USE OF THE BACTERIOPHAGE IN AN OUTBREAK OF INSTITUTIONAL DYSENTERY

BY

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Dysenteric infections in homes and hospitals for sick children are common and very hard to control. These difficulties were accentuated in the outbreak here described, as it happened in a home for blind babies. It was inadvisable to close the home, and impossible, as will be explained, to secure effective isolation. In these circumstances treatment with bacteriophage was assiduously carried out in the hope that the infectivity of those affected might be reduced by some alteration in the bacteria, such as is supposed to be produced by the action of the bacteriophage upon micro-organisms. So successful does this appear to have been that the experience seems worthy of record.

The home had thirty-two blind children aged from a few months to 7 years. It is managed by a devoted matron, with a staff of eight skilled nurses, three teaching staff, and five domestics. All are under the regular medical supervision of an experienced local medical practitioner, with ready access to consultant advice. The medical officer is a regular visitor to the home.

The Cases

The first patient, on February 20, 1937, was hardly ill at all, although there was a little blood in the stools. This child was not suspected of having dysentery, and after a few days' segregation was allowed to join the other children freely. Whether there was a connexion between this case and the epidemic that followed six weeks later is uncertain, but the child was again ill on April 22. On the latter occasion the first stool to be examined showed no dysentery bacilli, but on April 25 *B. dysenteriae* Sonne was obtained (Table I, Case 4).

TABLE I.—*Cases from which B. dysenteriae Sonne and/or "Atypical" Bacilli were Obtained*

Case No.	Date	Result of Stool Examination	Examined by
1	5/4/37	Sonne present	Dr. Selous
	2/5/37	" "	D.H.
	7/5/37	" "	D.H.
	20/5/37	"Atypical" bacilli present	D.H.
	27/5/37	Negative for dysenteries	D.H.
2	12/4/37	Sonne present	Dr. Selous
	25/4/37	"Atypical" bacilli present	D.H.
	7/5/37	Sonne present	D.H.
	24/6/37	"Atypical" bacilli present	D.H.
	7/7/37	Negative for dysenteries	D.H.
3	18/4/37	Sonne present	Dr. Selous
	4/5/37	" "	D.H.
	19/5/37	Negative	D.H.
4	22/4/37	Negative	Dr. Selous
	25/4/37	Sonne present	D.H.
	14/5/37	Negative	D.H.
5	25/4/37	Sonne present	D.H.
	6/5/37	Negative	D.H.
6	25/4/37	Negative	D.H.
	6/5/37	"Atypical" bacilli present	D.H.
	7/7/37	Negative	D.H.
7	25/4/37	"Atypical" bacilli present	D.H.
	24/5/37	" " "	D.H.
	3/6/37	" " "	D.H.
	7/7/37	Negative	D.H.
8	25/4/37	Sonne present	D.H.
	10/5/37	Negative	D.H.
9	25/4/37	"Atypical" bacilli present	D.H.
	6/5/37	Negative	D.H.
10	25/4/37	"Atypical" bacilli present	D.H.
	6/5/37	Negative	D.H.
11	27/4/37	Sonne present	D.H.
	27/5/37	Negative	D.H.

Following this presumed first case, on February 20, there were three cases on April 4 and 5. Of these, two were mild and one moderately severe. The last-mentioned case passed blood and mucus, and from a specimen of the stool Dr. Selous isolated *B. dysenteriae* Sonne (Table I, Case 1). After an interval of four days there were four more cases on April 10 and 11. From the stools of two of these *B. dysenteriae* Sonne were obtained (Table I, Cases 2 and 3), and from the other two "atypical" dysentery bacilli—that is, Gram-negative, non-motile, non-lactose-fermenting bacteria, which fermented mannitol with the production of acid only, but did not, however, conform to any of the recognized dysentery strains: they failed to agglutinate with standard Oxford sera for the Sonne, Shiga, or Flexner groups. Three of these four cases were febrile and toxic, and a tendency to cyanosis was a feature of their condition.

A week later, April 18, another febrile case of dysentery occurred, and from this also *B. dysenteriae* Sonne were obtained (Table I, Case 3). On the 22nd the first case was again reported ill. This was a mild attack. The first stool examined gave a negative result, but from a stool on April 25 *B. dysenteriae* Sonne were obtained (Table I, Case 4). It is possible that this patient may have harboured *B. sonnei* from February 20 and thus have been the source of the other infections. Whence her infection came in the first instance could not be ascertained. On April 25 three more cases occurred (Table I, Cases 7, 9, 10). Two of these patients were nurses (Table I, Cases 9, 10), only slightly indisposed, but from them "atypical" dysentery bacilli were obtained. The accompanying chart conveys a clear idea of the pattern of the epidemic.

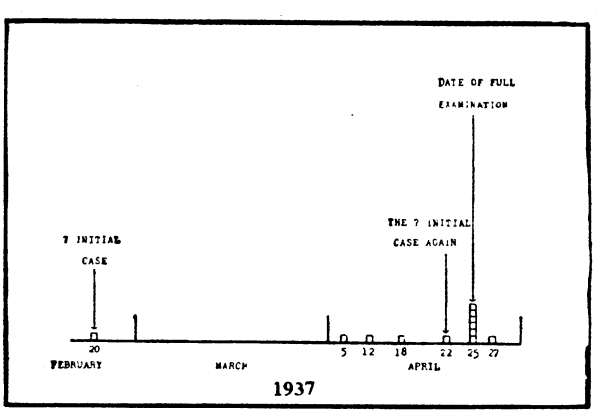

Chart showing a graphic representation of the epidemic

The Investigation

On April 25 I was consulted by Dr. Eric Pritchard, and was asked to investigate and to suggest a way of dealing with the outbreak. The home is situated in a very commodious and well-converted mansion, standing in its own extensive and attractive grounds. The appended sketch-plans of the two lower floors show the internal arrangements, and it will be seen how difficult was the problem of effective isolation in this epidemic. The water supply was from the town mains. There was no evidence of any epidemic in the rest of the area supplied. The milk was from local farms. It was not pasteurized, but was sterilized by boiling when received at the home.

These blind children are encouraged to lead as normal a life as possible. Vision, of course, plays a major part in the education of children; but in blind children this is perforce replaced by stimuli from touching, tasting, smelling, and hearing. It is desirable that they handle everything, and inevitable that they taste many things. Hence the control of an epidemic of a highly infective disease offers even more difficulties than those met with in institutions for more normal children.

Owing to the peculiar nature of the home there is no ward for the treatment and efficient isolation of cases of sporadic disease, and great reliance has to be placed upon "bed-isolation" (always a matter of difficulty, but more so in an institution of this kind).

Cases 9 and 10 were nurses, and were at no time really ill; they harboured "atypical" bacilli, and would never have been found had it not been possible to examine the stools of all the inmates and staff. Every case discovered at this time, with the exception of Case 11, was of the minor or carrier type, and in the ordinary course of events such cases would certainly have been overlooked.

There were then, on April 27, seven cases either known to have had dysentery or found on that date to harbour dysentery bacilli; one child negative on culture who subsequently developed the disease (Table I, Case 11); and two nurses (Cases 9, 10), who were shown to harbour "atypical" dysentery bacilli. The remainder of the children (twenty-two) were hitherto unaffected and presumably healthy. There were also seventeen nursing, teaching, and domestic staff. Efficient isolation seemed impossible without upsetting the routine of the home and thus nullifying much of the laborious and excellent work of the devoted staff, who were doing all that seemed possible to segregate the sick. It was very undesirable to close the home and disperse the children to isolation hospitals.

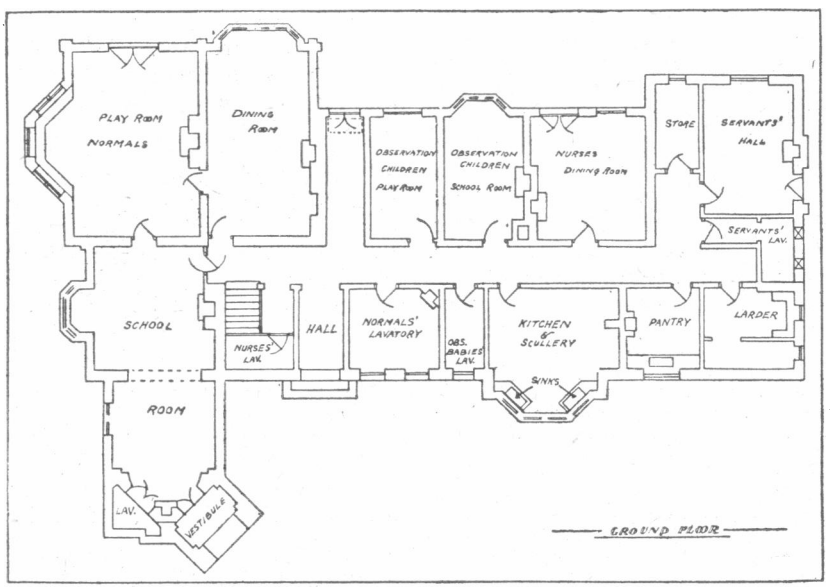

FIG. A.

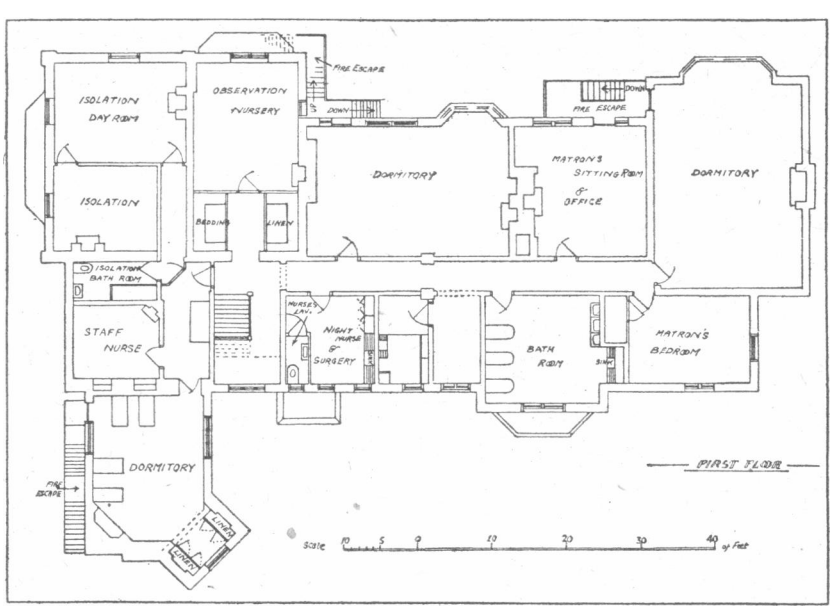

FIG. B.

Treatment

Accordingly I recommended that those who had been sick, those unaffected and therefore presumably at risk, and all the staff should receive one dose of a reliable anti-dysentery bacteriophage three times daily for a fortnight, and thereafter one dose daily. All those in bed and upon bed-isolation received one dose of the bacteriophage three times daily until the stools were reported "free from *B. dysenteriae* Sonne, and from 'atypical' dysentery bacilli."

An examination of the stools of all the inmates and staff was begun. In the first batch of stools examined on April 25, 1937, there were thirty-six specimens—eighteen from child inmates and eighteen from the adult staff. Of this batch three were positive for *B. dysenteriae* Sonne and two showed "atypical" dysentery bacilli (these were the two nurses). The rest did not show dysentery organisms. On May 4 four more specimens were examined; of these only one showed *B. dysenteriae* Sonne. On May 7 eight more stools were examined and two showed *B. dysenteriae* Sonne. The examinations were continued at varying intervals until, at the end of the epidemic on July 7 a total of sixty-six stools had been examined.

Bacteriophage treatment of the sick was started on April 25 and was extended to the whole institution on April 27. On the latter day, the second day after treatment was begun, one further case occurred. This was the last; and now, over a year later, there has been no fresh case.

This sudden cessation of the epidemic may have been a coincidence: but there was nothing to suggest that the cases between April 4 and 27 were being infected from

outside the home. The repeated findings of *B. dysenteriae* Sonne suggested that this infection was being spread. The "dropping" cases during the three weeks were what might be expected in an outbreak spread by contact infection; and even though the separation of the healthy from the sick was tightened up, the activity of these children, unbelievably quick in touching, smelling, and putting things into their mouths, made the transfer of infection probable.

The treatment aimed at the bacillus causing the disease: it sought by the action of the bacteriophage to modify the bacillus, and thus render it less capable of giving rise to dysenteric infection. Some modification did apparently occur, as towards the end of the epidemic there were more "atypical" bacilli and steadily fewer typical dysentery bacilli isolated. There was no change in the technique used, so it appears that the modification was truly in and of the bacilli. (It is open to argument whether "atypical" dysentery bacilli can be produced from *pure strains* of known dysentery organisms, but there is some evidence in the authorities which appears to support the proposition.) No medicinal treatment other than bacteriophage was administered. No case was removed from the home. Inquiries at the home at the end of April, 1938, elicited that no further case had occurred.

The bacteriophage was prepared at the Usher Institute of Public Health, Edinburgh. In its preparation races of bacteriophage active against strains of dysentery occurring in this country are largely used, and these include *B. dysenteriae* Sonne from a variety of sources.

I should like to express my thanks to Dr. Eric Pritchard for consulting me about this outbreak, for allowing me to use the bacteriophage treatment, and for his never-failing help and consideration in this and other matters; to Lieutenant-Colonel J. Morison, to whom I am indebted for the supply of bacteriophage, and much kindly help, advice, and friendly criticism; to Dr. W. E. Wallis, medical officer at the home, for his courteous assistance, for the efficient supervision of the outbreak, and for placing his records at my disposal; to the National Institute for the Blind for allowing the publication of this paper and for so readily supplying plans, documents, etc., relevant to this work; and, finally, to Mr. H. Clouston, my senior technician, for invaluable help in the isolation of the dysentery bacilli, and to the other members of my staff for their technical assistance.

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"Problems of the Nations" will be discussed in a series of talks to be held in the Halls of City Livery Companies in aid of King Edward's Hospital Fund for London. The subjects will be "China" on October 6 in the Hall of the Vintners' Company; "Russia" on October 26 in the Hall of the Goldsmiths' Company; "Eire" on November 10 in the Hall of the Clothworkers' Company; and "Czechoslovakia" on November 24 in the Hall of the Drapers' Company. Ticket holders will be given an opportunity of seeing the premises and historical relics before the talks, which begin at 5.30 p.m. Further information and tickets (price 3s. 6d.) can be obtained from the Secretary, King Edward's Hospital Fund for London, 10, Old Jewry, E.C.2.

OBSERVATIONS ON THE POTENCY AND STABILITY OF DICK TEST TOXINS

BY

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The Dick test is less reliable than the Schick test, and is therefore employed much less in clinical work. From time to time questions are asked about the possibility of improving the Dick toxin used clinically in many hospitals in this country. Is it of optimum potency at the time of preparation, and does the diluent ensure that undesirable deterioration does not occur before use?

We have recently been able to compare the poteney of two toxins, one of which, Toxin A, was diluted in boric acid borate buffer solution (B.B.S.), and the other, Toxin B, in 0.4 per cent. phenol saline and in B.B.S. The former toxin is the preparation now used clinically by many workers in this country. We have taken the opportunity to inquire into the stability of the various reagents and also to endeavour to assess the error of the skin method of comparing two toxins in human subjects.

Reagents and Technical Details

The following toxin dilutions were available for injection:

1. Toxin A, diluted in B.B.S. 2 to 3 days previously
2. " " " " " 1 month "
3. " B, " " phenol saline 2 to 3 days previously
4. " " " " " " 1 month "
5. " " " " B.B.S. 2 to 3 days previously
6. " " " " " 1 month "

Dilutions 1, 3, and 5 were posted on the day of preparation, and dilutions 2, 4, and 6 had been kept at 4° C. for four weeks and were sent by post at the same time as dilutions 1, 3, and 5. The tests were made on the anterior surfaces of the forearms of Dick-positive individuals, separate syringes being used for each dilution. The sites of injection varied in different patients; thus a dilution might be injected on the forearm near the elbow in one patient and near the wrist in another. Readings were made after sixteen to twenty-four hours, the key to the order of injections being unknown to the persons making the readings. Throughout the investigation the greatest care was taken to exclude conscious and unconscious bias. The dimensions of the reactions were recorded in millimetres and notes made of their intensity.

Results

An analysis of the comparisons made at the different hospitals is shown in the table.

The following conclusions may be drawn:

1. Toxin A is considerably stronger than Toxin B.

2. Toxin A deteriorates slightly after four weeks in cold storage followed by two to three days at room temperature.

3. Toxin A which has been kept for one month is still considerably stronger than Toxin B freshly prepared.

4. Toxin B deteriorates slightly after four weeks in cold storage followed by two to three days at room temperature.