During an epidemic where there is a probability that infection has actually occurred prophylactic inoculation would be best withheld until the incubation period has been passed, otherwise, generally speaking, prophylactic inoculation is advisable.

In conclusion there is no disease in which the motto "safety first" is more applicable than in the case of typhoid fever.

Case 1 (E. H. S., a man aged 58).—Onset occurred on October 20, 1937, with malaise and abdominal discomfort. There was an irregular pyrexia of mild degree (98° – 101°) up to November 9. Agglutination reaction: $1/50$ *B. typhosus* November 1. The patient was admitted to the London Fever Hospital November 9, 1937; temperature 99.5° , pulse 80. The temperature ranged between 97° and 102.5° up to November 20. It was normal from November 20 to December 18; then a relapse occurred, with a temperature of 99° – 102° up to December 31. It was normal again from December 31, 1937, to January 9, 1938. From January 9 it ranged between 101.5° and 96° . Death occurred on January 24, 1938. This case was characterized by severe and persistent toxæmia with comparatively slight pyrexia and absence of delirium until the last five days of the illness. On December 30, 1937, a local slight perforation occurred in the right iliac region, the symptoms of which cleared up in five days with treatment. Pain in the left leg over the tibia occurred on December 20, due apparently to periostitis. On January 10, 1938, pus was found over the left tibia by exploration, and on January 11 a subcutaneous abscess over the left tibia was opened and drained, *B. typhosus* being found in the pus. Pyelitis occurred on December 18 *et seq.*, the urine containing pus and albumin and *B. typhosus*. Myocarditis was present during the last three weeks of the illness. On three occasions there was a sudden drop in temperature, with rapid feeble pulse and cardiac collapse. Vomiting due to toxæmia occurred several times during the last three weeks. On January 11, 1938, the liver became enlarged, and toxic jaundice in mild but definite degree persisted till the end.

Case 14 (P. T., a woman aged 43).—The patient was admitted to the London Fever Hospital on November 13, 1937, with a history of malaise and mild fever for the previous twelve days. Agglutination reaction: $+1/1000$ *B. typhosus*. The temperature reached 102.5° on November 16, 17, and 18, and subsided to normal on November 24. A relapse occurred on November 25 with intermittent pyrexia up to January 24, 1938, after which date the temperature remained normal and the patient made a good recovery. Melaena occurred on December 3, 1937. On December 25, 1937, there was a rigor due to pyelitis. The urine contained pus and albumin and *B. typhosus*. A rigor with sudden fall of temperature from 103° to 97° occurred on December 26 and 28, and January 1, 2, and 6, after which date the temperature became intermittent and gradually subsided. Hexamine salicylate was given intravenously daily for twelve days with benefit; afterwards hexamine was administered by mouth.

Case B (a man aged 63).—Onset occurred on February 5, 1931, with typical symptoms. The temperature ranged up to 103° and gradually fell to normal on March 4. On February 15 *B. typhosus* was found in the stool. Agglutination reaction: $+1/1000$. On February 18 acute distension of gall-bladder occurred, with collapse. This cleared up quickly after atropine hypodermically. The temperature was normal from March 4 to March 15. During this period severe toxæmia with delirium occurred. On March 15 the temperature rose and became remittent in character. During the last five days it reached a height of 105° . On March 24 a blood transfusion was followed by some improvement. A second transfusion on March 25 was followed by a rigor and temperature rising to 105.6° on the following day. Streptococci were found on blood culture on March 25—probably a terminal auto-infection. Death occurred on March 27, 1931.

This case was characterized by a continuous acute toxæmia, which persisted although the temperature was normal for the

eleven days previous to the relapse. During the period of the relapse the symptoms of toxæmia became greatly increased—due, no doubt, to a secondary streptococcal infection.

My thanks are due to Dr. G. Lewin of Croydon for kindly giving me notes of cases under his care, also to my colleague, Dr. C. E. Lakin, for the use of his case notes.

I am greatly indebted to Dr. Richard Massingham, medical superintendent of the London Fever Hospital, for providing me with notes and charts of all the recent cases treated at that hospital; also to my son, Dr. Philip Willcox, for help in the copying of charts.

[The blocks for Charts A, F, and G have been kindly lent by the Medical Society of London.]

PROPHYLACTIC USE OF ANTI-TYPHOID SERUM IN A LOCALIZED OUTBREAK

BY

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During October and November, 1937, there occurred in Kensington a small outbreak of typhoid fever involving five cases.

History of the Outbreak

The first case was that of Mrs. S., who fell ill on October 9, 1937, and was sent to a general hospital on October 16, by a private practitioner, with a diagnosis of bronchitis. On October 26 she was transferred to a fever hospital as a suspected case of typhoid fever. This information was reported to the Public Health Department on October 27, and that day the rooms occupied by Mrs. S. and her family were disinfected. The family consisted of Mr. and Mrs. S. and six children, the eldest of whom was 14 years of age. Two other families also occupied rooms in the same house—the N. family, consisting of Mr. and Mrs. N. and two daughters aged 14 and 12 years, and another family consisting of three persons. The house was of the three-storied tenement type, there being two water-closets, which were used indiscriminately by all the occupants.

On November 17 the same practitioner was called in by the N. family, and he found both Mr. and Mrs. N. very ill. He diagnosed typhoid fever in the case of Mr. N., who was removed to a fever hospital, and died on Saturday, November 20. In the case of Mrs. N. he did not suspect typhoid fever, but recommended her transfer to a general hospital. This offer was refused.

On Thursday, November 18, the Public Health Department heard that Mr. N. had been removed to hospital suffering from typhoid fever, and when inquiries were made at the home it was learnt that Mrs. N. had died there during the night. A post-mortem examination was arranged for the same day, and this was performed by Sir Bernard Spilsbury. The cause of death was peritonitis due to perforation of a typhoid ulcer. It was estimated from the condition of the organs, and from the history, that the case was then of about three weeks' duration. That day all the occupants of the house were examined by the deputy medical officer of health; one contact,

Mary N., aged 14 years, was found to be suffering from typhoid fever and was transferred to a fever hospital. The duration of the disease in her case was estimated to be about twelve days.

All the home contacts and Mrs. B., a married daughter of Mrs. N. who lived in a house in the same street and who had also been in close contact with the N. family, were visited daily by the sanitary inspector, and were reported to be in good health. On November 21 the deputy medical officer of health visited all the contacts, including Mrs. B., and they reported well. A hint from another contact to the effect that Mrs. B. was not well led him to insist upon making a clinical examination. He found her to be suffering from typhoid fever of about fourteen days' duration. Her reason for not admitting to any symptoms—which, although mild, she had nevertheless guessed were due to typhoid fever—was that she "wanted to go to her mother's funeral."

Mrs. B., her husband, a child aged 3 years, and a baby aged 3 months lived in a house similar in type to that occupied by the other patients. There were two other families in the house, numbering twelve persons. In both houses it was the common practice to pass food from one family to another, and there were abundant opportunities for infection to have passed from the various patients to the contacts in other families, both by means of their food supply and by means of the lavatories, which were in common use.

The situation on November 21, 1937, was that there had occurred in two houses five cases of typhoid fever, two of which had proved fatal. Twenty-six intimate contacts were involved in the two houses, whilst a further family, consisting of man, wife, and three children, were also involved, the wife—another married daughter of Mrs. N.'s—and her family having visited the N.s' house and had meals there during the previous week.

Prophylactic Dose of Serum for Contacts

The question now arose as to whether some form of immediate protection could be given to these thirty-one contacts. T.A.B. vaccine was considered, but was rejected in view of the fact that some of the contacts might in fact be incubating the disease. The use of anti-typhoid serum as prepared at the serum department of the Lister Institute by Felix's method was then discussed. There was no record of the use of this serum for prophylaxis in the past, but as the contacts were all known to the Public Health Department, were localized, and had all been in intimate contact with the patients and therefore subjected to grave risk of infection, and might in fact be incubating the disease, anti-typhoid serum was given in the belief that it would confer immediate protection. This was offered to and accepted by all contacts. The dose given was 10 c.cm. to each adult and 5 c.cm. to each child, administered by the intramuscular route. The injections did not produce any symptoms of serum sickness or other unpleasant reactions.

No cases of typhoid fever occurred among these contacts. This fact is not in any way considered a proof that the serum did actually prevent the onset of typhoid fever in any of these persons: the present report of the outbreak is intended more to illustrate the type of circumstance in which inoculation with anti-typhoid serum is, in our opinion, the correct course to pursue—a course that might well be adopted in similar circumstances in the future.

NOTE ON THE PREVIOUS COMMUNICATION

BY

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The administration of a prophylactic dose of anti-typhoid serum to the group of persons referred to in the communication by Fenton and Hay (see p. 1090) provided the opportunity for estimating the concentration of the circulating antibodies that had been passively transferred with the prophylactic serum. It was thought that some indication might be obtained in this way of the effective dose of anti-typhoid serum for prophylactic use. Such information would be helpful, because doubts had arisen as to whether the dose recommended by the serum department of the Lister Institute was not too large. The prophylactic dose for an adult had been arbitrarily chosen as one-third of that recommended for the treatment of typhoid patients—namely, one dose of 33 c.cm. of serum, injected intramuscularly: three doses of 33 c.cm. are recommended for the treatment of adult cases of moderate severity; the dosage for children is correspondingly smaller.

The Serum used in the Outbreak

The anti-typhoid serum used by Fenton and Hay was derived from two different batches. The titres of the various antibodies present in the serum from the two batches are shown in Table I.

TABLE I

Anti-typhoid Serum	Titre of Antibodies Estimated by Agglutination		
	H	O	Vi
Batch No. 11 (issued March, 1936) ..	200,000	100,000	700
Batch No. 19 (issued September, 1937) ..	50,000	100,000	3,000

When the serum was used for the inoculation of the group of contacts the difference in the concentration of the antibodies in the two batches was unknown to Fenton and Hay. The two sera were therefore given in equal quantities—namely, 10 c.cm. to each adult and 5 c.cm. to each child under 14 years; the number of the batch from which the dose had been given was recorded in each instance. Two days after the administration of the anti-typhoid serum samples of blood were taken from nineteen persons out of a total of thirty-one contacts who had been inoculated. The No. 11 serum had been given to eight of these persons (three adults and five children), and the No. 19 serum to eleven persons (eight adults and three children). The antibody content of the blood serum from the nineteen contacts was estimated according to the same technique as that employed in the examination of the therapeutic horse serum, and the result is shown in the following table:

TABLE II

Anti-typhoid Serum Injected	Average Titre of Antibodies present in the Serum from 19 Contacts 48 Hours after the Administration of the Prophylactic Dose			Averages Calculated from
	H	O	Vi	
Batch No. 11	200	200	<5	8 observed titres 11 observed titres
Batch No. 19	50	200	<5	

When the figures shown in Table II are compared with the corresponding figures recorded in Table I it is seen that the H titres of the sera from the contacts were 1,000 times lower and the O titres 500 times lower than the titres of the two therapeutic sera that had been used for the injections. If account is taken of the fact that the titre of the natural H antibody in normal human serum is extremely low, whereas the O titres for the sensitive typhoid strain 0901 often reach a dilution of 1 in 50 or 1 in 100, it may be concluded that the H titres give the correct measure of the degree of dilution of the passively transferred antibodies. Judging from the dilution factor, one could not expect to demonstrate the Vi antibody in the serum from the inoculated persons even in a dilution of 1 in 5, which, according to my experience, is the limit of the natural Vi agglutinin in human serum. Actually only two out of the nineteen sera tested produced marked Vi agglutination in a dilution of 1 in 5. One of the two persons who gave a positive Vi reaction was re-examined twelve days after the administration of the prophylactic dose. The Vi reaction was then negative in the dilution 1 in 5, and the H and O titres had fallen to less than half the values that had been established two days after the inoculation.

Comments

It is not suggested that these observations indicate that the prophylactic doses administered by Fenton and Hay were too small. The results of experiments in mice show clearly that the potency of the Vi antibody in protective action is very striking when contrasted with the comparatively low titre of its *in vitro* action in agglutination tests. It is quite conceivable that adequate protection may be afforded when the circulating Vi antibody is not demonstrable by agglutination even in the undiluted serum. However, in the absence of adequate data relating to the results of the prophylactic use of the serum in man it would appear to be inadvisable to reduce unduly the amount of the specific antibodies that are injected.

The titre of the Vi antibody in the concentrated anti-typhoid serum as issued at the present time is 1 in 3,000. Until serum with a considerably higher content of this antibody can be prepared the following recommendation seems to be justified: for prophylactic use one intramuscular dose should be given, and this should lie between the limits of one-sixth and one-third of the full curative dose, which is 99 c.cm. for an adult and proportionately less for a child. When deciding on the dose to be administered account should be taken of the degree of risk and of the length of exposure to the infection.

The Association of Special Libraries and Information Bureaux (31, Museum Street, London, W.C.1) held a luncheon at the Café Royal on April 27 at which over eighty people were present. The president, Sir Harry Lindsay, Director of the Imperial Institute, spoke of the three stages of science: first scholasticism, dominated by the great scientists; then the period of the authoritative textbooks; now the era of the individual specialist. The results of modern scholarship were scattered in innumerable technical journals, and in order to keep abreast search must be made over a very wide field. The same was no less true of other spheres of knowledge. "ASLIB" was therefore formed to act as a guide to specialist sources of information. Sir Clement Hindley said that members of the Association were eager to facilitate the dissemination of knowledge, and Sir Ian MacAlister spoke of "ASLIB" as a valuable and essential part of the great movement to make the instruments of civilization work.

OUTBREAK OF SONNE DYSENTERY DUE TO CONSUMPTION OF MILK

BY

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The following account of an outbreak of Sonne dysentery due to milk may be of interest.

Course of Outbreak

On January 5, 1938, information was received in the Public Health Department, Bedford, to the effect that five persons employed in a neighbouring office, all of whom had drunk raw milk there on the morning of Tuesday, January 4, had been taken ill with diarrhoea and vomiting on the evening of the same day or early the following morning. Since all members of the office staff came from different homes, the milk drunk appeared to be the only food common to the individuals concerned. Moreover, all those who partook of the milk were affected, and none of the office staff who had not drunk it had had similar symptoms. The milk was delivered daily by a retailer who obtained all his supplies from a farm about seven miles away, the retailer's dairy being the only one in Bedford to receive this milk. It arrives in churns, and is distributed raw to the consumers, some in bottles and some "loose." The bottling is done by the retailer. No other persons but the retailer and his wife, who is employed mainly in the shop connected with the dairy, lived on the premises or worked in the business. The retailer was interviewed by a member of the sanitary staff on the morning of Wednesday, January 5, and stated that he had had no complaints from his customers of any illness caused by the milk. This statement seemed at first to throw some doubt upon milk as the source of the illness.

Samples were, however, obtained from milkings of the evening of January 5 and the morning of January 6 and sent to the County Medical Officer, Dr. C. G. Welch, in whose area the farm is situated, with a suggestion that a veterinary inspection of the cows might also be made. This veterinary inspection was undertaken, with negative results. At the same time a physical examination of samples showed that the milk was "clean." The County Medical Officer had meanwhile ascertained that another customer in the town had suffered from similar symptoms. On January 7 he obtained a sample of milk as delivered, and still sealed, at the house of this customer, and sent it to the Ministry of Health for examination.

On the same day, in a telephonic communication, Dr. Seymour of the Ministry of Health suggested that useful information might be obtained by house-to-house inquiries among the customers of the milkman. A list of these was accordingly secured. A preliminary inquiry in the evening of the same day showed that in two among the six houses then visited one or more members had suffered from similar symptoms. As in the original cases, the symptoms occurred on the evening of Tuesday, January 4, and the morning of Wednesday, January 5. In the original cases the milk supply had been stopped after the occurrence of symptoms, but in the households investigated no suspicion attached to milk, and members continued to drink it. It therefore appeared likely from this preliminary investigation that any infection of the milk had been limited to one day—namely, Tuesday, January 4. Though this presumption was subsequently found to be erroneous it was at the time decided, on the evidence available, not to take steps to stop the milk supply.