THE CONTROL OF DYSENTERY BY PROPHYLACTIC INOCULATION.*

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THE term " dysentery " in mental hospitals may be regarded as applicable to a clinical entity characterized by symptoms of abdominal pain, rise of temperature and passage of blood and mucus. The causative organisms are various, but that occurring most frequently and persistently is the *Bacillus dysenteriæ* of Flexner. This paper deals exclusively with this type of asylum dysentery.

Endemic at Caterham Hospital for many years, dysentery of the Flexner type has necessitated elaborate precautions for its control. Caterham Hospital is perhaps unique amongst mental defective institutions in having over 2,000 patients, the majority of whom are low grade, accommodated in a building opened in 1864 for chronic insane patients. Blocks of three wards each jut out at right angles to long covered corridors, the first and second floors of alternate adjacent blocks being connected by bridges. There is no suitable isolation block, and infectious diseases such as dysentery have to be treated where they occur, the affected ward remaining meanwhile in quarantine. No doubt better results would be obtained if a scheme of control such as that instituted by Prof. Shaw Bolton at Wakefield, and described by M. J. McGrath† in 1928, could be put into effect, but unfortunately this has not been found practicable at Caterham. Since 1932 it has been the practice to rely upon simple isolation combined with inoculation of contacts, and the results have been surprisingly good.

The procedure followed is to isolate the ward on the occurrence of a case of suspected dysentery. If confirmed by laboratory findings all contacts are inoculated, and the ward remains in isolation until the case of dysentery under treatment has cleared up and at least three negative stools reported from the laboratory. This is admittedly not the ideal method; better results might have followed immunization of the whole institutional population. Prophylactic inoculation with the Flexner organism has, however, been looked upon as experimental, and accordingly we have been cautious in its use. In any

* A paper read at the Quarterly Meeting of the Royal Medico-Psychological Association, November 24, 1937.

† M. J. McGrath, "A Description of the Steps taken in a Mental Hospital to Prevent the Spread of Dysentery and Allied Infectious Diseases", *Journ. Ment. Sci.*, October, 1928.

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case the limited method used has enabled definite conclusions with regard to the efficacy of inoculation to be arrived at, such as would not have been possible if it had been used indiscriminately.

During the period under review, 1928 to 1936, conditions at Caterham Hospital have remained relatively stable, and little change has occurred in the number and grade of population, quality of food and general environment, as well as the keen standard of clinical and laboratory diagnosis.

In 1931, when dysentery was assuming epidemic form, inoculation was at first cautiously carried out on relatively few cases. As no unpleasant reactions ensued it was decided to inoculate all contacts, and this has been done since 1932.

The four years, 1928 to 1931, can conveniently be called the "control period", and be compared with the five-year period 1932 to 1936 called the "inoculated period", some adjustment in figures being, however, necessary on account of the previously mentioned cases inoculated during 1931.

Vaccine and Dosage.

The vaccine used throughout the period of inoculation was prepared for us by the Central Laboratory of the L.C.C. Mental Hospitals. It was made from cultures of *B. dys.* Flexner (all types) isolated from cases of dysentery at Caterham and four other L.C.C. mental hospitals, equal quantities of the five organisms being pooled. It contained 500 million organisms per cubic centimetre, the dosage being ½ c.c., followed by 1 c.c. at an interval of a week, subcutaneously. Given in this way no unpleasant reactions occur, and none were noted.

Particulars of the preparation of this vaccine have been kindly supplied to me by Dr. S. A. Mann, and are as follow:

"*Preparation of Vaccine*, B. dys. *Flexner*.

"The organisms are isolated in pure culture and identified by morphological, cultural, biochemical and serological methods. The organisms are agglutinated first against polyvalent serum and finally against monovalent Flexner types. Cultures are kept in stock on agar, and when a vaccine is required, heavy inoculation is made on to nutrient agar slopes in 12-oz. medical flat bottles and incubated for 18 hours at 37° C. The resultant growth is washed off under aseptic conditions with as little as possible of sterile 0·5% phenol in normal saline (i.e., two washings of 10 c.c. each bottle) into another sterile 12-oz. medical flat bottle containing glass beads, thoroughly shaken and heated in a water-bath at 60° C. for ½ hour. Cultures are then taken and incubated at 37° C. for 48 hours. The emulsion is again heated for ½ hour at 60° C. if there is any growth. When the emulsion is found to be sterile, the strength is estimated by comparison with opacity tubes, and the vaccine diluted with 0·5% phenol solution in saline to contain 500 million organisms per c.c. This is placed in appropriate rubber-capped bottles, and by means of a sterile syringe or glass capillary pipette cultures are again taken from each bottle and grown

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aërobically and anaërobically for at least 48 hours to check sterility. After taking this culture the cap of the bottle can be sealed."

It is sometimes helpful at the beginning of an investigation of this nature to obtain some sort of idea as to the probable duration of induced immunity. Prof. Golla in 1932 very kindly supplied a vaccine of similar strength to the stock one, but containing the organisms from a pure culture of *B. dys.* Flexner

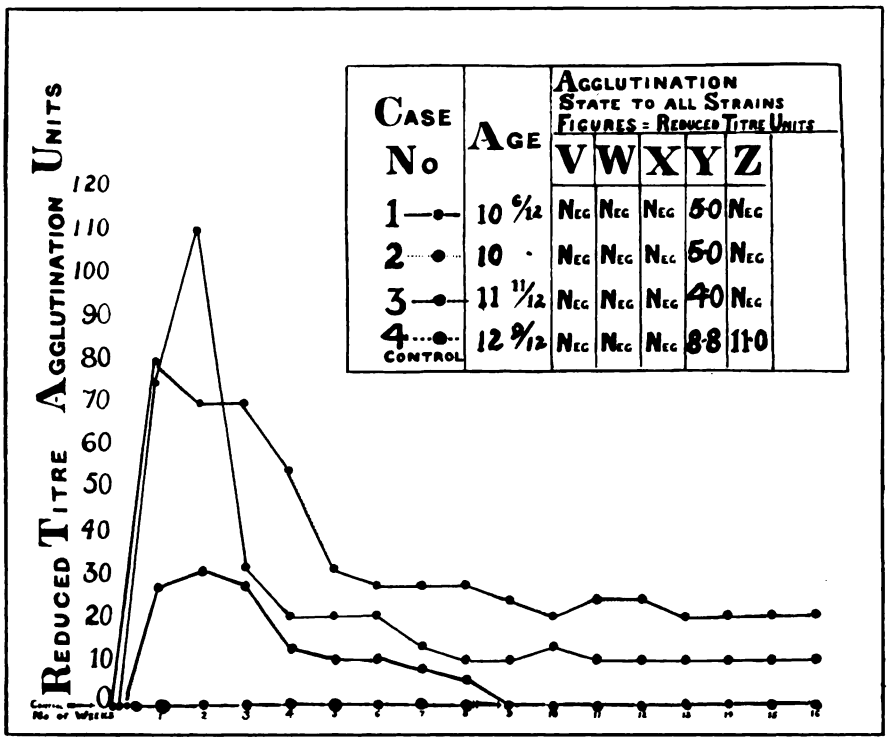


FIG 1.

"W". Using this vaccine, the agglutinating response of the sera of three healthy patients was ascertained in the following way:

A number of boys from a ward that had been free from dysentery for many years had their blood-sera tested for their Widal reaction against all five types of *B. dys.* Flexner, and four of these boys were chosen whose blood-sera gave a completely negative titre to the Flexner "W". Three of the four boys were then inoculated with the Flexner "W" vaccine in the usual way, the fourth being kept as a control. All four then had the agglutinating properties of their blood-sera against *B. dys.* Flexner "W" estimated (in R.T. units)

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weekly over a period of 16 weeks. The results are given in the form of a graph (Fig. 1), from which we see :

1. The control has remained negative throughout.

2. There appear to be individual differences in response, No. 2 case becoming negative in 9 weeks only.

3. That even at the end of 16 weeks the agglutinating properties of the blood-sera of two of the three cases are still above 10 R.T. units—a figure probably indicating a fair degree of immunity.

In a ward which has been free from infection for some time a single fresh case of dysentery is often followed by one or more others within a few days. Sometimes the interval is one of a few weeks or even months, when presumably an undetected carrier is responsible. For purposes of analysis and comparison it has been found convenient to define certain terms used in this paper :

1. *Primary cases of dysentery:* A primary case is one which was not preceded by another within a minimum period of 16 weeks.

2. *Secondary cases of dysentery:* A secondary case is one which followed a primary case within 16 weeks.

Both primary and secondary cases refer to patients of the same ward.

3. "*Contacts*": These are patients of a ward where a primary case of dysentery occurs and are referable to such case.

The total number of cases of dysentery in the control period was 77, and in the inoculated period 45. In the control period 31 primary cases occurred with 1,504 contacts. Of these, 46 developed dysentery, or 1 in 33. In the inoculated period 29 primary cases occurred, with 1,585 contacts. Of these, 16 only developed dysentery, or 1 in 99 ; thus, over a longer period of time not only was the total reduced, but the incidence amongst contacts was also considerably diminished.

It will be noted that whereas the total number of primary cases has remained approximately equal, there has been a considerable reduction of secondaries in the inoculated period.

In the inoculated period as many as 21 primary cases were not followed by secondary ones, whereas in the control period only 13 primary cases were similarly free.

A study of the chart illustrating primary followed by secondary cases of dysentery (Fig. 2) reveals entirely different distributions in these two groups. In the inoculated period practically all the secondary cases occur within 16 days of the primary ones ; in the control period, on the other hand, many more secondary cases occur after the first 16 days.

During the inoculated period, out of a total of 11 primary cases on the female side, only one was followed by secondaries. On the male side 7 out of 18 primary cases were followed by secondaries. The better results obtained on the female side would seem to be due to more prompt inoculation of contacts

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on that side. In fact in the only instance where inoculation was unavoidably delayed for some eight days, three further cases occurred.

Moreover there are two further examples that well illustrate the value of inoculation :

1. *In M.C. 3 ward.* On February 25, 1932, a primary case of dysentery occurred and was followed after three days by a secondary one. Due to some

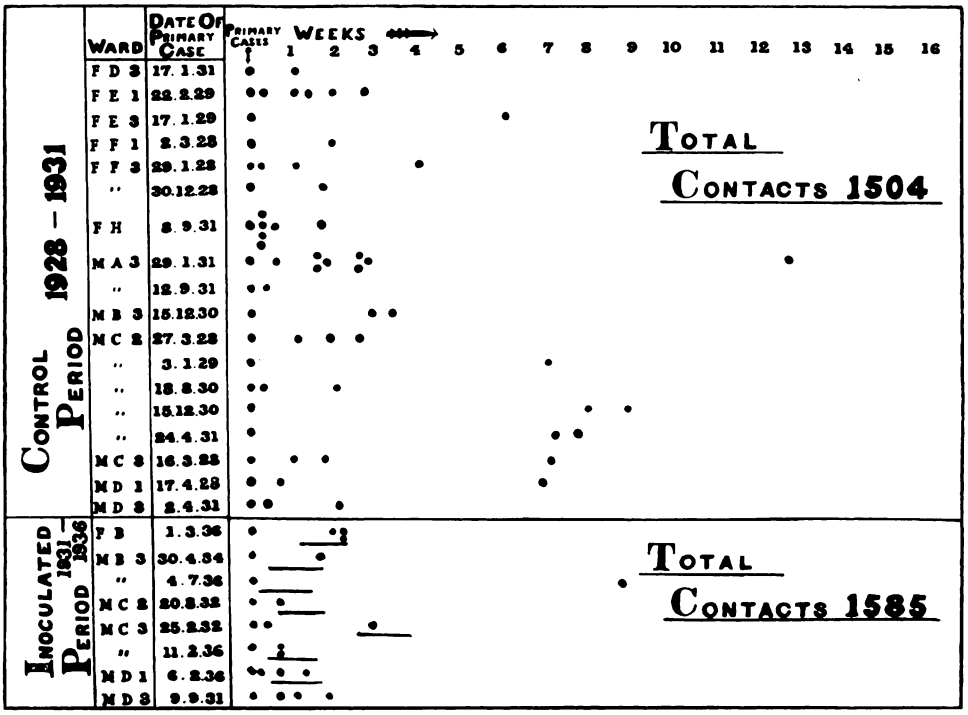


FIG. 2.

misunderstanding contacts were not inoculated until the end of the third week. One further case occurred before the completion of inoculation.

2. On July 4, 1936, a primary case of dysentery occurred in M.B. 3 ward. All contacts were inoculated and there were no further cases until the end of the eighth week, when a patient went down with typical dysentery, confirmed by laboratory findings. It looked at first sight as if an inoculated case had developed dysentery within only eight weeks. On further inquiry, however, it was discovered that this patient had been, rather incautiously, transferred to this ward, and that he had never been inoculated at all. Furthermore, the primary case, although now up and about, was found to be still passing *B. dys.* Flexner in large numbers without showing any clinical signs of the disease.

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TABLE I.—*Giving Comparative Figures relating to Cases of Dysentery during Control and Inoculated Periods.*

	Control period. (four years).	Inoculated period. (five years).
Total number of contacts	1,504	1,585
,, ,, cases of dysentery	77	45
,, ,, primary cases of dysentery	31	29
,, ,, secondary cases of dysentery	46	16
Primary *not* followed by secondary	13	21

TABLE II.—*Showing Incidence of Dysentery amongst the Grades, during Control and Inoculated Periods.*

	Control period.		Inoculated period.	
	Average total population. (%.)	Developed dysentery. (%.)	Average total population. (%.)	Developed dysentery. (%.)
Idiots	14·4	44·3	15	44
Imbeciles, low	38·2	40	38	40
,, medium	23·5	7	23	7
,, high	8·5	3·5	9	4
Feeble-minded	15·4	5·2	15	5
	100·0	100·0	100	100

Note the high incidence of dysentery amongst the idiots and low-grade imbecile.

TABLE III.—*Showing Number of Patients Developing Dysentery within 6 months of Admission (called New Admissions).*

	New admissions.	Total cases of dysentery.	%.
Control period	6	77	7·8
Inoculated period	4	45	6·6

Here, for two months, was a state of affairs ideally suited to the dissemination of dysentery amongst inoculated contacts, yet not one developed it. No sooner was a non-inoculated patient admitted than he fell a victim. This case of dysentery should, of course, never have occurred ; it is, however, put on the chart as it falls within the definition of a secondary.

Finally I should like to point out that with 1,584 inoculated contacts there has not been a single secondary case of dysentery after the completion of inoculation.

My thanks are due to Dr. D. Magrath and to Mr. Stunnell for their invaluable assistance. I am indebted to Dr. Thomas Lindsay, Medical Superintendent, Caterham Hospital (L.C.C.), for kind permission to publish details of this work.

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Discussion.

The PRESIDENT (Dr. Douglas McRae) said members would agree there was no doubt that Dr. Paddle had amply justified his position from what he had stated that afternoon. He, the President, had been accustomed to reside in places where the inhabitants were not usually massed together in large bodies, and in his hospital there was no dysentery, except for an occasional sporadic case. But in the large institutions, such as those in England especially, these infectious cases were certainly troublesome. It was satisfactory to know that there were men of scientific knowledge and energy who had found a way of controlling these epidemics.

He congratulated Dr. Paddle on his work, and wished him prosperity and happiness in his new post.

Dr. W. M. FORD-ROBERTSON: Before drawing your attention to one or two implications arising out of Dr. Paddle's paper, I should like to express my appreciation of the contribution he has made to a subject about which nearly all of us here will have exasperating recollections. We have had, I believe, practical and satisfactory evidence of the value of prophylactic immunization carried out under conditions that were not ideal.

The first point I should like to mention is the significance of the diminished incidence of secondaries following on primary cases. The occurrence of secondaries at all, however, shows that, if protection afforded by inoculation is really to be effective, immunization should be begun at the earliest possible moment after the primary case has been discovered. Related to this is the condensation of the secondary cases to within the sixteen days in what is called the "inoculated period", with the few exceptions Dr. Paddle has stated. Unless some other system of inoculation is devised, it would seem impossible to prevent infection being spread before the primary case becomes evident clinically, since dissemination may well occur during the pre-symptomatic phase, that of invasion or perhaps re-invasion. A regular prophylactic regime of vaccine treatment would be the most satisfactory method, but the time and labour involved for a large patient population is considerable. Therefore, it is worth while considering very briefly if some other equally satisfactory method is available and the evidence in support of such an alternative. I refer, of course, to *per os* immunization.

The study of the subject dates back to 1919 when Besredka (1) of the Pasteur Institute first published his papers and stated that the buccal route gave distinctly better results than the subcutaneous method. The literature since that date has emanated mainly from Europe and the East, less attention having been paid in America and this country. The many interesting theoretical considerations put forward by Besredka, Finder (2) and others will have to be omitted, but a short review of the practical results in a mental hospital and also in a crowded general community are, I think, worth mentioning.

Johns and Chalk (3), 1933, following the work of Cathcart and Gordon (4), 1924, give, in a preliminary report from the mental hospital at Ontario, the results of oral vaccine therapy against *B. dysentericus* Flexner, covering a treatment period of ten years from 1923–33. From a group of 46 patients selected at random and given the prescribed course of vaccines *per os*, it was ascertained that 65% developed agglutination titres of over 1/160, twelve a titre between 1/40 and 1/80, and only four a titre of under 1/40. None were negative.

The vaccine was made from the strains isolated from patients in the wards. Four-day agar cultures, killed by heat only administered without preliminary preparation of the patients. Five doses were given in six days, replacing the evening meal, while the quantity of the emulsion was 10 c.c. for the initial dose, followed by three doses of 20 c.c., and finally a single dose of 40 c.c.

It seems apparent from the evidence given that the method was successful as a prophylactic measure in controlling bacillary dysentery endemic in a mental

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hospital. In 1923 thirty-seven cases were reported, whereas in 1931 and 1932 no proved cases occurred. Cessation of the vaccine prophylaxis at certain periods resulted in prompt recurrence, and the disease was brought under control with its resuscitation. This fact would, of itself, indicate a favourable influence of the vaccine. To draw a parallel between these results and Dr. Paddle's seems permissible, if allowance is made for the different method employed and the route of administration. The authors report no untoward reaction and state that immunity is effective for one year.

Referring to similar investigations amongst the ordinary community, the work of Iguchi and others (5) from the Sanitary Section of the Metropolitan Police Bureau of Tokio is of interest. They report a tendency of dysentery to spread in spite of every known measure of prevention. It was therefore decided to try the effect of *per os* immunization. The bacteriological strains used were what they call " atypical 1 and 3 " and the " Ohhara " bacillus in pill form, a total of 90 mgrm. being divided into three doses, one each morning when fasting. In the years 1930 and 1931, more than 130,000 children were thus immunized, four towns being selected and divided into treatment and control areas. In 1930, 12,000 children were treated as soon as the disease appeared epidemically, and in 1931, 120,000 were treated just before the epidemic broke out. Toxic reactions were reported to be slight. The results in regard to morbidity were as follows: it is claimed that by buccal immunization against dysentery and ekeri, an acute and fatal form of diarrhœa found in Japan, the morbidity was reduced to about one half, with a conspicuous lowering of mortality. Taking 1931 as an example, the morbidity per 10,000 child population based on 11,500 cases treated, was 35·4, whereas in the control group of over 22,000 the incidence was 80·8 per 10,000.

Dr. Paddle's work and that of the investigators I have just mentioned should serve, I think, to stimulate others to study this important matter more than we have done hitherto.

References.—(1) Besredka, *Immunity in Infectious Diseases*, Williams and Wilkins, Baltimore, 1930.—(2) Finder, J., and Simons, J., *Journ. Med. Illinois*, April, 1932.—(3) Johns, E. P., and Chalk, S. G., " Prophylactic Oral Vaccine in Bacillary Dysentery ", *Canadian Med. Assoc. Journ.*, 1933, xxix, pp. 40–43.—(4) Cathcart and Gordon, *Ontario Journ. of Neuro-Psychiatry*, 1924, p. 52.—(5) Iguchi, J., and others, " Prophylaxis of Dysentery by *Per Os* Immunization ", *Kitasato Arch. Exper. Med.*, 1932, ix, pp. 218–223.

Dr. DOUGLAS TURNER said he also would like to congratulate Dr. Paddle on having chosen this subject for discussion, as it was interesting in an unfortunate way to nearly all members. If a report of a case of dysentery was received, the medical superintendent worried more than he did over scarlet fever or diphtheria. At Colchester many cases had occurred with practically no symptoms except a little diarrhœa, with the passage of a little mucus, and blood passed once or twice. They had all tried various remedies, and all had hoped that they had stopped the epidemic or the cases of dysentery. Years ago he tried izal—a filthy substance to take—and for some years he felt convinced that he had stamped out the disease. After the war there were instituted improvements in dietary, butter and milk being given in greater quantities. He isolated permanently every case, however mild, but he did not stamp out the disease. This year he had had twenty-five cases of it. One difficulty he had was in making sure whether there was a positive or a negative bacteriological result.

He asked what was the duration of the induced immunity. During the process of immunization, was there any period when the cases which were being immunized were more susceptible to infection in comparison with their susceptibility before immunization? He thought there were cases which were more likely to get typhoid if they had been immunized than if they had not. He would like to know how soon immunity developed after inoculation; he gathered it was sixteen days. He also asked how long, when a case occurred and the ward had been isolated, it remained isolated before receiving new admissions. And even

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when inoculation was working, were the new admissions to the ward inoculated before being sent to that ward? Or were they inoculated after they arrived?

Dr. T. LINDSAY (Caterham) wished to make a few remarks as the Superintendent of the hospital where Dr. Paddle's work was done. After the President's words of commendation he felt that anything said by him on that theme would be superfluous. He, the speaker, went to Caterham as Superintendent just before Dr. Paddle, who was appointed from Wakefield. He knew Caterham by reputation; cases transferred to Tooting Bec from Caterham were referred to as coming from a "dirty place", and the other patients were anxious not to associate with them. Dr. Paddle used often to say to him, "What about this isolation hospital? We shall never do any good until we have got it". That was the Wakefield idea—that an isolation hospital should be built, and that all the cases that had had dysentery or had been suspected of having it in the last four or five years should be put into it and kept there for an indefinite period. He, the speaker, felt obliged to discourage the transfer of all grades of patients, from the highest to the lowest, to an isolation hospital for this indefinite period. He thought it would amount to cruelty.

There must be a considerable amount of team-work which was quite difficult to establish in carrying out a routine of this kind, but once the machinery was in order, and the team entering into the spirit of the work, it went well and easily. In any case, a great deal of peace of mind had been the result.

In answer to Dr. Turner's question, the shortest period of immunity after experimental inoculation was nine weeks. If the outbreak could be stopped for nine weeks then that individual outbreak was practically at an end. At Caterham they did not now look on dysentery as formerly, and those present who were superintendents would appreciate what he said. Here was a method, which one could say and believe would stop the individual attack of dysentery which in the past had periodically almost brought the work of the institution to a standstill.

Dr. J. J. B. MARTIN (Bristol) said he felt that a word of caution was necessary, especially in view of the remarks of the last speaker. He, Dr. Martin, came from a hospital which was full of dysentery to one where there was none, and his present hospital claimed that it had no dysentery because all recent admissions were inoculated with the Flexner vaccine. He would like to believe it, but he was certain it was not true. The hospital from which he came was, for four years, more saturated with the disease than any mental hospital in the country, yet they were all inoculated four times a year, and some had a titre up to 500 induced by giving inoculations. Dysentery was still prevalent there. At the speaker's institution they had used the same methods as Dr. Paddle on a large number of occasions, and they found there was a tremendous individual variation. Some patients, indeed, showed no response. They found that the most constant result and the longest titre in the blood was achieved by intravenous inoculation. By mouth they gave relatively enormous doses, but they did not find anything like the titres which Dr. Ford Robertson had quoted; they found it difficult to get a titre of 20. They were not working with Flexner W, but with what Dr. Scott called ZX.

He felt that if medical superintendents were likely to go away from this meeting with the idea that once they inoculated a patient against dysentery they had stamped out the disease, they would have disappointing results in the next few years. If members studied the history of dysentery in any hospital they would find it went in cycles; that it appeared for no known reason in conditions which were constant. Undoubtedly there was a variant of some sort, some virulent type of Flexner which, when it appeared, would cause an epidemic despite active inoculations. He had seen cases of dysentery occurring in people with an R.T. of 500. He agreed that one thing which inoculation did was to modify the severity of the disease to such an extent that there might be practically no disease at all. On the other hand, one did not stop the activity of the carrier, and there was the

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constant fear that the disease was in one's hospital, but was rendered symptomless by the inoculation.

Dr. A. C. SINCLAIR (Dorchester) remarked that as he came from the hospital which Dr. Martin had just left he would like to say a word. An interesting feature was that the hospital population had been inoculated entirely once a year for some time past. The types of Flexner were X and Z. During the past fortnight there had been another outbreak in that hospital, and this time it was proved to be Flexner W, which had never before appeared in that hospital; that bore out the contention as to the efficacy of specific immunization.

With regard to Dr. Turner's difficulty in securing a diagnosis, Dr. Paddle had stated that one must first catch one's hare and then treat the contacts. For some years at Brentwood and Dorchester experiments had been carried out with rectal swabs. Often when ordinarily obtained specimens were repeatedly negative, these swabs proved positive. That was a useful measure in helping to stamp out dysentery. In the last threatened epidemic the disease was prevented from spreading.

Dr. S. MANN (L.C.C. Central Pathological Laboratory) said he had not much to add to what had already been said. One question he wanted to ask Dr. Paddle was how often, in relation to the blood agglutination findings, he would re-inoculate. He was able to say that Dr. Paddle's prophylactic technique had been adopted by some of his colleagues in the London County Mental Hospitals, and in each case they had considered it to be effective. The fact that a so-called immunized case broke down with an attack of dysentery was not a very serious criticism. One could not expect to give total immunity to a case, and a great deal depended on the intensity of the infection and the immunizing dose. In the hospital which was said to be saturated with dysentery the infection seemed to have been very intense.

With regard to Dr. Douglas Turner's difficulty in getting a bacteriological diagnosis, in any institution lacking immediate laboratory facilities the same difficulty would be experienced because of the lapse of time between the collection of specimens and the bacteriological examination. He had experienced a similar difficulty with an outbreak of Sonne dysentery, but afterwards they had plated directly in the ward, losing no time between the collection of the specimens and the preparation of the plates, and they obtained a positive result every time. As to the type of vaccine used, in the L.C.C. service they might have been lucky. The vaccine prepared at the Central Laboratory caused no reaction, and apparently had done the job. He thought the reason was that they had, at the time, a nice collection of fresh cultures, some from Dr. Paddle's cases, and representing together what might be called the " L.C.C. autogenous vaccine ". If inoculation had to be done, that was important. If, on the appearance of the first case, a vaccine was made rapidly, that type of vaccine might be very much more effective than a stock vaccine obtained from any other source.

Dr. A. A. W. PETRIE (Banstead) asked what effect Dr. Paddle's inoculations had on his carriers, as carriers were an essential feature of the problem. The symptomless carrier was what kept epidemics going. There were different types and variations within the standard V, W, X, Y, Z types; VZ types, XZ types, WX types, WY, and so on; and the efficacy of the vaccine depended partly on how much the titre went up after inoculation to the particular Flexner organism concerned.

One thing Dr. Mann mentioned touched a problem the speaker had at Banstead: that where they had previously been having Flexner dysentery, they suddenly got a crop of the Sonne, and that accounted for the return of some negative reports. The Sonne organism partly accounted for the spread of an outbreak in his neighbourhood last year, known as the Sutton outbreak. At the time no causal organism could be traced, but now people were being warned that Sonne dysentery was in the neighbourhood. Probably the public health bacteriologists had changed their

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method and now looked for a lactose fermenter. That might account for Dr. Douglas Turner's difficulty, because until recently laboratories had not been looking for the Sonne type of dysentery.

His chief purpose in rising had been to ask what was the effect of the inoculation on the carriers, the symptomless people who were carrying and excreting large numbers of the organisms, with only very slight diarrhœa. The slightest loose motion might be a recurrence of dysentery, and no one looking at the stools would think it was that disease. He would be interested in hearing Dr. Paddle's opinion as to how inoculation affected those.

Dr. PADDLE, in reply, thanked the President for the very kind remarks he had made about him. He thought the President had been lucky not to have had dysentery at his mental hospital at Ayr. He, the speaker, had had a few suspicious cases recently at his new institution, though he had not been able to call them dysentery.

He fully agreed with Dr. Ford Robertson's remark that immunization should be conferrred early; he thought the success of inoculation would be found to depend very largely, indeed almost entirely, on whether it was given as soon as possible after the outbreak of dysentery.

He had not had any experience of giving the vaccine by the mouth, but it seemed to be an interesting method, and it had advantages over inoculation, if the same good results could be obtained by that method.

Dr. Douglas Turner had asked whether cases which passed a little blood and mucus should be classed as dysentery. He, the speaker, thought they should be so classed, but whether they should be called the Flexner or the Sonne type must be left for the laboratory to decide. At Caterham it had almost always been of the Flexner type. In practically every single case blood and mucus were passed, though a few passed mucus only, and the Flexner bacillus was demonstrated. From his own experience at Caterham and Wakefield, when stools were examined after a four-hour interval they were almost invariably found to be negative. The specimens should be plated almost immediately they were voided, or withdrawn by rectal tube, or by the method which Dr. Sinclair mentioned.

The question as to the duration of the induced immunity was not an easy one for him to answer, but from the figures he had given he would infer it was probable that the immunity lasted about 4½ months in a small minority of the cases. In the large majority of those inoculated the immunity lasted from one to two years. As to the question whether patients were more susceptible at one stage of immunization, there was no evidence to show that any cases became more susceptible at any time. Another question asked was how soon immunity developed. If one were to judge immunity by the titre, it developed within three days, and was probably at its maximum in seven days. He had been told by Dr. McCartney, the Director of Research in the L.C.C. Laboratories, that immunity was a relative thing; it varied in an individual from day to day, sometimes even from hour to hour, and it must always be considered in terms of relativity as between one person and another. Dr. McCartney said that if a person received a sufficient dose of a virulent organism, it mattered little whether he had been immunized or not, he would probably develop the disease; but if he had a small dose of organisms and was immunized he might not develop the disease.

Another question was how long a ward remained in quarantine. At Caterham the ward remained in quarantine until the case of dysentery being treated there showed no clinical signs and the bacteriological report was negative three times.

He much appreciated the remarks made by Dr. Lindsay. He still thought an isolation hospital should be provided, where these cases of dysentery could be isolated from the rest of the colony, especially as many were carriers and were difficult to detect. It might appear to be cruelty to isolate them, but it would be still more cruel if the rest of the colony were allowed to have dysentery.

He believed Dr. Lindsay said the shortest period of immunity was nine weeks,

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He thought that was a mistake; it was just over sixteen weeks. The one case of dysentery which appeared at nine weeks had not been inoculated at all.

He had read Dr. Martin's paper in the *Journal of Mental Science* and was most interested. He thought Dr. Martin and he were in agreement in respect of about 80% of the statements made. The problem of dysentery was one of low-grade cases, i.e., wet and dirty cases, and if those were immunized, or any other method was used, the problem of dysentery could easily be controlled. Dr. Martin's method of intravenous inoculation had given extraordinarily good results, and he felt it was a pity it was not tried at Caterham.

With regard to dysentery occurring in cases with R.T. units of 500, he did not see why that should not occur. He was not certain whether the immunity and the titre curve always went hand in hand; but perhaps a real bacteriologist might give an opinion on that; he did not claim to be one himself.

Dr. Sinclair had said he had had cases of dysentery after inoculation, but that it was the W type which appeared, whereas he had inoculated with X and Z. That would be likely to occur. The vaccine supplied to Caterham by Prof. Golla contained all the organisms likely to be met with.

In answer to Dr. Mann, in the graph which the speaker showed the first inoculation was 250 million, followed by 500 million in a week's time.

In reply to Dr. Petrie, the effect of the vaccine on carriers was a very interesting matter. He remembered giving the first dozen carriers a vaccine of 250 million, and then finding that a few cases were passing the Flexner bacillus without showing the clinical signs of dysentery. He liked to call those cases "bacteriological" dysentery. He had not included them on the chart, which was confined to cases of clinical dysentery, which were confirmed as of Flexner origin. When inoculating, especially after the first dose, one found a certain number of cases were passing the Flexner organism; they were possibly carriers.

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