On the Pathology of Asylum Dysentery in England.

by

David M^c Kinlay Reid

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

and Dr. Barwise, M.O.H. for Derbyshire. What was termed a "virulent" form of B. Enteritidis Sporagenes was here regarded as the cause of the disease, having been isolated from eight cases: but a "non-virulent" form was also found in the stools of healthy patients. All these observers, so far as I can gather, employed agar only for primary cultivation and none of them carried out any satisfactory agglutination tests.

In the first volume of Mott's Archives of Neurology, Durham[7] published the results of some work emanating from the Claybury laboratory. He claimed that from the blood, bile and certain abdominal viscera of seven out of eight patients who had died from Dysentery, he had cultivated a coccus so minute that it was able to pass through the pores of a Berkefeld filter. Cultures were never made from the faeces; subcultivation in a series of generations was found impossible; and the results of agglutination and animal experiments were negative. Dr. Eyre[8] of Guy's Hospital was certainly the first in Britain to show asylum researchers the way to a sounder bacteriological knowledge of the disease. Using the Conradi-Drigalski medium in 1904, he recovered Shiga's bacillus from the faeces of four out of five Claybury patients suffering from the acute form of the disease and post-mortem from two out of four additional cases, agglutination being obtained with the organisms and an antidysenteric serum in a dilution of 1-200. As a result of further investigation he found the bacillus of Flexner also present in several of the series and in a private[9] communication stated that he had detected it altogether in six out of

nine acute and fifteen out of thirty-five chronic cases, none of the latter yielding Shiga's bacillus. Hewlett[10] (1904) tested the sera of two asylum Dysentery patients with B. Dysenteriae (obtained from Flexner), and obtained a positive result in 1-50 in one case and 1-100 in the other. In a paper read before the Royal Academy of Medicine in 1905 McWheeny[11] described a bacillus of the mannite-fermenting Dysentery group which had been isolated from a severe (subsequently fatal) case in Clonmel Asylum. This organism was noteworthy inasmuch as it produced no indol, and caused the death of several rabbits while an attempt was being made to immunize them. In the following year Candler[12] of Claybury investigated the faeces of six cases suspected to be suffering from Acute Dysentery. "In five of them an organism resembling the Flexner type was isolated and submitted to the usual tests. The sixth was subsequently found to have Intestinal Tuberculosis." As the result of an examination of five cases occurring in one of the Sussex County asylums in 1908 Bushnell[13], using Conradi plates, found no Dysentery bacilli present, but his report is short and incomplete. An important research was made by Aveline, Boycott and Macdonald[9] of the Lister Institute in 1909. They obtained specimens of dysenteric faeces from Cotford Asylum, and from seventeen out of nineteen Flexner's bacillus was recovered. Spleen and mesenteric gland of a fatal case yielded it also. MacConkey's bile-salt-lactose-neutral-red agar was employed for separation of the organisms by these investigators for the first time in this work. Agglutination was obtained with patients' serum and organism up to 1-200 and 500, and a multivalent dysentery horse serum was

shown to agglutinate in a dilution of 1-1000 and when tested to 1-10,000, time allowed being two hours.

In 1910 Dr. Macalister[14], also of the Lister Institute, had material sent him from Cheddleton Asylum in Staffordshire. His work was particularly directed towards finding evidence of Dysentery carriers, but he examined twenty-eight specimens from acute cases and was able to grow B. Flexner from thirteen. "Among the remaining fifteen negative samples there were seven from which some other pathogenic form was isolated, which may have masked or replaced the primary infection..... Twenty-five serums from acute cases gave seventeen positive results. Four of the remaining eight negative samples were obtained at the very commencement of the attack, that is to say, before the development of specific agglutinins." Further investigation was carried out by Candler in conjunction with Professor Dean[12] in 1911. They state that "out of sixteen cases at Claybury which had symptoms of Dysentery during life or in which lesions of a dysenteric character were found after death, five yielded a group of organisms known as Morgan's Bacillus No. I, and four yielded bacilli spoken of for convenience as Morgan's No. 3., i.e. a percentage of thirty-one of Morgan 1 and twenty-five of Morgan 3." Although admitting that in two cases an organism of probable Flexner type (and afterwards proved to be such) was isolated, these authors remark on the absence of bacilli of that group and suggest that they have "died out pari passu with the more acute form of the disease, and that their place has been

taken by the organism described by Dr. Morgan, and which he has shown to be associated with summer diarrhoea in children." Previously they say: "It must be stated, however, that whereas in some of the cases the majority of the colonies which appeared on the MacConkey plates were non-lactose fermenters, and a large number of which were picked off and transplanted on to slopes of agar-agar, some of these unfortunately died out before they could be fully examined. It is possible, therefore, that some of these more delicate colonies may have been those of the true Shiga or Flexner bacilli." In this research no agglutination tests were carried out with the Morgan organisms.

In 1912 Tebbutt[15], working at the Lister Institute with material from Cheddleton Asylum, examined twenty-eight cases (unclassified clinically). Eight of these were found to be excreting Dysentery bacilli. In another "all the non-lactose fermenting bacilli found showed identical characters and corresponded with Morgan's No. 4^a (apparently with some affinities to the Dysentery group) which was also found twice in Claybury by Candler and Dean. The other most common non-lactose fermenters found were Morgan's No. 1, in seven cases, No. 5 in three cases and No. 4^b in two cases. "Many of these associated bacilli," he says, "were tested with the patient's serum from whom they were isolated and in no case was any agglutination observed though positive with Bacillus 'Y' in each case." At the West Riding of Yorkshire Asylum[16] an investigation of Dysentery cases was commenced last year by the pathologist Dr. Nabarro, and in a preliminary note it is

stated that "Flexner's bacillus was found in the faeces of four cases out of eighteen and that ten of the bloods agglutinated the Flexner or 'Y' Dysentery bacillus."

From the foregoing it will be seen, therefore, that in the great majority of cases of Asylum Dysentery satisfactorily investigated, the organism regarded as responsible for the disease has been some type of Flexner's bacillus. The bacillus of Shiga has been detected in only one series of cases and in that it was associated with the former. B. Morgan 1, in the absence of convincing serological tests, cannot be definitely held to have a causative rôle, although its relation to the Summer Diarrhœa of Infants seems certain.[17] It is possible that some member or members of the Coli group may take on a specific pathogenic character in connection with the disease but such has not been proved.

It can hardly be wondered that the ratio of positive findings of a Flexner organism to number of cases examined is no higher, for as Macalister aptly remarks, "a minute portion only of a small sample of a single stool is examined, and thus much territory must be left unexplored."

The present research, begun towards the end of 1911, has been carried out at the London County Asylum, Horton; and I wish here to acknowledge my indebtedness to Dr. Lord, the Medical Superintendent, for kindly allowing me every facility towards furthering it, and to Mr. E.S. Dean, laboratory attendant, for much routine assistance and many valuable suggestions. Some of the cases have occurred in slight epidemic

form, but for the most part they have cropped up at varying intervals. Care was taken to make the clinical diagnosis accurate (as opposed to other diarrhoeas); and when possible corroborative evidence was obtained post-mortem. A patient attacked with the disease is as a rule sent to bed complaining (if mentally able) of headache, seediness and general pains. The temperature is found to be 101-104°. Later, vomiting may occur and abdominal spasms be felt, and marked tenderness over the colon, especially on the left side, may obtain. Within twenty-four hours diarrhœa generally begins, and this is frequently associated with tenesmus. The appearance of the motions varies, but in typical cases they are scanty and consist of fresh blood intimately mixed with sticky mucus, and some thin faecal material which has a heavy, foetid and (to the nurses) characteristic odour. As many as 20-30 stools may be passed in the twenty-four hours, but 8-12 is a usual number. In favourable cases the temperature falls by rapid lysis within four or five days and diarrhoea ceases within ten days; but in the fulminating type the patient may present a more or less complete picture of an acute abdominal affection, with much constitutional disturbance and rapidly increasing collapse, ending in death.

TECHNIQUE.

The technique has been that adopted by most recent investigators, with a few minor modifications. All cases of diarrhœa necessitating treatment in bed have been examined, and as soon as possible after a motion has been passed a flake

of mucus (preferably) or particle of faecal material is collected by means of a sterilised platinum needle and dropped direct into a tube of sterile normal saline. The fluid is shaken up and from it two or three drops are placed upon a plate of MacConkey's medium, and carefully spread by means of a delta-shaped glass rod which was previously kept in alcohol and was flamed before use. A second plate is inoculated by smearing the surface with the rod without re-charging it. In many of my recent cases I have used also an agar plate for the purpose of obtaining a truer picture of the flora present, the bile salt medium having an inhibiting effect on the growth of certain organisms.[18] Some have recommended the direct application of the mucus to the plate, but so far as I have seen the resulting growth tends to become too confluent. After thirty-six hours in the incubator at 37° C, growth is usually well advanced and it is possible to distinguish lactose- from non-lactose fermenters. While theoretically one ought to pick off all the white colonies, the expense of time and media is such a consideration when the work is being done merely in one's leisure, that I have made it a practice to select three, these having been chosen because of showing some differences under the hand lens or low power. As a rule, however, such differences depend chiefly on the varying conditions of the medium and the abundance of the red colonies. The presence of B. Proteus and B. Pyocyaneus, too, quickly alters the state of the plate. Consequently I am unable to endorse the statement[9] that "the colonies of B. Dysenteriae on MacConkey's

agar are to some extent characteristic in that each white colony is surrounded by a clear zone distinctly more yellow (i.e. more alkaline) in colour than the rest of the medium." Subcultures from the selected colonies are then made in lactose glucose and mannite broths. Lactose is used to confirm the previous reaction; glucose to separate gas from non-gas producers (Dysentery bacilli being of latter type); and mannite to determine whether the organism belongs to the Shiga or Flexner group. A stock culture of such growth is kept on an agar slope. This is subcultured every two months, and from it, when time is more convenient, further tests are carried out with various sugars, glucosides and alcohols. Litmus milk is also inoculated and Peptone water (1%) for the Indol reaction. In some of my later cases where it was necessary to obtain an early diagnosis for isolation or curative (autogenous vaccine) reasons, I have examined the lactose culture for motility after eight hours and tested for agglutination with a Flexner immune serum.

RESULT OF CULTURES.

Cultures have been made from the faeces of thirty-five patients suffering from Acute Dysentery, and in twenty-four instances dysentery-like (Flexner) organisms have been recovered. Three of the negative cases, however, and two additional ones from which cultures were not made during life proved fatal, and bacilli of the type were found in the large intestine. Thus, out of thirty-seven cases examined the

bacilli were isolated from twenty-eight. In the remaining nine lactose fermenters only were grown twice; organisms of the Gaertner group three times; and B. Proteus, B. Pyocyaneus, B. Faecalis Alkaligenes and a bacillus with some resemblances to that of Shiga once each.

As regards the general appearance of the plates nothing remarkable has been observed. In only a few instances have the pale colonies outnumbered the red (e.g. Case 23, ratio equals 116:23) and in those plates from which Dysentery organisms have been recovered the proportion of non-fermenters to fermenters has nearly always been low. This, I take it, is not due to any real paucity of the bacilli in the faeces but to my preference (vide ante) for using a washing of the mucus rather than the mucus itself for inoculating the medium. That the percentage (75.5) of positive findings of Dysentery bacilli is not higher may partly be due to this, and also to the fact that only occasionally was more than one primary culture made.

CONTROL CULTURES. Twenty cases of diarrhoea not dysenteric in origin have also been examined (seven of these died later and no dysentery lesions were found), and in no instance has B. Dysenteriae or its like been found. Further, cultures have been made from the faeces of eighteen patients who died from diseases quite unassociated with diarrhœa, and in none of these did dysentery-like organisms appear. While admitting that it is not always easy to distinguish between Dysentery and severe diarrhœa due to other causes and that the diagnosis may sometimes have been at fault, still it is

striking that in the pure controls these bacilli were not isolated. It is, however, in accordance with the experience of Aveline, Boycott and Macdonald, who obtained "no evidence of the presence of the bacillus (Flexner) in the faeces of ward contacts (twenty-six) with either normal or diarrhœic stools." Ledingham[19], on the other hand, in an extensive investigation on Typhoid-carriers in different parts of the country recovered dysentery-like strains not infrequently.

TABLE A.

Showing in detail organisms isolated from faeces or post-mortem from cases clinically considered Dysentery.

Case No.	Type of Disease.	Date of Onset.	Date of Culture From Faeces.	Result.	Organisms isolated from Faeces.	Organisms isolated P.M.	If Dysentery Lesions present.
1.	Slight attack.	21.9.11.	23.9.11.	Recov^{d}.	B. Dysenteriae (Group A)	-	-
2.	Severe.	23.9.11.	23.9.11.	"	" "	-	-
3.	Moderately severe.	23.9.11.	23.9.11.	"	" "	-	-
4.	" "	24.9.11.	26.9.11.	"	" "	-	-
5.	Severe in debilitated patient.	23.9.11.	-	Died.	No cultures made.	B. Dysenteriae Group B. (caecum).	?
6.	Moderately severe protracted.	27.9.11.	28.9.11.	Recov^{d}.	B. Proteus.	-	-
7.	Very severe.	11.10.11.	15.10.11.	Died.	B. Pyocyaneus.	Lactose fermenters only.	Yes.
8.	Severe & complicated with Pneumonia.	12.10.11.	-	Died.	No cultures made.	B. Dysenteriae Group B. (caecum).	Yes.
9.	Slight.	19.10.11.	24.10.11.	Recov^{d}.	B. Dysenteriae (Group A)	-	-
10.	Very severe in debilitated patient.	14.12.11.	14.12.11.	Died.	" (Group C)	B. Dysenteriae Group C. (liver) B. Morgan I. (caecum).	Yes.

TABLE A. (Con'd.)

Case No.	Type of Disease.	Date of Onset.	Date of Culture From Faeces.	Result.	Organisms isolated from Faeces.	Organisms isolated P.M.	If Dysentery Lesions present.
11.	Very severe in debilitated patient.	24.12.11.	27.12.11.	Died.	B. Dysenteriae (Group C)	B. Dysenteriae Group C. (liver)	Yes.
12.	Slight.	1.1.12.	2.1.12.	Recov^{d}.	" "	-	-
13.	Very severe.	29.12.11.	3.1.12.	Died.	B. Morgan I.	B. Dysenteriae Group C. (caecum)	Yes.
14.	" "	7.1.12.	15.1.12.	"	Lactose fermenters only.	Lactose fermenters only.	Yes.
15.	Severe and very protracted.	18.9.11.	21.1.12.	"	B. of Gaertner group.	B. Dysenteriae Group B. (caecum)	Yes.
16.	Severe with tendency to relapse.	8.3.12.	8.3.12.	Recov^{d}.	B. Dysenteriae (Group B)	-	-
17.	Fairly severe and protracted.	6.3.12.	8.3.12.	Died.	B. Morgan I.	B. Dysenteriae Group B. and B. Morgan I. (caecum and blood)	Yes.
18.	Slight.	23.3.12.	24.3.12.	Recov^{d}.	B. Dysenteriae (Group C)	-	-
19.	Moderately severe.	26.3.12.	27.3.12.	"	" (Group A)	-	-
20.	Fairly severe but of short duration.	6.4.12.	6.4.12.	"	" (Group B)	-	-
21.	Severe attack in debilitated patient.	14.4.12.	19.4.12.	Died.	" (Group C)	B. Morgan I.	Yes.

TABLE A. (Con'd.)

Case No.	Type of Disease.	Date of Onset.	Date of Culture from Faeces.	Result.	Organisms isolated from Faeces.	Organisms isolated P.M.	If Dysentery Lesions present.
22.	Moderately severe but of short duration.	7.6.12.	9.6.12.	Recov^{d}.	B. Dysenteriae (Group B)	-	-
23.	Severe but of short duration.	11.7.12.	15.7.12.	"	" (Group A)	-	-
24.	Slight.	19.10.12.	20.10.12.	"	B. Faecalis alkaligenes.	-	-
25.	Very severe and protracted.	24.10.12.	25.10.12.	"	B. of Gaertner group.	-	Colon not examined.
26.	Severe with relapses.	20.10.12.	31.10.12.	"	B. Dysenteriae (ungrouped)	-	-
27.	Very severe.	10.11.12.	10.11.12.	Died.	" "	B. of Gaertner group.	Yes.
28.	" "	25.11.12.	25.11.12.	"	" (Group B)	B. Dysenteriae Group B. (caecum)	Yes.
29.	Severe and protracted.	18.2.13.	19.2.13.	Recov^{d}.	" "	-	-
30.	Fairly severe.	28.2.13.	3.3.13.	"	B. of Gaertner group.	-	-
31.	Severe and protracted.	9.3.13.	10.3.13.	Recov^{d}.	B. Dysenteriae (Group B)	-	-
32.	Very severe.	16.3.13.	17.3.13.	Died.	" "	Lactose fermenters only.	Yes.

TABLE A. (Con'd.)

Case No.	Type of Disease.	Date of Onset.	Date of Culture from Faeces.	Result.	Organisms isolated from Faeces.	Organisms isolated P.M.	If Dysentery Lesions present.
33.	Moderately severe and protracted.	20.3.13.	20.3.13.	Recov^{d}.	B. Dysenteriae (Group B)	-	-
34.	Very severe.	23.3.13.	24.3.13.	Died.	"	B. of Gaertner group.	Yes.
35.	Severe and protracted.	26.3.13.	31.3.13.	Recov^{d}.	B. of Gaertner group.	-	-
36.	Severe.	1.5.13.	5.5.13.	Died.	"	B. of Gaertner group.	Yes.
37.	Recurrent slight case: thought to be a "carrier".	14.5.13.	14.5.13.	"	? B. Typhosus.	B. with resemblances to B. Shiga.	Yes.

The foregoing table presents a few points of interest. (1) It shows roughly what Macalister has proved from an examination of a large number of cases, viz:- that the earlier in the disease the cultures are made the greater the likelihood is there of Dysentery bacilli being recovered. Of the nine cases in which the faeces were examined on the day of the onset of the disease the bacilli were found in each, and out of ten in which a specimen was obtained four or more days after the onset no such organisms were found on six occasions. (2) It need hardly be said that on many plates more than one type of growth resulted and that the usual intestinal bacteria were not wanting. Only those most abundant or noteworthy for other reasons have been included. B. Morgan I. for instance, has always been noted. This was obtained twice from the faeces and once from the intestine unaccompanied by B. Dysenteriae and twice in conjunction with the latter. It was found, however, in three of the eighteen controls . B Pyocyaneus has been looked upon with suspicion in connection with the disease, but it occurred only once; besides, Andrewes[20] has pointed out that it is met repeatedly in the intestine. (3) The large number of fatal cases will be observed. This gives quite an erroneous impression of the average mortality rate of the disease. The attacks for the most part were certainly severe, but the majority of the patients who died had been weakened by previous illness and had little resistive power against a disease so exhausting as Dysentery. (4) As post-mortems are made in the high percentage

of 96.4 of all deaths in the asylum it was easy to obtain evidence corroborative or otherwise of the clinical diagnosis. In only one case was the colon not examined. In a second the lesions present were not regarded as definite. All the others showed signs of Dysentery. (5) Although cultures were made not only from the intestine but generally also from liver, spleen, mesenteric gland and blood, no dysentery-like organisms were ever isolated from spleen or gland and once only were they detected in the blood (possibly due to contamination as bowel yielded them in this case).

CLASSIFICATION OF THE DYSENTERY-LIKE BACILLI ISOLATED.

Attempts have been made to classify the various groups and sub-groups of the Dysentery bacilli by the usual methods with indifferent success. The non-mannite fermenters (Shiga type) seem to show little or no tendency to variation, but it is otherwise with those that split mannite (type of Flexner, etc). Agglutination tests (Widal and Bordet-Durham reactions) show marked differences between the members of the various groups but these differences do not appear to be constant. And the absorption method of Castellani has indicated such extremely fine variations even among strains supposed on other grounds to be closely allied, that it is regarded as of theoretical interest rather than practical value. According to Arkwright, too, the results obtained thereby have been found to be inconsistent and it has been unfavourably commented on by Lentz[21], Bainbridge and Dudfield[22], Morgan[23] and Wassermann[24]. At present it seems uncertain what to include in the Flexner group: one writer would admit strains which another would dis-

card. In the absence of more accurate knowledge, therefore, and as at least a practical guide it seems reasonable to regard as members those non-motile, non-gram staining bacilli which do not ferment lactose, produce acid but no gas in glucose, and which acidify mannite; whose ability to produce indol in peptone solutions is generally but not necessarily positive; and cultures of which are not markedly virulent to laboratory animals. The group of organisms answering to such a description would necessarily be extensive, and sub-divisions have been made by various workers according to the cultural reactions shown on certain media. Hiss[25] for instance, has arranged them into three main groups. The first group is represented by bacillus "Y" which ferments mono-saccharids and mannite generally within twenty-four hours. The second group, represented by Strong's Phillipine culture, ferments mono-saccharids and mannite with ease: saccharose is fermented comparatively readily and at times maltose, but slowly. The organisms comprising the third group, represented by Flexner's Manila cultures and Duval's Baltimore culture, ferment mono-saccharids, mannite, maltose and dextrin with ease. But even such a broad classification as this has been found to be inadequate now and again, its divisions being broken down by organisms which were proved to have a definite pathogenic rôle in connection with Dysentery. It is little wonder then that further subdivision is only of use for the comparative study of, say, the members of one series of cases.

In the following table (B) the reactions of the various bacilli isolated are set down. The sugars, glucosides and alcohols have been observed daily and the results noted at the end of the week. Any change in litmus milk was observed one, three and fifteen days after inoculation. The para-dimethyl-amido-benzaldehyde test for indol was made on the seventh day.

TABLE B.

Showing cultural reactions of organisms isolated from the cases: with reactions of other British and foreign strains of Dysentery bacilli.

	Lactose	Glucose	Mannite	Galactose	Laevulose	Maltose	Raffinose	Arabinose	Isodulcite	Cane Sugar	Dextrin	Inulin	Salicin	Sorbite	Dulcite	Adonite	Erythrite	Amygdalin	Glycerine	Litmus Milk 1 day	Litmus Milk 3 days	Litmus Milk 15 days	Indol	Motility	
B. Shiga.	-	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	Alk.	-	-	
B. Flexner "I.I.P.M."	-	A	A	A	A	A	A	A	-	-	A	-	-	-	-	-	-	-	-	A	A	Slight alk.	+	-	
B. "Y" (Hiss & Russell)	-	A	A	A	A	A	A	A	-	-	SA	-	-	-	-	-	-	-	-	A	A	" "	+	-	
B. "Strong"	-	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	-	-	-	O	A	A C	+	-	
B. pseudo-dysenteriae D. (Kruse)	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	Slight alk.	+	-	
B. 162 U.P. (Willmore)	-	A	A	A	A	-	A	A	-	-	SA	-	-	-	-	-	-	-	-	A	A	" "	+	-	
B. infant's diarrhoea (Willmore)	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	+	-	
B. Morgan 16.	-	A	A	A	A	A	-	A	A	-	A	-	-	-	-	-	-	-	-	A	A	A C	-	-	
Case 1.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 2.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 3.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 4.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 9.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 19.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 23.	-	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	A	A	A C	-	-	
" 5.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	Slight alk.	-	-	
" 8.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 28.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 29.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 31.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 32.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 33.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 34.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 15.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	Trace	-	
" 16.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 17.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 20.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 22.	-	A	A	A	A	-	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 10.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 11.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	-	-	
" 12.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	Trace	-	
" 13.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 18.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 21.	-	A	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 26.	-	A	A	A	A	A	-	A	-	-	-	-	A	-	-	-	-	-	-	A	A	" "	"	-	
" 27.	-	A	A	A	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 34.	-	A	A	A	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	A	A	" "	"	-	
" 37.	-	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	O	A D	+	-	

Group A. (Cases 1, 2, 3, 4, 9, 19, 23)

Group B. (Cases 5, 8, 28, 29, 31, 32, 33, 34, 15, 16, 17, 20, 22)

Group C. (Cases 10, 11, 12, 13, 18, 21)

Group D. (Cases 26, 27)

A = acid.
SA = slight acid.

A C = acid and clot.
D = decolourized.

Among the thirty-seven cases it will be seen that there are various differences but it is possible to group them (with two exceptions) into four. No.37, however, is not a mannite fermenter. It corresponds to no well-known intestinal inhabitant and differs from Shiga's bacillus in producing indol, fermenting glycerine, and in its action on milk. Only as regards the production of indol was there any difficulty in grouping, and as it was practically impossible sometimes to determine whether the reaction was positive or negative this test was not given much weight. Sorbite has lately (Tebbutt) been given prominence as a differentiating medium and the rapid production of indol in peptone beef broth by fermenters of that medium has been pointed out. But the only sorbite-fermenter of the series (No.26) produced only a trace of indol in seven days. Some of the media were entirely unaffected by all the bacilli, viz:- cane sugar, dextrin, inulin, salicin, dulcite, erythrite and amygdalin: and only those of Group A affected isodulcite. This latter group differs from the others notably in the formation of acid and clot in milk. While it agrees with Strong's bacillus in this respect it is distinguished from it and other recognised types in various ways. It will be noticed, however, that but for dextrin, it is identical with Morgan's B 16 - a strain isolated from a case of Dysentery at Claybury. Group B corresponds to an organism isolated by Willmore in an epidemic of children's darrhœa in Alexandria, and differs from B. Flexner and bacillus "Y" in producing no acid in maltose, arabinose and dextrin. It may here be mentioned, however, that not too much stress should be laid on these media, Macalister[26] and others discounting their reliability. There is a close similarity between Group C and one of Kruse's Pseudo-dysenteriae bacilli as

tested by Willmore[27], the only difference being in the decided indol-formation by the latter. The two members of Group D fail to show acid in Arabinose and Dextrin and give a negative indol reaction, thereby differing from "Flexner" and "Y". Lastly, No. 26 corresponds exactly to a strain obtained by Tebbutt from Cheddleton Asylum.

The series accordingly shows six distinct strains, as tested culturally, and all of these fail to correspond in some respects with recognized types of Dysentery bacilli. But surely, as has been pointed out, "it seems somewhat unreasonable to regard a bacillus as a true Dysentery bacillus or not, according to whether it corresponds with a bacillus found in another part of the world, separated possibly from common ancestors by many generations subject to different climates and other factors which might lead to variations in character," (Tebbutt) And after all, is not the relation of germ to disease as tested by serum reactions, not the best ground for determining admission to a group?

AGGLUTINATION TESTS.

A. With patients' organism and serum.

Arkwright[28] states that the reaction in Dysentery should not be considered positive unless it recurs in a dilution of 1 - 100. With this I do not agree. Certainly in the majority of cases positive results are obtained in dilutions considerably higher than that, but in several of my cases 1 - 80 clumping has occurred very early in the disease, and its specificity has been proved by agglutination in higher dilutions later or by the presence of signs of Dysentery post-mortems. Nor have I found much difficulty in excluding

non-specific agglutination. In each case I have made hanging-traps of culture and normal saline, and in the absence of any tendency to spontaneous clumping, it has been found that control serum does not agglutinate when diluted greater than 1 - 40. As the research progressed, therefore, I found it unnecessary to heat patients and control serum, as recommended by Raymond[29]. One can understand, however, such measures being adopted when Shiga's is the organism under observation, for with it results are regarded as positive when obtained with dilutions as low as 1 - 20 ~ 40. (Shiga[30], Castellani[31] and others).

The microscopic method has been used throughout, time allowed being one and a half hours at room temperature. At first I adopted dilutions of 1 - 20, 1 - 40, and 1 - 80 but soon found that these could readily be exceeded and so used 1 - 50 up to 1 - 400. Only where the disease was of fulminating type and the patient already so debilitated that death occurs withn a day or two are positive results lower than with 1 - 100 obtained. The only two cases which agglutinated with 1 - 80 and no higher were of such a nature. Most of the others gave agglutinations in dilutions varying from 1 - 160 to 1 - 320. The time at which a positive result first appears varies. I have found it in a dilution of 1 - 180 on the third day, but as a rule it is a few days later and by the end of a fortnight is well established in all cases. The agglutinating power of patients' sera often varies considerably from day to day. This was proved thoroughly in two cases which were tested daily for the first month of the disease and every two days during the second month. Further, and as one would expect, the period of

maximum agglutination varies within wide limits. In a few instances this has been reached within the second week and has thereafter declined until no positive result was obtainable: but frequently the best result was found only after the lapse of months. After what time agglutination ceases to occur at all it is impossible to say except by repeated examinations of each case. Macalister gives the following summary from his cases:-

	Positive agglutinations.	Negative agglutinations.
During the attack	17	8
After 6 months	5	6
6 months to 1 year	7	6
1 - 3 years	12	12
3 - 5 years	4	5
5 - 8 years	1	4

This question is of course of the greatest importance in connection with Dysentery carriers, and I am at present engaged on further investigation with regard to this.

B. With patients' serum and B. Flexner.

The various sera were tested with a culture of Flexner's bacillus obtained from the Lister Institute, same dilutions being used as in the previous tests. The tendency on the whole was for these to agglutinate in rather lower dilutions, only one giving a positive result as high as 1 - 320; but the results were fully confirmative of the specific relation of organism to serum.

C. With patient's organism and rabbit Flexner immune serum. The serum (titre 1 - 20000) of a rabbit immunized against an asylum strain of B.Dysenteriae (Flexner) has been used to further identify the bacilli isolated from the cases. 64% were agglutinated in dilution of 1 - 20000, 33% in 1 - 10000 and 3% in 1 - 5000.

A few cases which I tested with "Y" serum showed that much lower dilutions were necessary than with the former. This is contrary to the experience of Morgan but the serum as used was old and may have deteriorated.

ANIMAL EXPERIMENTS.

It is generally conceded that cultures of the Shiga type of organism are much more fatal to laboratory animals than those of the Flexner group. Nevertheless, evidence is not wanting to show that the latter may possess considerable toxic power. McWheeny's case has already been referred to. Firth[32], testing his two strains named Flexner I and III, found that subcutaneous injections of "from $\frac{1}{2}$ - $\frac{1}{4}$ of a twenty-four hours old agar slope culture produced merely a temporary fall of temperature following an initial rise, but in larger doses (varying from $\frac{1}{3}$ - $\frac{3}{4}$ according to the size and weight of the rabbit), after an initial rise in temperature there was a marked lowering of body heat, with paralysis of the hind legs, progressive enfeeblement, and death about the fourth or fifth day." The larger bowel was found to be the site of "lesions bearing a striking resemblance to those characteristic of the disease in man." On the other hand, Firth's strains II and IV when injected "gave rise to practically no intestinal disturbance or lesion or any symptoms other than a temporary fall in temperature of about 1° C. lasting about a couple of days."

Captain A.T.Wells[33], having isolated a mannite fermenting strain in nine cases of Dysentery occurring in Hyderabagh Central Jail in India, found that when injected intraperitoneally into rabbits in doses of ½ to 4 c.c. of broth or agar cultures it produced symptoms such as paralysis of the hind legs, diarrhoea, emaciation and weakness, and finally death within 1 - 6 days. Post-mortem, injection of the peritoneum and colon, haemorrhages in the caecum and and lymphy flakes of mucus in the intestinal contents were present. Flexner[34] in one of his early articles says that his organism when injected subcutaneously into rabbits "gives rise to a localised swelling which is sometimes followed by death. At other times an abscess forms and perforates the skin, after which recovery may take place." Some years later he writes of lesions being caused by intraperitoneal and intravenous injections which correspond with those of the observers previously mentioned, but points out its weaker pathogenicity as compared with Shiga's bacillus.

It seems that few or no experiments on rabbits or guinea pigs have been carried on with strains actually isolated from asylum cases. None of Morgan's cultures so tested had this source and Tebbutt's attempts at infection were confined to a monkey (these it may be said were of various means and all were negative). In this part of the work I have unfortunately been handicapped, as the Asylums Committee of the London County Council prohibit animal experiments in their laboratories. Dr. Macalister of the Lister Institute, however, was good enough to inoculate two rabbits with cultures of Groups A and C respectively. Each received an

intravenous dose of the whole of a twenty-four hours broth culture and each died within thirty-six hours but I was unable to obtain information as to what symptoms had arisen, if any beyond an acute toxaemia. The animals were brought to Horton as soon after death as possible and I made the examination myself. The appearances on section were remarkably similar in each case, viz:- Peritoneum showed some increase of fluid: mesenteric glands enlarged and congested: small intestine slightly congested: large intestine - contents fluid and mixed with mucus, mucous membrane more or less generally congested with some tumescence, submucous haemorrhages in places but no actual ulceration. The resemblance between such findings and those characteristic of the early disease in man will be at once apparent to anyone who has performed many autopsies in an asylum. The doses given were of course large and death was anticipated, but the localised nature of the lesions was very remarkable. Two guinea-pigs inoculated at the same time with 1cc.doses of eighteen hours-washed agar cultures were unaffected.

Being desirous of having some feeding experiments carried out I approached my friend Dr. J. Walter Macleod of Charing Cross Medical School. At my suggestion he had the rabbits carefully isolated and cultures of Group A and Group C were intimately mixed with their respective foods (oats). Each received three 10 cc. broth cultures, followed five days later by the washings of four agar slopes. The feeds were well consumed but with the exception of some apparent seediness on the part of Group A rabbit no untoward symptoms resulted. The animals were killed on the 10th. day and examined by myself. The organs were found tp be perfectly normal: nothing suggestive of intestinal lesions was seen and

in the rectum well-formed faeces were present. Considering the large number of bacilli that must have been ingested such a result is rather surprising, especially in view of the fact that one of Flexner's assistants who accidentally drew a small quantity of a culture into his mouth, developed a typical attack of Dysentery, and that despite having immediately used an antiseptic wash. It cannot well be attributed to a difference in virulence between the cultures, for Flexner's organism itself has been employed for mixing with the food of laboratory animals, for direct introduction into the stomach by means of an oesophageal tube, and into the peritoneum or bowel itself after laparotomy - with negative results constantly.

A NOTE ON TREATMENT.

Vaccine treatment does not seem to have been tried in the case of Dysentery due to Flexner's bacillus or its variants. In a few cases I have injected patients with a vaccine prepared from their own strain but the results have been indefinite. The dosage is a matter of difficulty and, in any case, favourable cases generally run such a short course under ordinary medical treatment that a vaccine is unnecessary. Chronic cases I have had no opportunity of studying, and, as has been said, the fatal acute cases occurred in patients with whom probably no treatment would have had any effect.

Nor has serum treatment been used to any extent where Flexner's bacillus is concerned. The number of patients from whom this organism was isolated and who were afterwards

treated with an acute bacterial horse serum by Ruffer and Willmore[35] was too small to allow of deductions being drawn, although their results in other cases of bacillary Dysentery were excellent. The Lister Institute prepares a serum which "consists of the serum of horses which have been highly immunised against the Dysentery bacilli (including those of Shiga, Kruse, Flexner, Duval, etc), and the toxic substances elaborated by these bacilli." I can find, however, no record of its extended use and my own limited experience of it in asylum cases is unfavourable. If further research on the bacteriology of Dysentery as it occurs in asylums were carried out in different parts of the country and if, as seems not unlikely, several similar strains of Flexner's organism came to be regarded as the cause of most of the cases, the use of an antiserum prepared from these for therapeutic use would be worth a trial at least.

CONCLUSIONS.

1. That strains of the mannite-fermenting group of Dysentery bacilli have been proved to be the cause of Dysentery in English asylums in the majority of cases satisfactorily investigated.
2. That these strains cannot be said to be identical with any of the well-known members of the group; but that, on the other hand, several isolated from different asylums have been shown to have the same cultural characteristics.
3. That consequently if further and more widespread research were carried out and similar conclusions reached, it is reasonable to believe that an immune serum prepared from a number of these strains would be of general value in the treatment of the disease.

REFERENCES.

1. KRUSE: Deutsche Medizinische Wochenschrift. 1901. XXVII

2. GOODELIFFE: Lancaster County Asylum Report. 1899.

3. GEMMELL : "Idiopathic Ulcerative Colitis."

4. CAMPBELL: Journal of Pathol. & Bacteriol. 1899. Vol. VI. No. ii.

5. CHANTEMESSE & WIDAL: Bulletin de l'Académie de Med. 1888.

6. LEGGE: Journal of Mental Science. 1899. Vol. XLV.

7. DURHAM: Archives of Neurology & Psychiatry. Vol. I. 1899.

8. EYRE: Brit. Med. Journal. 1904. April 30th.

9. AVELINE, BOYCOTT & MACDONALD: Journal of Hygiene, Vol. VIII, No. 3.

10. HEWLETT: Trans. Pathol. Soc. Lond. Vol. LV. 1904.

11. MCWHEENY: Brit. Med. Journal. 1906. June 30th.

12. CANDLER & DEAN: Archives Neurol. & Psychiat. Vol. V. 1911.

13. BUSHNELL: Brit. Med. Journal. 1908. Sept. 19th.

14. MACALISTER: " " " 1910. Nov. 12th.

15. TEBBUTT: Journal of Hyg. Vol. XII. No. 2.

16. REPORT OF COMMISSIONERS OF LUNACY, England 1912. P. 93.

17. MORGAN: Brit. Med. Journal. 1906, April 21st, and 1907, July 6th.

MORGAN & LEDINGHAM: Proc. Roy. Soc. Med. (Epidem. section), 1909. Vol. II, p. 133.

18. MACCONKEY: Journal of Hyg. Vol. VIII, No. 3.

19. LEDINGHAM: "Enteric Fever Carriers." L.G.B. Report, 1910.

20. ANDREWES: Proc. Roy. Soc. Med. (Discussion on Alimentary Toxaemia), 1913, March.

21. LENTZ: Handbuch für Micro-Organism. (Kolle und Wassermann). Bd II. Ergänzung.

22. BAINBRIDGE & DUDFIELD: Journal of Hyg. Vol.XI, p. 356.

23. MORGAN: Journal of Hyg. Vol. XI, p. 1.

24. WASSERMANN: Zeitschrift für Hyg. Bd. XLI.

25. HISS: Journal of Med. Research. 1904. Dec.

26. MACALISTER: Private communication.

27. WILLMORE & RUFFER: Brit. Med. Journ. 1909. Sept. 25th.

28. ARKWRIGHT: Art. Dysentery in "Carrier Problem in Infectious Diseases" (Ledingham & Arkwright).

29. RAYMOND: Annales de l'Institut Pasteur. 1911. Aug.

30. SHIGA: Art. Dysentery in Osler & Macrae's "System of Medicine."

31. CASTELLANI: Journ. of Hyg. 1904. Vol. IV.

32. FIRTH: Trans. Path. Soc. Lond. 1904. Vol. LV.

33. WELLS: Scientific Memoirs by Officers of Medical & Sanitary Departments of Gov. of India. No. 52.

34. FLEXNER: Brit. Med. Journ. 1900. Sept. 19th. Art. Dysentery in Rolleston & Allbutt's "System of Medicine."

35. WILLMORE & RUFFER: Brit. Med. Journ. 1910. Nov.

36. Forster: Indian Medical Gazette. 1907. June.

---

addendum.

A statement on vaccine treatment needs explanation. Dysentery due to Flexner's bacillus has not so far as I am aware been treated with vaccines prepared from that organism. On the other hand Forster[36], & others claim to have secured excellent results in their from 2 the disease (chronic type) with a vaccine made from Shiga - Kruse strains. But