 12.9%	67 14%

RESULTS OBTAINED.

Table I shows the results obtained in 480 cases of acute dysentery. An exact laboratory diagnosis was arrived at in 86% of the total cases examined - (73.1% bacillary and 12.9% protozoal). It is interesting to note that a diagnosis upon which treatment could be at once definitely settled was arrived at in over 70% of cases by microscopic examination alone; as this included many specimens received by post, which, as already pointed out, were not so satisfactory as fresh specimens, the microscopic diagnosis is probably possible in well over 80% when fresh specimens only are dealt with. This places the physician, who can and will use a microscope, in the absence of a laboratory, in a very strong position for accurate diagnosis and treatment of such cases. Moreover it is one of the few occasions upon which the laboratory ⁿcases often give an immediate diagnosis the report being handed to the person who brought the specimen from the Wards. The proportion of bacillary dysentery to protozoal cases in those definitely diagnosed was 5.8 to 1. This corresponds with the findings of Cunningham ⁽⁶⁾ who states that 86% of the dysentery in jails of Eastern Bengal was bacillary in origin and also with

Acton and Knowles⁽⁷⁾ who state that in their experience in Calcutta between 1920 and 1923 bacillary dysentery was at least five or six times as common as protozoal dysentery.

If the same proportions hold good in the 67 cases in which laboratory findings were negative then of these cases approximately 56 were bacillary and 11 protozoal. It is therefore possible to say that of the 480 cases examined 407 (i.e. 351 definitely diagnosed plus 56 undiagnosed in the laboratory) were bacillary in origin. The difference between the total cases diagnosed as bacillary (351) and the number diagnosed bacteriologically (231) indicates that 120 cases showed a typical exudate with negative bacteriological results (Although no figures are available it may be taken that in practically every case in which the causative organism was isolated a bacillary exudate was present. This point will be referred to later when the carrier question is discussed)

The reason for this is, I think, because the disease as seen in the Army is definitely mild; the Report on the health of the Army for 1929 Table 60 page 133 records that in India there were 1039 cases of dysentery and only one death amongst men. This often means that the patient does not come to hospital until he has been ill for about 48 hours; the exudate persists long after

the excretion of dysentery bacilli has ceased or become very intermittent, in fact it is a moot point which will be discussed later whether, even in convalescents or so-called carriers, dysentery bacilli are ever present in the stools in the absence of an exudate.

The presence of the exudate, therefore, does not mean that dysentery bacilli are present in the stools, it does mean that there is still an inflammatory process going on kept up by secondary invading organisms while the dysentery bacilli, if they were the cause of the original inflammation, are deeper in the submucous coat of the intestine and are only excreted at intervals.

There are, of course, other factors in the production of negative results; insufficient numbers of colonies may have been examined, delay may have occurred in the despatch of the specimen and faulty glycerine saline solutions may have been used.

While the laboratory worker must consider these 120 cases unsatisfactory yet for the physician the diagnosis of bacillary dysentery is all that is required; in fact so mild are the vast majority of cases that, by the time the laboratory has elaborated its original finding of a bacillary exudate present into a bacteriological result, the patients are convalescent.

I can quite imagine a physician who had 480 cases of acute dysentery examined at a laboratory and received a definite diagnosis in 413 cases (86%) being more than satisfied.

BACTERIOLOGICAL FINDINGS.

Table 2.

Cases diagnosed bacteriologically.	B. dys. Flexner	B. dys. Shiga	B. dys. Sonne.
231	199 (86.1%)	21 (9%)	11 (4.9%)

The large preponderance of flexner infections is in keeping with the mild character of the disease. Mixed infections of Shiga and Flexner bacilli in one patient were never met with. Apart from those organisms recognised as causative of dysentery certain other organisms not generally so accepted but about whose pathogenicity there is some doubt were isolated frequently, the commonest being B. Schmitz and B. morgan; the latter organism is so very frequently present late in the disease that one

The W. strain showed a very definite preponderance. Of the 11 unclassified cases two became auto-agglutinable while the remaining 9 gave the same percentage titre with more than one anti-serum.

The anti-sera used had a minimum titre of 1-500. A further 45 flexner organisms isolated by me in Poona from cases of acute dysentery were sent to the Ministry of Health Pathological laboratory London and these were classified by Dr. Scott to whom I am indebted for the following figures.

Table 4.

Number tested	Classified as							
	V	W	X	Y	Z	Sonne	Shiga	Unclassified.
45	3	11	2	5	4	5	1	14

These results correspond fairly closely to those obtained by me in India. The five organisms which Dr. Scott classified as Sonne were considered by me to be inagglutinable flexners as they did not ferment lactose in my hands. These organisms were all isolated about the same time and it is a common experience of bacteriologists in India that too much reliance cannot be placed on sugar fermentation results especially

Lactose and Saccharose.

The Shiga bacillus was sent in error.

Of the unclassified cases 7 were stated as "possibly not Flexner" 2 were dead and 5 were not typed.

Again the W strain predominates.

Part II. THE METHOD OF INFECTION AND SPREAD
OF THE DISEASE.

The causative organisms are present in nature in the intestinal canal of man, sometimes in dogs, in their excreta and nowhere else (the question of their presence in the intestinal canal of the fly is discussed later.)

It follows, therefore, that, as man can only be infected per os, (infection per rectum is possible but must be extremely rare) food or drink contaminated by human excreta is the common method of infection or as Vaughan ⁽⁸⁾ puts it "Dysentery is always due to the transfer of the excreta of one person to the ingesta of another."

While this is the direct cause there must be many indirect or predisposing causes because when investigating the question of infection it is common, in fact usual, in endemic areas to find that the ingesta of the sporadic case have been shared by many others many of whom have quite probably had the same dose or a larger dose of the organism and yet none have become infected. This escape may be due to many causes and it would almost appear that the true solution of the spread of bacillary dysentery is not the number and prevalence of sources of infection

flies etc. but the receptive state of the tissues, gastric and intestinal, at the time of exposure to infection. Kettle⁽⁹⁾ writing of work by Gye & Cramer on infection says that their conclusions appear to be, that, in infection the state of the tissues is of the first importance. There are certain observations which bear on this question of infection. Virchow⁽¹⁰⁾ noticed during the prevalence on several occasions of epidemic contagious dysentery (undoubtedly bacillary) in the Charité hospital Berlin the disease chiefly spaced the syphilitic wards in which, at that time, the patients were treated without mercury by a plan in which laxative medication was a prominent feature. Kauntze⁽¹¹⁾ observed that in the early stages of bacillary dysentery there is a disturbance of liver function and an increased flow of bile and later a diminished excretion of bile. Besredka showed that administration of bile to rabbits renders them susceptible to infection by *B. typhosus*.

Again, experimental infection by feeding with cultures (Strong and Musgrave) was produced in normal individuals only after alkalisising the stomach. Scheer⁽¹²⁾, making experiments on the bactericidal action of the gastric juice on certain

organisms amongst which were the dysentery group, found that normal gastric juice kills pathogenic bacteria in two minutes the essential ingredient being not the free hydrochloric acid but its salts. It would seem, therefore, that constipation, liver disturbance resulting in an increased flow of bile, and diminished bactericidal activity of the gastric juice are necessary for infection. Unfortunately infection has occurred before the patients come under observation but a history of constipation is frequently obtained while liver disturbance is a commonplace in endemic areas. This problem of infection is not confined to bacillary dysentery but applies equally to many other diseases where the infection is per os, such as cholera, typhoid fever etc. and it means that while the bacteriologist and hygienist can prove definitely how the organism is obtained and conveyed to the individual it lies with the bio-chemist to explain the factors prevailing in the body which permit the bacillus to obtain a footing.

The Source of infection.

It is safe to say that every text book on tropical medicine will state that "carriers" are the source of infection in bacillary dysentery. A "Carrier" in the accepted sense of the word is an individual showing no signs or symptoms who is either convalescent from the disease and still excretes the causative organism or an apparently healthy person who may or may not have a history of the disease and who also excretes the organism. In endemic areas it is practically certain that carriers play a negligible part in the spread of the disease. The main source of the disease is the mild case who is not under treatment, in other words the uncontrolled or missed case. It has already been shown that in Europeans the disease is generally mild and in Indians also, mild attacks are very usual, the latter, accustomed as they are to bowel complaints, treat a slight diarrhoea with perhaps the passage of some blood and mucus as an inevitable event which will pass off and the vast majority never think of seeking treatment far less of becoming hospital patients. Cunningham⁽¹³⁾ found in Madras and Bengal that 22% of the population were suffering from what he termed latent dysentery, that is passed blood and mucus at

intervals. Many of these mild cases become chronic cases of dysentery who secrete organisms at intervals and who would show lesions could they be examined with the sigmoidoscope. Europeans in endemic areas are surrounded by these uncontrolled cases, some acute, some chronic all more or less infectious. The sanitation is primitive and the vectors of the disease have free access to infected material practically continuously as native latrines are usually emptied once in twenty four hours.

Is there such a person as a healthy carrier?

(14)
Perry who has studied this question states that in the great majority of the carriers he examined there was some obvious ulceration of the large intestine and that the disappearance of the organism from the stools coincided with the improvement clinically of the cases, in other words the cured case was non-infectious.

(15)
Saisawa and Tanabe examining recruits for the Japanese army found that out of 2847, 15 i.e. 0.52% were excreting dysentery bacilli and that sigmoidoscopic examination revealed ulceration or inflammation, in most cases they conclude that so-called healthy carriers are very mild cases of the disease. In Bangalore I examined 649 Indians and found the

B. dysenteriae flexner on two occasions and in other 2 cases a bacillary exudate that is 0.6% showed signs of bacillary dysentery, both cases in which a bacillus was isolated showed blood and mucus in the stools.

If the different organisms are considered it will be found that while the individual from whom the flexner bacillus is obtainable during convalescence or later, is apparently in perfect health, the shiga excretor generally shows definite signs of ill-health - his bowels are irregular, he passes blood and mucus at intervals, he suffers from severe mental depression and is quite unfit for work.

If the Flexner excretor is questioned one frequently elicits a history of occasional passage of excessive slime in the morning and I have on several occasions examined such stools and found a typical bacillary exudate present showing that the individual has still active intestinal inflammation.

Out of 1817 examinations of convalescent cases after the alleged disappearance of blood and mucus from the stools dysentery bacilli were isolated 23 times (22 flexners 1 shiga) i.e. 1.2% of these 23 positive cases further careful examination showed a typical bacillary exudate present in 15 at a later date, 6 were not further examined and 2 showed no

exudate present in two further examinations. The so-called carrier of bacillary dysentery is not comparable with the carriers of other diseases such as typhoid fever. In the vast majority of cases he has signs of the disease which can be detected either by naked eye and microscopic examination of the stools or by the sigmoidoscope, he is either a missed case or a chronic case, in any event he is a case of the disease and the reservoir of infection; the disease is spread from case to case by the vectors which have to be considered.

It should be noted that dogs may be the reservoir of the organism Dold ⁽¹⁶⁾ found that of seven sporting dogs suffering from diarrhoea at Shanghai four were harbouring dysentery bacilli (one Shiga three Flexner)

The Vectors of infection.

The disease may be spread direct from one case to another when a case is not isolated in hospital. Everything he touches may be infected and if he has anything to do with the preparation or serving of food his scope is considerably enlarged. His clothing will be specially dangerous to those handling it before it has been washed.

(17)

Zinsser states that the bacilli may live in clothing for a month.

This is the direct method of spread.

Indirectly the disease is spread by

- (1) Human beings
- (2) Dust and Sand
- (3) Water
- (4) Milk and its derivatives
- (5) Flies.

1..Human beings. The healthy human may transmit the disease from a case to others without himself becoming infected. Cooks may use infected latrines and convey the infection to the food of others; the native servant handles and attends to his sick child and then serves his master's food.

2. Dust and Sand. The bacilli if not exposed to direct sunlight will stand dessication well and it has been suggested that dried and powdered faeces blown about might contaminate food. If this were a potent means of spread one would expect a high incidence in the dry season in the tropics whereas the rainy season and immediately after is the time of greatest incidence when dust is at its minimum. Dust plays little direct part in the spread of the disease, indirectly by irritation of the intestinal canal sand and dust may be a pre-

disposing cause. Zinsser states that in damp sand the bacilli may live for 39 days so that cleaning food utensils with unsterilised sand - a practice common in the tropics - may be a source of infection and this was said to have been the cause of an outbreak in Scotland during the great war.

3. Water. The bacilli are rapidly outgrown by other organisms in water, but in sterilised water they can live for several weeks. In ice bacilli can remain alive for longer than a month (Zinsser). Theoretically therefore water may be infected but practically water borne epidemics seldom occur.

4. Milk and its derivatives. These may be infected by flies or by an uncontrolled case and an outbreak may arise; such an outbreak was reported in St. Andrews some years ago due to the Sonne bacillus.

Tinned butter is a frequent article of diet in India, much of it is made there under conditions which are more than favourable to infection but I have never heard of a single case being traced to such an infection. I obtained several tins of Indian made butter and infected them with cultures of *B. flexner*, a heavy infection, but after a month at room temperature the bacilli

had disappeared, the butter was very acid so that even if it is infected when made the acidity is sufficient to destroy these organisms, which are sensitive to acidity, after a short period of storage.

5. The fly. It has been shown often that in many localities the maximum incidence of dysentery corresponds closely to the maximum incidence of flies. A great deal of work has been done to prove the guilt of the fly as an infecting agent much of which has been in connection with the enteric group of bacilli.

(18)
Faichnie states that out of 13 flies bred from a typhoid stool 6 contained *B. typhosus* in their intestines and the bacillus was recovered from a fly 16 days old; these findings have been confirmed by Tebbut (19) and in his experiments the *B. dysenteriae* (Flexner Y) was used and his results seem to show that this bacillus is more adaptable to the fly than *B. typhosus*.

(20)
Orton writing of an outbreak of bacillary dysentery in an asylum considers the fly entirely responsible. He experimented with *B. prodigiosus* exposing cultures in the laundry where the bedding and clothing were

cleaned and from some of the flies caught in other parts of the asylum this bacillus was isolated.

(21)

Manson Bahr isolated dysentery bacilli (Shiga) from the intestines of flies in Fiji in 1910 and later also in Sinai, of the latter he states the flies had no direct access to dysenteric stools so far as could be ascertained "there would seem therefore to be some unascertained vital association between the house fly and the dysentery bacilli."

Experimentally it has been proved that dysentery bacilli can survive in the intestinal canal of the fly for at least 5 days.

(22)

Dudgeon examined 1000 flies caught in a dysentery hospital in Salonika; from one of these caught in a kitchen a typical flexner bacillus was isolated.

(23)

Graham Smith from experiments conducted with *B. prodigiosus* comes to certain conclusions. Infected flies carry the bacillus on their legs and wings for 18 hours after infection and up to 4 or 5 days in large numbers in the crop and intestine, the maximum period in the intestine being 18 days.

They infect not only food but other flies by

their deposits.

He also found that the alimentary canal of the fly contains many bacilli which do not ferment lactose and closely resemble pathogenic organisms. I can confirm this last finding because examining flies in Bangalore I found all sorts of coliform organisms in their intestines and also non lactose fermenting organisms including Morgans bacillus on several occasions.

Manson Bahr's suggestion of an intimate and vital connection between dysentery bacilli and the fly is of great interest and if proved would be of far reaching importance.

Can it be that the bacillus of dysentery undergoes some change in the fly or that some of these organisms commonly present in the flies intestine are really dysentery bacilli in process of change, becoming later pathogenic to man again. The mutation of organisms has been suggested many times but has never been proved.

The case against the fly is proved, as far as it seems possible to prove it; the fly is probably responsible for the rise in the number of cases in endemic areas just after

the rainy season, while the causation of the sporadic cases is shared with the fly by the human vector especially the Indian.

PART III.

THE MEANS OF PREVENTION.

The measures to be adopted for the prevention of the disease can conveniently be considered under three heads according as they are applicable to -

- A. The sources of infection
- B. The vectors of infection
- C. The potential cases.

A. Methods applicable to the sources of infection.

It has been shown that the mild uncontrolled cases and the uncured cases are the sources of infection. If these could be detected early, isolated in hospital and not discharged until cured then the greatest source of infection would be controlled. This is a counsel of perfection quite unattainable in the primitive countries which the disease mainly affects; firstly these people regard a mild dysentery much as a European regards a cold, and secondly apart from the expense of providing sufficient hospital accommodation which would be formidable the vast majority of natives are extremely averse to hospital treatment. In every cantonment in India there is a

hospital for the treatment of Indians who live in cantonments but it is quite the exception to have any cases of dysentery under treatment there or even to see cases apply for such treatment as outpatients. Europeans also are often inclined to minimise mild bowel complaints; every locality has its own peculiar name for them e.g. "Poonaitis", "Bangalore tummy"; most of these are mild Flexner dysenteries, which yield quickly to saline or castor oil treatment. They can be readily diagnosed if subjected to laboratory examination early but this is seldom done because the local doctor is forced by popular opinion to call them by the local name and treat them in the local manner.

The solution of this part of the problem is bound up with the public health policy of the country and the education of the inhabitants. Europeans living in endemic areas can do a great deal to assist incidentally protecting themselves by insisting that all their servants are medically examined frequently and that any who are ill are properly treated and removed to hospital if necessary. It is clear, therefore, that in endemic regions

until the inhabitants can be educated up to a much higher standard of public health these sources of infection will remain uncontrolled and uncontrollable.

The periodical examination of the stools of all personnel employed in cook houses, restaurants, supper bars, hotels and boarding houses is now carried out in many endemic areas but the fact that the chronic case of flexner dysentery generally secretes organisms at intervals only, renders this procedure of doubtful value; it is valuable in that it prevents mild acute cases carrying on their work undetected. Moreover it is fraught with difficulties which at first seem improbable; it is an undoubted fact that when specimens are selected by subordinate personnel a single stool may provide specimens labelled with half a dozen different names.

If a particular set of food handlers appear to be associated with several cases of the disease the only satisfactory method of dealing with them is to get them into hospital, examine their stools for traces of blood and mucus over a definite period say three to five days, release those who show no signs.

and do bacteriological examinations on those passing blood and mucus or excessive amounts of mucus. This of course is difficult and sometimes impossible to carry out, but it can be done and on two occasions by such methods I have found a chronic case of flexner dysentery amongst food handlers associated with a number of cases of the disease.

Part B.

Methods applicable to the vectors of infection.

The human vector who carries the disease from a case can only be dealt with by education in cleanliness and by the provision of facilities for cleanliness. This is specially necessary in all food handlers and is carried out only when strictly supervised. Even when provided with all modern appliances the native cook loves to revert to his primitive methods and it is no uncommon sight to see him seated on the floor icing cakes, the cakes reposing on the floor beside him.

Too often even in well supervised places the appearance of cleanliness stands for its practise and a basin of potassium permanganate

covers a multitude of sins.

The most important vector is the fly.

There is a voluminous literature on the subject of fly destruction and on the methods by which the human being should be protected from its disease carrying proclivities. It will be sufficient if general outlines of the campaign against the fly are given. This campaign should be in force all the year round in endemic areas but should be intensified at the beginning of each fly season.

It consists in

- (a) Prevention of breeding
- (b) Prevention of access to human excreta
- (c) Destruction of larvae and adults.
- (d) Protection of ingesta.

The methods to be adopted under each of these heads vary with local circumstances and it is unnecessary to enter into details. It is my own conviction that most can be done by the prevention of breeding, the breeding places being systematically found and dealt with according to their merits. The number of fly proof latrines is legion which goes

to show that none are really satisfactory and it has to be remembered that the provision of a water carried system of sewage disposal is completely ruled out in most of the endemic areas for many reasons.

The campaign against the fly in these primitive countries should be directed by one who knows the country well and is well up in the bionomics of the fly, he will find it easy to rouse a fleeting interest but very difficult to get that sustained effort which alone can prove effective in reducing numbers.

Part C.

Methods applicable to the potential case.

The factors predisposing to individual infection have been shown to be, constipation, liver disturbance, diminished bactericidal power of the gastric juice and possibly intestinal irritation caused by the ingestion of quantities of sand or dust. These are matters of personal hygiene well known to most educated people; constipation is a very common complaint in Europeans in the tropics and the majority in my experience take some form of aperient with great regularity. After considering the statement of Virchow quoted above I believe that a daily dose of Sodium Sulphate sufficient to produce one or two liquid motions is a prophylactic well worth individual trial. I have contemplated a large scale trial of this method but have been unable to overcome local difficulties in carrying it out. Apart from its prophylactic value, which is very difficult to prove, it would seem probable that it might quite easily prevent the bacilli from gaining a footing and thus abort the disease.

It has apparently no deleterious effects even when taken over long periods as I have known many individuals who have done so. Of late years in the United Kingdom habitual morning salines have become very popular and they apparently have no ill-effects. The liver disturbance and diminished bactericidal action of the gastric juice are due to a variety of causes which operate specially in the tropics - over indulgence in alcohol, heavy, highly spiced meals and sedentary habits or the reverse, over-exercise, being the most common. These are of course avoidable and again the daily saline helps.

The ingestion of sand and dust were thought in Gallipoli to render the individual more susceptible to bowel complaints particularly dysentery and in places where dust storms are frequent and sudden it is quite possible that the quantity of sand ingested may be considerable. But that is not the time of the year when dysentery is at its height and I have never been able to satisfy myself that it in any way predisposes.

Production of artificial immunity.

The striking success of inoculation with vaccine in diminishing the incidence of the enteric group of diseases leads one naturally to look for a similar form of protection against bacillary dysentery. Many attempts have been made to produce a satisfactory vaccine for bacillary dysentery some of which have been very promising. There are certain difficulties the first of which is the toxicity of the shiga element of the vaccine and the second, the confusion in the Flexner group and the very variable response to inoculation of vaccines prepared from this group. In spite of these difficulties certain of the vaccines prepared seem to have been of use and deserve mention.

(24)
Whitmore, Fennel and Peterson prepared a lipo vaccine containing Shiga bacilli and the Flexner Y group and injected large doses into human beings without marked local or general reaction. They found production of agglutinins, precipitins and bacteriolysins in the blood of inoculated men and animals and some evidence of complement fixation - that is several tests showed the presence of a degree

of immunity. The vaccine is difficult and expensive to make.

Perry and Coppinger ⁽²⁵⁾ describe a vaccine made from anaerobically grown Shiga bacilli and found they could inject up to 20,000 million Shiga bacilli into human beings without excessive local or general reactions.

Their conclusions were very guarded but they prepared a mixed Flexner group and Shiga vaccine which could be inoculated into human beings and which produced demonstrable agglutinins for both types of organisms.

Dumas, Ramon and Bilal ⁽²⁶⁾ describe the preparation of anatoxin from B. Shiga. With this they have easily immunised rabbits although the serum of the rabbits shows no agglutinin production. The anatoxin retains its antigenic properties for at least twelve months. It has been used to immunise horses for the production of antitoxin. Doses of 0.5 and 1 c.c.m. can be given to human beings with but slight local inflammatory reaction and rise of temperature.

Many other methods have been adopted for getting rid of the toxic effects of the Shiga element Blaine and Canunopetros ⁽²⁷⁾ state that the

Shiga bacillus is non-toxic so long as it is uncontaminated with water of condensation. While Castellani⁽²⁸⁾ states that vaccines made from bacilli grown on broth give severe reactions. The toxicity of the Shiga element can therefore be overcome but the confusion in the Flexner group is still not cleared up and the very variable response given by animals when injected for the purpose of preparing specific anti-sera against Flexner group organisms is discouraging. My own experience of preparing specific Flexner antisera in rabbits has been that it was impossible in India to get an anti-serum of a higher titre than 1-500 and that one had frequently to be satisfied with a much lower titre. When this is compared with the very high titres obtained after injection of the *B. typhosus* it becomes evident that immunity production as measured by the agglutinin response in rabbits injected with *B. flexner* is very small. At the same time this agglutinin response cannot be relied upon as a definite measure of immunity for individuals recovered from a Flexner dysentery it is often impossible to demonstrate any

agglutinins in the serum and even when they are present they never approach the quantities found in a convalescent enteric group case. Again a single attack of bacillary dysentery does not produce in the individual that lasting immunity from further attacks which an infection with *B. typhosus* does; second and third attacks are common but whether these are fresh injections or recurrences of the original one is a matter of conjecture. It would seem therefore that, while a flexner vaccine prepared from strains of the bacillus isolated in one place might have a local success in preventing attacks, it is not possible to produce a flexner vaccine likely to be generally successful until a very large number of strains have been further investigated.

Oral vaccination.

This method of prophylaxis is based upon Bes^rnedka's theory of local cellular immunity has been tried fairly extensively. The method consists in the administration by the mouth of tablets of dried sterilised bacilli pulverised and made into tablets by means of a machine and coated with varnish. Bile pills consisting of sterilised concentrated ox bile coated with

gluten are given first to prepare the intestinal mucosa. Each pill contains the equivalent of 20 centigrammes of fresh ox bile. A bile pill is swallowed in the morning before any food is taken and quarter of an hour later a vaccine tablet, no food is taken for one hour this is repeated on two following days; three bile pills and three vaccine tablets completes the course.

In the Warsaw bilivaccin the bile is incorporated with the bacilli in one tablet 0.05 gramme of bacilli (70-80 billion) and 0.15 gramme of ox bile.

There are conflicting opinions regarding its usefulness.

(29)
Fulton & Berry found that infants were not protected by oral vaccination when 2000 million of five different strains of Flexner organisms were given every month on three successive days.

(30)
Alivisatos and Joranoric state that oral immunisation has been statistically shown to immunise human beings quickly and for a dysentery season.

Unfortunately there is no method except the statistical one of proving whether oral immunisa-

tion does immunise because animal experiments only prove that the particular animal can be protected and the method does not result in the production of demonstrable antibodies in the blood such as are found after subcutaneous vaccinations. No such antibodies can be demonstrated in the blood even when *B. typhosus* is used for oral immunisation.

It is unfortunate that the method should have been commercialised before adequate scientific proof of its efficacy was forthcoming.

Immunity production by means of the bacteriophage

(31)
D'Herelle has immunised rabbits to two surely fatal doses of *B. dysenteriae* Shiga culture by injection of a quarter of a cubic centimetre of a suspension of Shiga bacteriophage.

The antitoxic immunity is established six days after the injection and persists for at least three months. He states that "the antitoxic immunity which develops after the injection of bacteriophage suspensions is also endogenous in origin due to the inoculation of the bacterial products in the suspension. These products seem here to be found in a physical state



particularly adapted to exciting an antitoxic reaction response on the part of the animal body." Nothing is however said about the amount of antitoxin produced or about similar work on human beings. The method requires further investigation.

While there have been many attempts to produce immunity by means of a vaccine none have yet been strikingly successful for reasons shown above. Oral vaccination requires very carefully controlled application and study before the claims made for it can be accepted and I have not been able to find any account of the use of the bacteriophage in prophylaxis; its use in treatment has not, as far as I am aware, been superior to other methods.

SUMMARY and CONCLUSIONS.

1. The laboratory methods employed have been described and the results in 480 cases of acute dysentery have been tabulated.
2. A diagnosis of the variety of dysentery was made in 86% of the cases examined. The importance of the presence of a typical exudate is stressed and its appearance described.
3. The bacteriological results are tabulated and the great predominance of the Flexner group shown; of this group the W. strain was most common.
4. The problem of infection has been discussed and the conclusion arrived at is that the state of the potential patients tissues are of the first importance in determining infection.
5. In endemic areas there are so many mild untreated and uncontrolled cases living under insanitary conditions favouring the spread of infection that they must be the most likely reservoir of the organisms and source of infection.

6. Carriers in the true sense of the term practically do not exist; those who excrete organisms are missed or chronic cases and have demonstrable evidence of intestinal inflammation.
7. Of all the vectors of the disease the fly is the most important.
8. The main line of prevention in endemic areas is a higher standard of sanitation and personal cleanliness. Progress is being made slowly in this way in India.
9. Periodical bacteriological examination of stools of food handlers is unsatisfactory unless these people are under control in hospital for a few days. It is useless to examine normal stools with no trace of blood and mucus or excessive mucus for dysentery bacilli.
10. A campaign to reduce the number of flies is necessary.
11. For personal prophylaxis Sodium Sulphate is worth trial, its use is based on sound observations.
12. No satisfactory vaccine has yet been produced although the toxicity of the Shiga element has

been overcome, the confusion in the Flexner group and their poor antigenic properties are responsible for this.

There is no definite proof that the oral bilivaccin or the bacteriophage produce immunity in man.

A P P E N D I X.

Litmus Lactose Bile Salt Agar

	Per cent
Agar	2.5
Peptone	2.0
Sodium Tamocholate	0.5
Lemco	0.5
Sodium Chloride	0.5
Tap Water	Q S.

The above are dissolved in the steamer at 100°C cooled to 60°C and cleared with white of egg; filtered first through lint then through Chardin filter paper. The medium is then adjusted to p^H7.4. To the hot filtrate add 2. per cent lactose and 5 per cent litmus solution. The medium is sterilised by steaming on three successive days for 15 minutes at 100°C.

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