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OBSERVATIONS ON FLEXNER DYSENTERY

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Initial Outbreak.—The first proven case of Flexner dysentery occurred in a female infirmary ward on 23.12.40. From that date up to 31.5.42, 357 cases of severe diarrhoea or definite dysentery have required treatment in the hospital—102 male and 255 female cases.

Apart from a minor epidemic of Flexner dysentery in 1931, which involved a total of 12 cases only, and which was readily controlled, this hospital had not had any cases of typhoid or Flexner dysentery since its opening in 1924. It was most unlikely that the disease was introduced by a newly admitted patient from an observation ward, since there was no direct contact between the admission ward and the infirmary ward where the disease commenced. On 16.11.40, because of severe air-raid damage to their hospital, some 50 female patients were hurriedly evacuated from one of the older mental hospitals, where dysentery has probably been endemic for years. These patients were housed together in the same ward block, and used the same gardens as did the patients of the infirmary ward where the first dysentery cases occurred, and there is a strong suspicion that one or more of the transferred cases conveyed the infection, although it is not impossible that a member of the nursing staff was responsible. An outbreak of Sonne dysentery confined to one of the female wards in the spring of 1940 was proven to be due to a non-resident nurse who was on duty in that particular ward at the time of the outbreak. Furthermore, gastro-enteritis amongst the sick non-resident staff has been of frequent occurrence during the

past three years, and we cannot help feeling that if the general practitioner had more adequate laboratory facilities a number of these cases would prove to be cases of Flexner or Sonne dysentery.

Seasonal Incidence.—While fresh cases continued to appear, during the whole course of the epidemic there were two peak periods, each occurring in the mid-winter and early spring months of the year. This seasonal variation corresponds to that often found in epidemics in mental hospitals.^{1, 2}

The explanation of this seasonal distribution may be due to the relatively closer segregation of patients in the colder months. In the warmer months patients obtain more exercise in the gardens and they are not packed so closely together over long periods. Moreover, it is highly significant that not one case of proven dysentery occurred in a parole or "open" ward, even in the winter months. Open ward patients spend a large part of the day away from the wards where they eat and sleep. The indoor accommodation (bed space, relative proportion of patients to size of ward, etc.) is the same as that of the "closed" wards, whilst dietary and laundering are common to the whole hospital.

At first sight it might appear that the prophylactic inoculation of autogenous dysentery vaccine in 1941 affected the subsequent incidence of the disease. However, the similar seasonal incidence at other hospitals, a similar seasonal incidence for the year 1942 in our own cases, and the low incidence of diarrhoea in non-inoculated female parole patients weighs against such an assumption.

Dissemination in the Hospital.—The first epidemic was confined to one ward on the female side; but although the usual precautionary measures were adopted, the disease began to appear in other wards about five weeks later. At the same time the first male case occurred, and again, after being limited to two infirmary wards, the disease soon became sporadic throughout most of the closed male wards. By the end of January 1942 the disease became almost entirely confined to one block on the female division of the hospital and to two blocks on the male side.

Collection of Fæcal Specimens and Bacteriological Methods.—Up to November 1941 fæcal specimens were collected in sterile glass containers as soon as possible after defæcation, and plated on MacConkey's medium with the least possible delay. The percentage of positive Flexner returns was low, approximately 12 per cent. for female cases. The Central

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Pathological Laboratory of the Mental Hospitals (L.C.C.) had, as a result of considerable experience of Flexner dysentery epidemics in mental hospitals, appreciated that MacConkey was not sufficiently sensitive or selective, and had noted when using this medium that most of the initial cases in an epidemic of severe diarrhoea gave no growth, whereas later cases occurring six to ten weeks later gave increasingly positive results. This was our experience in the early months of the outbreak. Up till then it had been thought that this was due to the organism becoming truer to type as a result of passage through several hosts. Now we believe it was due to the insensitivity of the medium.

From November 1941 onwards an improved technique was adopted in the collection of faecal specimens, and the desoxycholate citrate medium of Hynes³ was used in place of MacConkey.

The technique of collection of faecal specimens is as follows⁴:— A special glycerine-saline solution is made by mixing 1000 c.c. glycerine with 2000 c.c. 0·85 per cent. saline, to which is added sufficient aqueous solution of phenol red to colour. A 5 per cent. solution of sodium phosphate is carefully added until the indicator registers a *pH* of 8·0. The mixture is tubed in 10 c.c. quantities in screw-capped bottles (universal containers) and sterilised for ten minutes at 10 lb. pressure. The *pH* should now be approximately 7·4 and the fluid a definite bright pink colour; when required for use any tubes which have lost their colour should be neglected. Immediately after defaecation a specimen of faeces is placed into the glycerine saline by a faeces spoon. There is no urgency about plating out. Specimens left for some hours yield as good and even better results than those dealt with at once.

As a result of these improved methods the percentage of positive Flexner findings in our cases of severe diarrhoea has remained consistently high (about 70 per cent. in female cases). Rectal swabbing was carried out in many cases, but we have now largely abandoned this procedure as our returns proved higher with a faecal specimen. Thus it was common to obtain a negative result from a rectal swab in a patient whose stools were positive. Finally, the organism grown from each positive case had at least one agglutination test carried out against serum specific for *B. dysenteriae* Flexner (polyvalent serum No. I., Standards Laboratory, Oxford).

Symptoms.—On the whole the disease has been a mild one—most cases showing symptoms for three or four days only. The symptoms and signs noted were those usually described: a

sudden onset of abdominal pain accompanied by tenderness over the colon, with or without vomiting, shortly followed by the passage of frequent loose stools containing mucus and often blood. The temperature was elevated moderately as a rule. The passage of blood and much mucus rarely persisted for more than one or two days, and loose motions and fever rarely continued longer than ten days. Severe dehydration was rare and complications uncommon. The faint spermin-like odour of the dysenteric stool was perceptible in many instances.^{1, 5}

Although most cases became symptomless ten days after the onset of diarrhoea, the organism continued to be excreted, on an average, for 32 days with extremes of 3 to 208 days, but by far the majority of cases passed the organism for 25 to 40 days.

Treatment.—Most of our cases were treated by the sodium sulphate method as described by Manson-Bahr¹ and satisfactory results were obtained. Sulphapyridine was tried on a group of patients in the earlier "peak" period, but owing to the insensitivity of the culture medium in use at that time no useful comparison can be made with sulphanilylguanidine (sulphaguanidine) which has been utilised recently. Table I (p. 133) summarises the results of the sulphanilylguanidine treatment. In all cases, except those especially commented on, a course of seven days sulphanilylguanidine was instituted as recommended by Anderson and Cruickshank² (9 grams a day in three doses of 3 grams for two days, followed by two doses of 2 grams each day for five days).

It is to be noted that in recent cases treated early with sulphanilylguanidine, the clinical results were wholly good and the average length of time the stools remained positive was low. The results in group B, where the treatment was commenced later in the course of the disease, appear less satisfactory clinically: in 3 of these cases additional sulphanilylguanidine was necessary. Group C consisted of a heterogeneous collection of cases of recurrent diarrhoea, all suspected at the time of being carriers. In 4 out of 8 cases the results of treatment appeared clinically good; 2 cases were recognised a little later to be suffering from pellagra (confirmed by the effect of specific therapy). Case 22, probably a true chronic carrier, continued to excrete the bacillus for eighty days after treatment, which was given for three weeks, and was still excreting the dysentery bacillus nine months after the original infection.

The effectiveness of sulphapyridine and of sulphanilylguanidine in the treatment of Flexner dysentery has been

TABLE I
Sulphanilylguanidine Treatment

Number of Case	Stools + or - in present attack (or in C. at time of commencing treatment).	Number of days elapsing between onset of present attack and date of commencing S.	Number of weeks stools + after S.	Clinical result treatment	Comments
<i>Group A.—Acute cases, treatment commenced within three days of onset</i>					
1	+	0	4	Satisfactory (no relaxed stool or other symptoms after S.)	...
2	+	3	1	" " "	
3	+	0	2	" " "	
4	+	2	1	" " "	
5	+	1	1	" " "	
6	+	0	0	" " "	
7	+	3	2	" " "	
8	—	2	0	" " "	Clinical dysentery
9	—	2	0	" " "	Doubtful dysentery
10	—	0	0	" " "	" "
<i>Group B.—Acute cases, treatment commenced seven or more days after onset</i>					
11	+	13	3½	Exacerbation five weeks after onset. Further S. satisfactory	...
12	+	14	1	No relaxed stools after treatment	Died
13	+	23	0	Occasional loose stools despite four weeks S.	Secondary carcinomatosis
14	+	17	1	Occasional relaxed stool for three weeks after S.	...
15	+	7	0	Satisfactory	...
16	+	12	1	No loose stools but fever persisted	Cerebral thrombosis
17	+	10	1	Satisfactory	
<i>Group C.—Cases of recurrent diarrhoea</i>					
18	—	...	2	Two weeks course S. satisfactory	First attack bacteriologically confirmed. Dec. '41
19	—	...	0	" " "	" " " Nov. '41
20	—	...	0	" " "	" " " Dec. '40
21	—	...	0	" " "	" " " Dec. '40
22	+	...	12+	Three weeks course S. Stools persistently + three months after S.	" " " Nov. '41
23	—	...	0	Diarrhoea persisted	" " " Dec. '40.
24	—	...	0	" "	Clinical pellagra
25	—	...	0	Three weeks course S. Diarrhoea persisted	Chronic diarrhoea. Clinical pellagra Chronic diarrhoea. ? Subclinical pellagra
<i>Group D</i>					
26	+	...	1	...	Asymptomatic dysentery

S. refers to sulphanilylguanidine treatment.

already reported.^{6, 7, 8, 9, 10} Sulphanilylguanidine has been the favoured sulphonamide on the grounds that "only a fraction" of the drug given by mouth is absorbed.² Firor¹¹ has lately stated that "the original claim that sulphanilylguanidine is poorly absorbed from the gastro-intestinal tract is incorrect. The drug is readily absorbed from the small intestine, and the low concentration found in the blood is due to rapid elimination of it by the kidneys." Firor claims that succinyl sulphathiazol is a compound of high antibacterial potency, low toxicity and poor absorbability from the gastro-intestinal tract, and he states further that *B. dysenteriae* (Shiga, Flexner and Sonne) are amongst those organisms particularly susceptible to it. Further, he thinks that whilst sulphanilylguanidine is often ineffective in the presence of an ulcerative lesion, succinyl sulphathiazol may prove successful. We have not yet had the opportunity of trying this new compound on fresh cases or on the chronic carrier, who presumably has ulcerative lesions. Cruickshank has lately advocated larger initial doses of sulphanilylguanidine.¹²

Deaths.—On the male side only 3 deaths could be directly attributed to dysentery. In 4 other cases where death occurred within seventeen days of the onset of diarrhoea the patients were already moribund from pulmonary tuberculosis or advanced cardio-vascular degeneration. Similar results were noted on the female side where, amongst 9 deaths shortly after the onset of the disease, several cases were known to have other gross systemic lesions. This gives approximately a mortality rate of under 4 per cent., and even in this small group the disease was usually the *coup de grâce*.

Prophylaxis

1. *Vaccine.*—When in early 1941 it became apparent that the disease was spreading to other wards, we decided to try a vaccine against Flexner as had been previously recommended by Paddle.¹³ Every male patient (1110 in all) received during January and February 1941 two injections of the vaccine: the first, 0.5 c.c., and the second, 1.0 c.c., a week later (500 million organisms per 1.0 c.c.). The greater proportion of female patients were inoculated at this time, but the parole patients were exempted. A stock polyvalent vaccine was used at first, but was replaced by an autogenous one as soon as it could be prepared.

The results were disappointing. Thus, the incidence of disease

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on the male side where everyone received inoculation was only slightly lower than that on the partially inoculated female side. To illustrate in further detail: between March and September 1941 (the period following the inoculation), out of 63 female cases of severe diarrhoea, only 8 cases occurred amongst the uninoculated parole patients. This figure is low, even taking into consideration the fact that the total number of patients in the non-inoculated wards was approximately one-fifth those in the inoculated wards. Moreover, only 20 of these 63 cases were non-inoculated. On the male side 4 patients contracted proven dysentery within thirty days after the second inoculation, 8 cases occurred fifty days afterwards, 17 cases seventy days afterwards, and 50 further cases before the end of one year. We conclude that immunity (if any) conferred appears to be of very short duration, with a probable optimum of about three to four weeks.

This belief is supported by the agglutination titres of 12 cases who were given 1.0 c.c., followed a week later by 2.0 c.c. of an autogenous vaccine of 1000 million organisms per c.c. There was no rise above normal in the amounts of agglutinin to V, W, X and Y strains in any of the 12 cases on specimens taken at regular intervals up to thirty days after the first injection. Only 6 cases showed an increase in the Z strain, and this was twenty days after the first injection—in later tests the value had dropped again to within normal limits. It must be recorded that in only one of these 12 cases did diarrhoea subsequently develop (ten months afterwards), and the diagnosis of Flexner dysentery was confirmed bacteriologically.

Reactions were rare, transitory and mild even when the vaccine was given in concentrated form as with the 12 cases. However, 6 of these cases were found subsequently to have active pulmonary tuberculosis.

We believe that prophylactic inoculation is of value if given immediately to other patients in a ward where one or two sporadic infections have occurred. We have lately used a dosage of 0.5 c.c. and 1.0 c.c. of 1000 million organisms per cubic centimetre.

2. *Non-specific.*—Every case of diarrhoea was transferred immediately to special infectious disease wards for investigation and treatment. Proven dysenterics were not transferred from the isolation ward until the stools were consistently negative. This entailed a sojourn of some six to eight weeks as a rule. Further, we frequently found that after a patient had passed three or more consecutive stools negative for dysentery the next

specimen was returned positive. This emphasises the danger of the temporary carrier, and the fallacy of the rule "three negative stools indicate recovery." Care was taken with those potentially dangerous cases who were not confirmed bacteriologically by utilising a "buffer ward" before they returned to the general wards of the hospital. At the peak of our last epidemic we were forced to set aside a further block in the hospital for isolation purposes owing to the large number of cases. Quarantine for twenty-one days was observed in wards where no more than one or two isolated sporadic cases occurred, and all patients in these wards had their stools examined bacteriologically during this period. The usual routine precautionary measures of disinfection of excreta, lavatories, crockery and clothing were followed, and garden lavatories had to be boarded up temporarily during ward epidemics to prevent "cross" infection of patients from adjacent wards who normally utilised the same lavatories. Bacteriological tests were made on the water from the outflow pipes of the "infectious" and ordinary laundries of the hospital; the effluents from the washing machines, hydros, floors, etc., were also tested bacteriologically. It was gratifying to find that this waste water was absolutely sterile even when left for several days on appropriate media.

Symptomless and Carrier Cases.—A detailed study of the epidemic in the H block of female wards which occurred mainly in February and March of 1942 has been made as it furnished many interesting facts. In this block are two wards, H1 and H2. The two wards are completely separated from each other as far as living and sleeping accommodation is concerned, except that they use the same lavatories. The patients in H1 ward are mainly deteriorated schizophrenics requiring every nursing care and attention, whereas the H2 patients are able to attend to their personal requirements and were able to co-operate with the medical and nursing staffs. They are capable of complaining when feeling ill and are able to give satisfactory histories on interrogation. The epidemic commenced with an isolated case in H1 on 13th January 1942, but the majority of cases occurred between 5th February and 1st March. Thereafter the epidemic tailed off to the end of March. When the diarrhoea had reached epidemic proportions on 5th February the usual precautions were taken, and these included the collection of stool specimens from all the contacts. An unexpected finding was that a considerable number of contacts were returned as positive Flexners who were

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not only not ill, but who had made no complaint, and who on interrogation and with careful observation were not observed to have any sign or symptom of the disease. Moreover, these "symptomless" cases occurred *pari passu* with the overt cases of the disease.

Of 151 patients in these two wards 40 developed symptoms, 29 had positive stools but were symptomless, and 82 did not become infected.

It was found that of the patients who had been previously inoculated, a rather higher percentage became infected than of those not inoculated, and clinical dysentery of all grades occurred whether the patients had been inoculated twice, once, or not at all. However, it may be significant that out of the 29 "symptomless" cases, 25 had received inoculation.

Table II expresses the average length of time the stools remained positive for Flexner amongst these patients, the grade of severity being correlated against inoculation.

TABLE II

Relationship between Inoculation against B. dysenteriae Flexner, Grade of Severity of Disease and Duration of Infectivity

	Average Number of Weeks Stools + for Dysentery.				
	Severe.	Moderate.	Mild.	Total Cases Clinical Dysentery.	Symptomless Cases.
Patients inoculated twice	6.3	3.8	6.0	4.4	1.5
Patients inoculated once	2.25	5.0	5.5	3.7	2.9
Patients not inoculated	5.4	6.5	2.0	4.5	2.25
Average . . .	4.5	4.4	4.5	4.3	2.2

The table serves to demonstrate that in this epidemic the average case of clinical dysentery, whether severe or mild, continued to excrete the bacillus on an average for about four-and-a-half weeks from the onset. The symptomless cases, on the other hand, excreted the bacillus for about only half that period.

A few isolated cases of asymptomatic dysentery have been noted in other ward blocks during minor epidemics.

Infection of Nursing Staff.—Bearing in mind the lessons ably exemplified by McMillan *et al*,¹⁴ a stricter vigilance is now maintained over the nursing staff, particularly when a case of

dysentery has occurred in any ward. A recent interrogation of the staff of the female isolation ward, where dysentery cases are nursed and treated, revealed that 9 out of 14 nurses admitted having had attacks which were suggestive of a Flexner infection, although only three had reported sick. In the majority of instances relaxed stools for only twenty-four to forty-eight hours were admitted, with or without abdominal pain. In 2 cases where non-resident nurses were treated by their own doctor, dysentery was apparently unsuspected. Moreover, one of the staff who was found to have positive stools on routine examination had no symptoms referable to the gastro-intestinal tract beyond a single vomit.

These observations support the findings and conclusions made by McMillan. The infected nurse may have transient symptoms which pass unnoticed, or, if she is ill, from a mistaken sense of duty she may carry on with her work. The danger is obvious when one considers that she handles the patients' food, often shares a communal lavatory with her fellow-nurses, and is liable to be transferred for duty to another ward in the hospital.

Summary and Conclusions.—The adoption of a careful routine for the collection of faecal specimens and the use of the new culture medium, desoxycholate-citrate agar, has resulted in the following findings.

1. A high proportion of cases of diarrhoea suspected of being dysentery (Flexner) have been bacteriologically confirmed.
2. The majority of cases infected with *B. dysenteriae* excrete the bacillus during convalescence, and the temporary carrier state may last for several weeks.
3. Contacts may become infected and produce very mild symptoms, or none at all.
4. Prophylactic inoculation with a *B. dysenteriae* vaccine has not prevented infection, but it may have modified the course of the disease in some instances.

The following factors are of importance in the spread of the disease: (1) Failure of the nursing staff from ignorance or from a mistaken sense of duty to report gastro-intestinal symptoms; (2) the common temporary carrier state following infection; (3) the occurrence of "missed" cases, formes frustes or asymptomatic cases.

Sulphanilylguanidine appears to be an effective anti-dysenteric agent. It probably shortens the course of the disease and appears to clear the stools of *B. dysenteriae* more rapidly than the sodium

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sulphate treatment. It is useful in cases of chronic diarrhoea following dysenteric infection, suggesting that it may be an effective treatment of the chronic carrier.

We wish to express our appreciation of the help given by Mr Partner of the Central Pathological Laboratory for all bacteriological and agglutination results.

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