

OBSERVATIONS ON AN EPIDEMIC OF PARATYPHOID FEVER IN DUNDEE, 1941

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I. THE EPIDEMIC

Introduction

An epidemic of paratyphoid B fever occurred in Dundee during the period from 19 February to 19 October 1941. There were 373 notifications and 357 patients were admitted for investigation and treatment to King's Cross (Infectious Diseases) Hospital. Information was also received of the occurrence of eight cases in other areas, and there is evidence that they were infected in Dundee.

The undernoted figures give a general idea of the extent of the outbreak:

Total number of confirmed cases in Dundee	331
Incidence of paratyphoid fever per 100,000 population	203.1
Total number of deaths	5
Case mortality percentage	1.5

Routine enquiries by the Public Health Department discovered 55 of the 331 cases; all the fatal cases were in women, three in the age group 25-45 and two in persons aged 65 years and over.

Age and sex distribution of confirmed cases appear below:

Total cases	All ages		0-5		5-10		10-15	
	M.	F.	M.	F.	M.	F.	M.	F.
331	103	228	26	36	22	21	13	23
	15-25		25-45		45-65		65+	
	M.	F.	M.	F.	M.	F.	M.	F.
	19	57	15	62	6	24	2	5

The distribution of cases among families was as follows:

One confirmed case in each of	236 families
Two confirmed cases in each of	31 families
Three confirmed cases in each of	5 families
Four confirmed cases in each of	3 families
Six confirmed cases in	1 family
Total number of families	... 276

Previous incidence of enteric fevers in Dundee

Prior to the epidemic of 1941, the highest number of cases of enteric fever (all varieties) notified in any one year in Dundee since the beginning of the century was

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206 in 1904; there were 180 in 1903, 131 in 1915 and 103 in 1919.

At the end of 1940, five atypical cases of paratyphoid B fever were discovered in the children's ward of the Municipal General Hospital. Specimens from seventy close contacts were investigated and two of these were found to be positive. There was no further spread of infection, and no connexion has been established between this group of cases and the epidemic now to be described.

The epidemic of 1941

The first notification was received on 19 February 1941, and by 24 March, when information of fourteen cases had reached the Medical Officer of Health, five within the previous few days, it was thought that an outbreak of epidemic proportions might be brewing. Steps were immediately taken to give warning of this to local general medical practitioners, neighbouring medical officers of health and local medical officers of the armed forces, so that they might be on the look out for cases.

The same day (24 March), and on the following morning, the local press inserted notices at the request of the Medical Officer of Health to warn the public of the presence of paratyphoid fever in the city and to recommend that all milk should be boiled before use. Notices were issued for display in dairies, bakeries and food shops to impress upon all food handlers the need to avoid contamination of materials for human consumption.

Basic investigations

Every infected house was visited in a search for missed cases and to inspect the sanitary conditions. A comprehensive inquiry form was also completed in respect of every case, and each day the results were reviewed. At an early stage there was discovered a common milk supply to fully 80% of the confirmed cases, but inquiries covered the whole range of food supplies.

Supervision of contacts

The period of supervision of contacts was fixed as 28 days from last exposure to infection, and child contacts were excluded from school for that length of time. They were supervised twice weekly, and at least one specimen of faeces from each was submitted for bacteriological examination. Food handlers were suspended from duty until three successive negative stool and urine results were obtained at weekly intervals and their blood sera were twice tested. As a result fifty-five cases of paratyphoid infection were discovered and removed to hospital.

Hospital accommodation

It was possible throughout the epidemic to admit every case for which hospital treatment was requested. Upon discharge every patient or guardian of a juvenile person received a printed statement urging the observance of personal cleanliness.

No return case has come to notice.

Water supplies

Routine weekly bacteriological and monthly chemical analyses of the Corporation water supply continued to be satisfactory, and suspicion was not cast on water as the vehicle of infection.

Milk supplies

Of all fourteen cases confirmed by 24 March, eight were children under 16 years of age and all but one of the adults were women. The majority were milk consumers, and dairy A supplied 57% of the infected families. That firm deals with about 80% of Dundee's

been immunized with T.A.B.C. vaccine, the titres ranging from 1/25 to 1/100, and freedom of stools from pathogenic organisms cleared them of suspicion. They are omitted from the following table, which comprises thirteen cases in which an abnormal reaction in blood, faeces or urine was obtained at the first examination.

The results of subsequent examinations of specimens from these employees are shown in the following paragraphs:

No. 1. Both faeces and urine were positive for *Bact. paratyphosum* B on 3 May and the young woman was admitted to hospital, where she remained for 10 weeks.

No. 2. This worker was also removed to hospital. A specimen of faeces submitted on 5 May contained *Bact. paratyphosum* B, and although kept in hospital until 5 June there was at no time any clinical evidence of illness. She was probably a missed case, and it was not until 23 June that the carrier condition had cleared up. A brother (aged 4 years) was found to harbour *Bact. potsdam* in the faeces on 7 April, while on 8 May two

No.	Sex		Suspended	Occupation	Widal (<i>Bact. paratyphosum</i> B) H antigen	Faeces upon initial examination
	M.	F.				
1	.	+	22. iv. 41	Cake packer	+ 1/25	Negative
2	.	+	22. iv. 41	Cookie creamer	+ 1/100	<i>Bact. rubislaw</i>
3	.	+	22. iv. 41	Baker	+ 1/100	Negative
4	+	.	24. iv. 41	Baker (cream cakes)	Negative	<i>Bact. thomson</i>
5	.	+	24. iv. 41	Cake packer	Negative	<i>Bact. potsdam</i>
6	.	+	24. iv. 41	Cake packer	Negative	<i>Bact. potsdam</i>
7	+	.	25. iv. 41	Baker (cream cakes)	Negative	<i>Bact. aberdeen</i>
8	.	+	28. iv. 41	Cake packer	Negative	<i>Bact. potsdam</i>
9	.	+	0	Clerkess	+ 1/25	<i>Bact. potsdam</i>
10	.	+	0	Baker (bread)	+ 1/25	Negative
11	.	+	0	Cake packer	+ 1/25	Negative
12	.	+	3. v. 41	Cake packer	Negative	<i>Bact. potsdam</i>
13	.	+	0	Greaser	+ 1/25	Negative

milk and regular samples had produced, not infrequently, plate counts of three and four million viable bacteria per c.c. and the presence of *Bact. coli* in 1/100 c.c. Attempts to locate the origin of the epidemic in these premises were, however, unsuccessful, although milk from that source was a common factor latterly in as high a percentage of cases as 85.

Bakeries

By 18 April 1941 extensive inquiries had been made into fifty-one confirmed cases of paratyphoid fever and in thirty-six (70%) the regular family baker was bakery A. Cream cakes had been consumed by thirteen of the thirty-six patients. Although bakery A probably supplies more Dundee families with bread, cakes, etc., than does any other single bakery, the frequency with which its produce was a common factor to so many cases of paratyphoid fever could not be ignored. It was considered too that, if they were the vehicles of infection, the baked goods were probably being infected centrally at the time of preparation or despatch, and the investigation was therefore concentrated upon employees of the bakehouse.

Specimens of blood and faeces were obtained from 127 employees. Serum reactions were found to be positive in certain Civil Defence Volunteers who had recently

other brothers (aged 10 and 11 years) were admitted to hospital with faeces positive for *Bact. paratyphosum* B and suffering from symptoms of paratyphoid fever.

No. 7. Specimens of faeces examined on both 3 and 7 May contained *Bact. potsdam*. He remained clear of infection till 26 May, when he was released from supervision.

No. 9. *Bact. potsdam* was again cultured from the faeces yet she did not complain of illness at any material time. Her brother (aged 10 years) was admitted to hospital on 24 April suffering from paratyphoid fever, and examination of home contacts led to the discovery of *Bact. potsdam* in the faeces of two other children.

Nos. 4, 5, 6, 8 and 12. Renewed examinations of stool and urine failed to disclose pathogens.

Nos. 3, 10, 11 and 13. On retest, serological reactions remained either constant in titre or became weaker, while excreta were free from disease-producing organisms. Perhaps no. 3 was a missed case.

To sum up, two persons were found to be infected with *Bact. paratyphosum* B and a third may have been a missed case. Seven others harboured various *Salmonellas*, especially *Bact. potsdam*, the association of which with paratyphoid infection was noticed in the course of the epidemic.

During these investigations a case of paratyphoid

occurred in the homes of two employees, and a female clerk who had been off work since 16 April was found to be suffering (as well as her mother) from paratyphoid fever.

It was hoped that 2 weeks after suspension from work of these employees there would be a reduction in the incidence of paratyphoid infection in the city, although it was realized that fresh cases might crop up in the bakery. The dates of initial suspension ranged from 22 April to 3 May, and from the week ending 17 May there was a steady fall in the number of confirmed cases until 14 June. It was then decided to resubmit specimens for bacteriological examination from all the bakehouse workers with the possibility of discovering another source of infection. The following additional positive results were thereby obtained:

No.	Sex	Suspended	Occupation
14	+	16. vi. 41	Cake packer
15	+	23. vi. 41	Confectionery assistant

No. 14. At this time she left her employment to take up factory work in another part of the country, and no further information about her health has been received.

No. 15. On being questioned, this woman admitted that during the preceding 2 weeks she had felt unwell by reason of lassitude and weakness, so that the date of infection may have been about 26 May. Her duties appear to have been confined to the manufacture and packing of confectionery and did not include the handling of cakes. It is interesting to note that although faeces and urine were examined in hospital on five subsequent occasions *Bact. paratyphosum B* was not again demonstrable.

Two weeks after the suspension from duty of employee no. 15 there was a steady fall in the incidence of paratyphoid fever in Dundee, and the last case that came to notice sickened on 12 September.

Equally extensive tests were carried out during the early part of the epidemic among employees of other bakeries and food stores because of the occurrence of a case of paratyphoid fever either among them or in their homes. In this way, two cases were discovered in home contacts out of some 150 persons tested, and an apparently healthy worker was found to harbour *Bact. aertrycke*.

Artificial creams

Only artificial creams may now be used commercially by bakers, and inquiries revealed that a proprietary brand, called here cream I, was being used by three of the principal bakeries including bakery A. Cream confections traceable only to the latter were associated with cases of paratyphoid fever, a factor suggestive of contamination on the premises. However, bakery A also employed a cream mixture of their own, and as the two kinds were so often admixed it was never possible to be certain of the true origin of any chosen sample. *Bact. coli* was recovered from every one of ten specimens of cream taken from cakes at the bakery and from retail shops. Once *Bact. coli* was present in 1×10^{-12} c.c. together with *Bact. proteus*, and on another occasion *Bact. coli* in 1×10^{-7} c.c. in company with *Bact. aertrycke*.

By 8 July, cream I was temporarily withdrawn from the public market, and coincident with this, bakery A resolved to give up the use of synthetic creams altogether. It is worth noting that when cream I became available elsewhere in Dundee in August it was sterile.

Five other proprietary brands were much less heavily contaminated than cream I, two being completely free of bacterial life.

Chemical analysis of synthetic creams revealed considerable variation in their contents. Energy values ranged from 319 to 457 cal. per 100 g. and averaged 380 over six samples.

Paratyphoid carriers

The minimum criterion of freedom from infection before discharge from hospital was to secure at weekly

Widal (<i>Bact. paratyphosum B</i>)	Faeces	Urine
H antigen		
Not examined	<i>Bact. potsdam</i>	Negative
+ 1/800	<i>Bact. paratyphosum B</i>	Negative

intervals three consecutive negative stools and urines from convalescents. This was not always possible of achievement, and twelve women and one youth regarded as carriers were discharged without having satisfied that condition. By October 1941 eleven remained in the city and they were prescribed a course of soluble iodophthalein after Saphir & Howell (1940). Doses of 4 g. were given orally three times in 6 days and then once weekly for 4 weeks, but only eight persons could complete the treatment by reason of the intestinal upset that accompanied it. In any case the results were disappointing, everyone continuing to excrete *Bact. paratyphosum B* in the faeces.

Early in 1942 one woman recovered from the carrier state—probably a natural recovery. In March 1942 the other ten were given 38 g. of sulphaguanidine over a period of 7 days in accordance with the scheme employed by Anderson & Cruickshank (1941). Four showed marked improvement and are now considered to be free from infection. Of the other six, one died after an operation, another left this area, and there remain under observation three women and a young man. Their stools are consistently positive and the urines intermittently positive.

To date no information has been secured regarding the progress of the three carriers who left Dundee.

Other concurrent *Salmonella* infections

The first two Dundee cases of *Bact. potsdam* infection were encountered on 19 March, and in the following months a further fifty-one were discovered. Twenty-nine were found as a result of stool examinations from paratyphoid contacts. The illness resembled acute bacillary dysentery, but no one was seriously ill. Twice the organism appeared in the urine. On one occasion *Bact. potsdam* was found in the faeces of a child whose father, sister and brother were concurrently infected with *Bact. potsdam*, *Bact. aertrycke* and *Bact. paratyphosum B* respectively.

Subsequent to the recovery of *Bact. aertrycke* in artificial cream, eight cases of illness from that cause

occurred a few days later. One of the patients was also infected with *Bact. potsdam*.

The recovery of *Bact. rubislaw* from faeces was associated with little intestinal upset.

General comments

The usual preventive action in the way of isolation, disinfection, supervision of contacts, etc., was applied to each case. Precautionary measures of a general nature were taken by advising the public to boil milk and instructing food handlers to adopt a high standard of cleanliness.

The geographical distribution of the cases suggested that the vehicle of infection was an article in general use. Water was excluded. Age and sex distribution cast suspicion on milk, but it was excluded although samples from a milk dealer with extensive business showed that cleanliness was not one of its qualities. Of 331 cases of paratyphoid, 231 (68.3%) purchased goods regularly from bakery A, and 152 of them admitted recent consumption of cream confections. Circumstantial evidence therefore supports the view that the vehicle of infection was artificial cream. Confirmatory bacteriological proof was not obtained, but reports on samples submitted to the laboratory show that the cream was heavily contaminated with organisms of intestinal origin. On one occasion *Bact. aertrycke* was recovered from a sample, and just afterwards a crop of cases of *aertrycke* infection was discovered in the city.

Search for the source of infection led to the discovery of four excretors of *Bact. paratyphosum* B out of 127 employees of bakery A. Some 2 weeks after the first three were put off work the incidence of paratyphoid declined only to rise again. When the fourth person was dealt with in the same way some weeks later, the epidemic quickly came to an end. Carriers of other Salmonellas were revealed among the staff of bakery A coincident with groups of cases in the city infected with the same organisms. Thus the investigations disclosed faecal carriers of pathogens who worked among food-stuffs including synthetic cream, and who were in a position to contaminate these goods by direct contact. That they did so is probable in view of what has been stated.

We are tempted to think that the epidemic originated among workers at bakery A, and that they carelessly spread infection throughout the city by means of food-stuffs, particularly synthetic cream. On the other hand, epidemics of paratyphoid occurred in other parts of the country about the same time, and these were associated with synthetic cream, believed to be cream I. So suspect was that material that action by the Ministry of Health caused its temporary withdrawal from the market in July 1941. After its reappearance in Dundee, samples were regularly found to be sterile. Cleanliness of that order might well be obligatory on manufacturers and a nutritive standard determined whereby artificial cream might have a positive food value.

To safeguard the future so far as possible, carriers of paratyphoid organisms resulting from the epidemic are being constantly supervised. The importance of this is borne out by the length of time the carrier state may persist. Three women and a youth continued in this condition some 19 months after infection. Limited ex-

perience of sulphaguanidine offers some prospects of success in the treatment of these persons.

II. SUBCLINICAL INFECTIONS

Introduction

The outbreak of paratyphoid was so extensive that an opportunity was presented to investigate the problem of subclinical infections.

Obviously subclinical, and possibly transient, infections may play an important role in the epidemiology of the malady and a study of this was the main object of the work herein described.

In this connexion the views of Madsen (1937) concerning the mechanism of intestinal infections deserve special consideration. Madsen proved that infections in experimental animals with members of the colon-typhoid group may remain limited to the intestine, may penetrate the mucosa but be arrested by the lymph glands of the intestinal canal, and only when these lymph glands in turn fail as a barrier to further infection does blood generalization occur.

If the same occurs in man it would follow that in outbreaks of enteric fever there should be numerous cases of 'transient infection', i.e. cases in which the invading micro-organism fails to penetrate the intestinal mucosa, or is arrested at the lymph glands. These, while unimportant clinically, present a special problem when the victims handle food-stuffs. Owing to the large number of contacts and of employees of catering firms examined, indirect information on this was obtained.

Laboratory investigations

(a) *Blood culture.* A bile-salt broth was prepared for blood culture in cases of suspected enteric fever.

(b) *Diagnostic agglutination tests.* These were performed macroscopically, the patients' sera being tested in dilutions from 1/25 to 1/1600 against suspensions of flagellate and deflagellate typhoid and paratyphoid bacilli, and also against *Brucella abortus*. The tubes were incubated at 55° C. for 4 hr.

(c) *Examination of urine.* Urines were centrifugized and the centrifugate plated directly on brilliant green eosin (B.G.E.) agar.

(d) *Examination of faeces.* Faeces were collected in wide mouth bottles with screw caps and rubber liners, each containing 5 c.c. of Teague's fluid (1916) neutralized as advised by Sachs (1939): one part of glycerin with two parts of 0.9% sodium chloride buffered to pH 7.8 with 20% Na₂HPO₄.12H₂O.

Tetrathionate broth (Muller, 1923) was inoculated with the faecal suspension using an iron wire loop $\frac{1}{8}$ in. in diameter to seed 5 c.c. of the broth. This broth was incubated at 37° C. overnight, and then subcultured on B.G.E. agar plates. Where *Bact. paratyphosum* B, or other Salmonellas, was present, a pure growth of typical salmon pink colonies was obtained, inhibition of *Bact. coli* being usually complete.

Suspicious colonies were picked off for preliminary rapid 'slide agglutination' and subcultivation on ordinary nutrient agar, the growth obtained being used to inoculate fermentation tubes and to make suspensions for serological tests.

Occasionally the inhibition of *Bact. coli* was incomplete, and it was thought that this possibly depended upon the period of incubation of the tetrathionate broths prior to subculture.

Ten stools were therefore inoculated each into one bottle of tetrathionate broth and incubated at 37° C. for a period of 72 hr. in all. Subcultures from them were made on B.G.E. agar at 16, 24, 40, 48, 64 and 72 hr. intervals. The plates spread from the 16, 40 and 64 hr. broths were incubated at 37° C. for 24 hr., while the others were examined after 16 hr. incubation.

The results obtained indicate that although the period of incubation of the tetrathionate broth does in some cases influence the number of colonies of coliform bacilli obtained by plating on B.G.E. agar, the more important factor is the time allowed to elapse between plating and the examination of the plates, i.e. 16 hr. incubation is preferable to 24 hr. incubation.

Media

(i) *Brilliant green eosin (B.G.E.) agar—modified from Teague & Churman (1916)*. This is prepared by mixing 500 c.c. of melted non-nutrient agar and 400 c.c. of 'double-strength' serum peptic digest Lemco broth (Brodie, 1942), the reaction being adjusted to pH 7.6. Quantities of 74 c.c. are bottled in 100 c.c. 'medical flats' with screw caps, and these are sterilized in the steamer for 30 min. on each of three successive days or once in the autoclave.

To make plates a bottle of 74 c.c. is melted, cooled to 60° C. and the following sterile aqueous solutions added:

Lactose	20 %	5 c.c.
Saccharose	20 %	5 c.c.
Brilliant green	0.1 %	5 c.c.
Tetrabrom eosin	3 %	5 c.c.

Mix thoroughly and pour plates directly.

When B.G.E. agar was first adopted in this laboratory for the isolation of Salmonellas, it was noted that different batches of the medium varied in their power to restrain the growth of coliform bacilli. Experiments using stock cultures of *Bact. coli* and Salmonellas showed tetrabrom eosin to be superior to dinitrodibrom eosin. Different batches of tetrabrom eosin were then tested and a stock of the most satisfactory batch procured for future use, with surprisingly good results.

On B.G.E. agar *Bact. proteus* and *Bact. coli* give purplish colonies with opaque centres. Colonies of *Bact. paratyphosum* B and of Salmonellas are from 2 to 3 mm. in diameter, salmon pink in colour by reflected light and transparent by transmitted light. Colonies of *Bact. typhosum* are 1-1½ mm. in diameter, clear, pinkish but not salmon pink.

(ii) *Broth for tetrathionate enrichment—modified from Muller (1923)*. To make 1000 c.c., 400 c.c. double-strength serum peptic digest Lemco broth and 500 c.c. of water are mixed and the reaction adjusted to pH 7.6. Chalk (50 g.) is added and the mixture sterilized in the steamer for 30 min. on three successive days or once in

the autoclave. Batches of 250 c.c. are convenient for storage.

To each 250 c.c. of this, well shaken, is added 12.5 g. of sodium thiosulphate dissolved in 25 c.c. of water and sterilized by boiling. When cool, 5 c.c. of a solution of iodine made by dissolving 5 g. of iodine and 4 g. of potassium iodide in 20 c.c. of water is added, the whole well shaken and distributed in 5 c.c. lots in screw-capped bottles.

Clinical classification of paratyphoid infections

A total of 305 cases were hospitalized and the findings in these—both clinical and bacteriological—are discussed below.

Upon the basis of symptomatology a simple clinical classification, admittedly crude, of the hospitalized cases was used so that outstanding differences between groups of cases would be revealed and such differences correlated with laboratory findings. This rough clinical classification divided the cases into the following categories:

(a) *Typical cases*. In the outbreak studied the symptoms which predominated were headache, listlessness and an intense feeling of fatigue. Before a case was considered as 'typical' it exhibited in addition to general upset at least one of these three predominant symptoms.

The 'typical' cases could be subdivided into two sub-groups depending upon whether (1) 'rose spots' were present, or (2) 'rose spots' were absent.

(b) *Cases in which gastro-enteritis was the predominant feature*. In these the symptoms recalled bacillary food infection, the notable features being abdominal pain, sickness, vomiting and diarrhoea. Headache, listlessness and intense fatigue were absent.

(c) *Symptomless contacts*. The majority of contacts exhibited no symptoms nor did they complain of being ill and are, therefore, designated 'symptomless contacts'.

(d) *Symptomless non-contacts*. Apart from known contacts, two further cases were investigated of which neither showed symptoms nor even complained of malaise.

(e) *'Unclassified.'* Except for eight cases, the above classification allowed of the grouping of all 305 hospitalized cases (see Table 4).

Bacteriological findings

(a) *Blood culture results*. Of twenty-nine cases so examined twenty-one were positive for *Bact. paratyphosum* B and in the remaining eight the micro-organism was subsequently isolated from faeces or urine, or both.

All cases diagnosed by blood culture did *not*, contrary to expectation, show a marked febrile disturbance. In a few such cases we failed to demonstrate *Bact. paratyphosum* B in faeces and/or urine, and, when isolated from the excreta, the period of time over which the organism could be recovered was not in all cases prolonged. In fact, in one instance *Bact. paratyphosum* B was never revealed on subsequent examination of faeces and urine; although several specimens of each were investigated. In three further cases the organism was isolated once only; in two instances a single positive faecal culture was obtained, and in one case a single positive urine.

If, as Madsen suggests, the infection can be held up at

the intestinal lymph follicles and lymph glands, it would seem that it may also be held up by the reticulo-endothelial cells of the liver and spleen, even when blood generalization has occurred. In such cases excretion of the bacilli via the biliary system would not occur. The above cases suggest this possibility, but the number of instances is too small fully to substantiate the suggestion. The findings are nevertheless interesting.

(b) *Agglutination tests.* These fall into two categories namely: (i) those performed for diagnosis, and (ii) those performed prior to discharge from hospital.

Widal tests. A total of 196 diagnostic and 191 discharge Widal reactions were performed, the results being given in Table 1.

Scrutiny of the diagnostic Widal results revealed that in five cases, from whom at a later date *Bact. paratyphosum B* was recovered from faeces or urine or both, the patients' sera failed to agglutinate either suspension even in a dilution of 1/25, i.e. the reaction—in a practical sense—was negative: furthermore, in four of these cases the discharge Widal reactions were also negative. The significance of negative or feeble serological response is dealt with later.

Taken collectively, the results show that the flagellate is a much more delicate test than is the deflagellate.

Table 1. *Widal reactions*

	With flagellate suspension		With somatic suspension	
	No. either negative or positive to 1/50 only	No. positive 1/100 to 1/1600	No. either negative or positive to 1/50 only	No. positive 1/100 to 1/1600
Diagnostic	25	171	143	53
Discharge	34	157	157	34

(c) *Faecal and urinary cultures.* One weekly specimen each of faeces and of urine from all hospital cases was examined. Patients were not released from isolation until three consecutive weekly specimens of faeces and urine had given negative results.

Results of examination of contacts. The total number of contacts examined by faecal culture was 1213, of whom fifty-five were infected with *Bact. paratyphosum B*. Urines were examined only when contacts were employed by catering firms; all were free from infection.

Thus of 331 cases of infection with *Bact. paratyphosum B*, no less than fifty-five, i.e. 16.5%, were revealed only by examination of contacts, and in the majority of these clinical manifestations were either absent or so slight that a clinical diagnosis could not have been made. Table 2 gives the gross findings concerning faecal and urinary cultures from all 331 cases.

(d) *Other investigations.* (i) Two patients required operative treatment for cholelstitis. In both cases the organism was isolated from bile drained from the site of the operation, and the infection, therefore, had presumably been septicaemic.

(ii) It was noted that in female cases urinary cultures

were more often positive for *Bact. paratyphosum B* than in male patients.

Urines from females were not catheter specimens and so the possibility that the genitalia might infect the urine during micturition arose. To investigate this possibility catheter specimens of urine and vaginal swabs were collected in the following manner. The external genitalia were cleansed with 1 in 1000 biniodide of mercury solution. Thereafter, using a speculum, a swab of secretion was taken from high in the vagina, immediately followed by the collection of urine by sterile catheter. The swab was used to inoculate a bottle of tetrathionate broth and the urine was centrifugized and the deposit plated directly on to B.G.E. agar. The writers desire to thank Dr Jamieson, Senior Resident Medical Officer, King's Cross Hospital, for his cooperation in the seven cases so investigated.

In cases 1-5 urines and vaginal cultures were negative. In case 6, *Bact. paratyphosum B* was isolated from vaginal cultures on two occasions when both faecal and urinary cultures were negative. In case 7 both urine and vaginal swabs were simultaneously positive. Vaginal infection in case 8 was shown only by the chance receipt of a vaginal swab submitted for examination other than for *Bact. paratyphosum B*.

Table 2. *Gross findings*

	Faeces	Urine
Number examined	2235	2063
Number positive	959	309
Number of patients with one or more positive result	273	138
Number of cases which were negative after 1 month	218	85
Number of cases which were negative after 2 months	254	113

The results obtained from these investigations indicate that

(1) Some positive urinary cultures in females whose faecal cultures are positive are due to contamination of the genitalia.

(2) Only when catheter specimens are positive is the focus of infection certainly in the urinary tract.

(3) In females, infection of the vagina may occur, and the causal bacilli may be demonstrated therein even when negative findings only are obtained on examining faeces and urine.

(e) *Transient infection and minimal serological response.* Peroral infection in animals produces two types of infection:

(i) Septicaemic type where the lymphatic barrier is broken leading to generalization of the infection, usually followed by reinfection of gut via the biliary system.

(ii) Transient type where the infection is successfully held up at the lymph follicles and lymph glands of the gut. Where such foci are situated in the lymph follicles of the gut, the possibility of bacteria from these being responsible for at least occasional infective stools must be considered.

The epidemic of paratyphoid fever under discussion presented an opportunity of investigating such transient infections.

In order to obtain indirect information concerning the degree of invasion it was intended to perform discharge Widal reactions on all hospitalized cases, but circumstances prevented this being done. The purpose of performing discharge Widal reactions was to assess the degree of serological response, it being probable that septicaemia would produce a marked response while transient infection would lead to minimal reaction. The discharge Widal results were, therefore, provisionally considered as a possible index of the degree to which invasion had occurred.

yielded only minimal response prior to discharge from hospital. In sixteen of these thirty-four cases diagnostic Widals had been performed, but of the sixteen only four gave a result positive to a dilution of 1/50, leaving a total of thirty cases in which minimal serological response was recorded either with diagnostic or discharge Widals.

Each of these thirty was scrutinized both as to laboratory findings and as to clinical classification. The results are given in Table 3.

Laboratory proof of septicaemia in any of the thirty cases was lacking, but in one instance there was pre-

Table 3. Cases showing discharge Widal positive 1/50 or under, excluding those with diagnostic Widal positive in dilution over 1/50

Case no.	Sex	Diagnostic Widal reaction		Discharge Widal reaction		Positive blood culture	No. of positive faeces	No. of positive urines	Clinical classification
		Flag.	Deflag.	Flag.	Deflag.				
1	F.	.	.	—	—	.	—	3	'Typical' rose spots absent
2	F.	.	.	—	—	.	—	1	'Typical' rose spots absent
3	M.	.	.	—	—	.	2	—	'Typical' rose spots absent
4	F.	—	—	—	—	.	—	1	'Typical' rose spots absent
5	F.	—	—	—	—	.	1	1	'Typical' rose spots absent
6	F.	.	.	—	—	.	1	1	'Typical' rose spots absent
7	F.	—	—	—	—	.	1	2	Gastro-enteric
8	F.	—	—	—	—	.	4	1	Gastro-enteric
9	F.	—	—	—	—	.	2	—	Gastro-enteric
10	F.	.	.	—	—	.	4	4	Symptomless contact
11	M.	.	.	—	—	.	2	—	Symptomless contact
12	F.	.	.	—	—	.	2	1	Symptomless contact
13	F.	.	.	—	—	.	1	2	Symptomless contact
14	F.	1/25	—	—	—	.	—	—	'Typical' rose spots absent
15	F.	.	.	1/25	—	.	—	2	'Typical' rose spots absent
16	F.	.	.	1/25	—	.	3	2	**'Typical' rose spots absent
17	F.	.	.	1/25	—	.	2	1	Gastro-enteric
18	F.	.	.	1/25	—	.	2	—	Symptomless contact
19	F.	.	.	—	1/25	.	2	1	Symptomless contact
20	M.	1/25	—	.	.	.	2	—	Symptomless contact
21	M.	.	.	1/50	—	.	3	—	'Typical' rose spots absent
22	M.	.	.	1/50	—	.	6	—	'Typical' rose spots absent
23	M.	.	.	1/50	—	.	24	—	†Symptomless contact
24	M.	.	.	1/50	—	.	4	—	Symptomless contact
25	F.	1/25	—	1/50	—	.	3	3	'Typical' rose spots absent
26	F.	1/25	—	1/50	—	.	1	2	Symptomless non-contact
27	F.	1/25	—	1/50	1/25	.	1	—	Unclassified
28	F.	1/50	—	1/50	—	.	—	1	'Typical' rose spots absent
29	F.	1/50	—	1/50	—	.	—	—	'Typical' rose spots absent
30	M.	1/50	—	1/25	—	.	1	1	'Typical' rose spots present

* Revealed in course of investigation of contacts.

† One of the carriers resulting from the outbreak.

It must be realized, however, that penetration leading to generalized infection, need not always do so. Instances of poor agglutinin response in such cases have been encountered, e.g. a recent case at Exeter (1942) in which blood culture was positive (*Bact. typhosum*) but Widal reactions performed at later dates failed to reveal agglutinin response.

The upper limit of agglutinin response for possible transient infections was arbitrarily chosen as 1/50 dilution of patient's serum, and cases falling into this group are herein referred to as showing minimal serological response.

Reference to Table 1 shows that thirty-four cases

sumptive evidence of blood infection—the occurrence of rose spots. This case—no. 30—had a diagnostic Widal positive to 1/50 using a flagellate suspension and positive to 1/25 with the same suspension on discharge. The case was transient in that only one faecal and one urinary culture were positive for *Bact. paratyphosum* B notwithstanding the probability of its being septicaemic. This is the only male case of the group which yielded a positive urinary culture.

Considering Table 3, the following facts are noteworthy:

(a) The small number of positive faecal cultures except in case 23 which, although clinically a symptomless

contact, became one of the carriers resulting from the outbreak. Indeed, omitting case 23, the average number of positive faecal cultures is 1.6 in this group of cases.

(b) The small number of positive urinary cultures—an average of 1%.

(c) Five cases only out of the whole series gave four or more positive faecal cultures each, and one of these gave four positive urinary cultures. Of these five cases, three gave discharge Widal results positive to a dilution of 1/50 using the flagellate suspension, and it was in two of these that several positive faecal cultures were obtained—cases nos. 22 and 23.

Table 4 gives all the hospitalized cases grouped according to their clinical features and in each category the number of transient cases is especially noted.

This table reveals that when the cases were typical clinically, and also showed rose spots (a1) the percentage of transient infections was small, whereas in categories b, c, d and e these transient infections were more numerous.

It is worthy of note that the two cases in category d were both employees of bakery A.

Table 4. *Transient infections in each clinical group*

Clinical classification	Total		
	no.	No. transient	%
(a1) 'Typical' rose spots present	108	1	0.9
(a2) 'Typical' rose spots absent	128	14	10.9
(b) Gastro-enteric	23	4	(17.4)
(c) Symptomless contacts	36	8	(22.2)
(d) Symptomless non-contacts	2	2	(100)
(e) Unclassified	8	1	(12.5)

The concurrent potsdam epidemic

Of a total of fifty-three cases of infection due to *Bact. potsdam*, twenty-nine were revealed during the routine examination of faeces from paratyphoid contacts (Table 5).

Clinically the infection gave rise in most cases to enteritis but in some instances simulated mild enterica and even dysentery. On the whole, however, the patients suffered only slight inconvenience.

Table 5. *Infections due to Bact. potsdam*

Revealed in course of examination of paratyphoid contacts	29
Suspected as being paratyphoid cases	5
Suspected as being dysentery cases	3
Suspected as case of enteritis	1
Revealed in routine examination of personnel of catering establishments	7
Others, no information available	8
Total	53

Findings concerning the 'alpha-beta' variation of Bact. potsdam. According to Kauffmann (1939), *Bact. potsdam* in its alpha phase possesses flagellar antigens 'lv', in its beta phase 'en' and in the 'mixed' phase 'enlv'.

Bact. potsdam was encountered in a few instances as a deflagellate variant in the outbreak under discussion. When these strains had been induced, by laboratory means, to become flagellate their flagellar antigenic structure was investigated.

Of the fifty-three strains isolated, forty-five were in the alpha phase, eight in the mixed phase and none in the beta phase.

Cases of double infection with Bact. paratyphosum B and Bact. potsdam

Eleven such double infections were encountered, and in two patients (both females) *Bact. potsdam* was isolated from urinary cultures.

In case A, *Bact. potsdam* was isolated from the urine on the same date as *Bact. paratyphosum B* was isolated from the stool.

In case B, *Bact. potsdam* was isolated from three successive specimens of urine at weekly intervals, *Bact. potsdam* was never demonstrated in the faeces and on two occasions *Bact. paratyphosum B* was isolated from the accompanying specimens of stool.

The isolation of *Bact. potsdam* from urines of female patients suggests either foci of infection in the urinary tract, in which case the infection might have been septicaemic, or contamination of the specimen by the genitalia during micturition.

What is of special epidemiological importance is that these eleven cases of double infection strongly suggest a common vehicle of infection of both *Bact. paratyphosum B* and *Bact. potsdam*.

Salmonellas other than Bact. paratyphosum B and Bact. potsdam revealed in the study of contacts

These are tabulated (Table 6) according to the organism isolated and the date of its isolation.

As previously stated, *Bact. aertrycke* was isolated from a sample of synthetic cream. The cases of infection which came to light immediately after this finding are grouped together in the table.

The results given in Table 6 show that an appreciable number of Salmonella infections are at all times present in the community without clinical manifestations, and these constitute a potential reservoir for future outbreaks should such infected persons ever handle food-stuffs which are suitable pabula for the growth of the micro-organisms.

Examination of waters, foodstuffs, etc.

All samples of these were investigated as to the cleanliness and presence of intestinal pathogens, for the latter the method recommended by Szper (1935) being employed.

As the findings have already been discussed by Dr Davidson, only an interesting finding revealed during the examination of aerated waters is mentioned here.

It was found that when small inocula of actively growing cultures of recently isolated *Bact. paratyphosum B* were added to lemonade as sold, the organisms died out within 48 hr. The reaction of this aerated water was pH 3 and probably the acid was responsible for the lethal effect on the bacillus because, on neutralizing the material by the addition of sterile alkali, growth of *Bact. paratyphosum B* occurred at room temperature. The high acidity was not due to carbon dioxide but to organic acids used for flavouring, and it would seem that when these were neutralized their salts could be utilized by the bacillus.

Table 6. *Other Salmonellas*

Organism	Date of isolation	Remarks
<i>Bact. enteritidis</i> (Gaertner) var. Dublin	18. iv. 41	Contact. Sporadic case
Do.	18. iv. 41	Contact. Sporadic case
<i>Bact. aertrycke</i>	24. iv. 41	Employee of dairy A
Do.	29. v. 41	Sporadic case
Do.	16. viii. 41	Sporadic case
Do.	9. vi. 41	Isolated from synthetic cream distributed by bakery A
Do.	12. vi. 41	Case of 'food poisoning'
Do.	13. vi. 41	Do.
Do.	13. vi. 41	Contact. <i>Bact. potsdam</i> also found
Do.	13. vi. 41	Contact
Do.	13. vi. 41	Contact
Do.	17. vi. 41	Suspected paratyphoid case
Do.	18. vi. 41	Suspected paratyphoid case
Do.	21. vi. 41	Suspected paratyphoid case
<i>Bact. thomson</i>	21. iv. 41	<i>Bact. paratyphosum</i> B also found. Employee of bakery A
<i>Bact. aberdeen</i>	21. iv. 41	<i>Bact. potsdam</i> also found. Employee of bakery A
<i>Bact. rubislaw</i>	7. iv. 41	Contact. Sporadic case
Do.	24. iv. 41	<i>Bact. paratyphosum</i> B also found. Employee of bakery A
Do.	25. iv. 41	Convalescent paratyphoid fever case

Group of infections due to
Bact. aertrycke related to
above infected cream

APPENDIX

Disposal of 'faeces outfits'

To render autoclaving and washing of these a less obnoxious procedure, a mixture consisting of equal parts of a saturated solution of sodium carbonate (ordinary household washing soda was used) and hypochlorite solution was evolved. The solutions were kept in separate bottles and mixed in equal volumes in a smaller bottle fitted with a pourer from which about 5 c.c. was added to every faeces outfit before autoclaving, after which the specimens were easy to handle and devoid of odour.

The hypochlorite solution is prepared by dissolving 80 g. of sodium carbonate in 2200 c.c. of distilled water. This solution is used to rub up 40 g. of chloride of lime in a mortar, the suspension being transferred to a bottle and shaken occasionally during the next 20 min. After standing for 10 min. the supernatant fluid is decanted and filtered.

CONCLUSIONS

From the foregoing study of the epidemic of paratyphoid fever, the following conclusions can be drawn:

(1) The views of Madsen concerning infection with members of the colon-typhoid group of bacilli as revealed by animal experiment may equally apply to natural infection in the human, caused by *Bact. paratyphosum* B.

(2) Transient infections usually show minimal clinical manifestations, may never require medical

attention, or, when such aid is sought, remain undiagnosed.

(3) Transient infections constitute a grave danger and may lead to extensive outbreaks whose source may be difficult to trace. Such outbreaks are especially liable to occur when these transient cases handle foodstuffs which are suitable pabula for the growth of the organism.

(4) Septicaemia need not result in prolonged excretion of *Bact. paratyphosum* B via the biliary system.

(5) Routine examination of contacts of cases of paratyphoid fever is essential since many of the infections termed 'transient' can only be revealed in this way.

(6) The value of the Widal reaction as a diagnostic procedure is very strictly limited and it often fails to reveal precisely those cases which are of paramount importance in public health.

(7) The response of patients to the somatic antigens of *Bact. paratyphosum* B was, in this outbreak, poor.

(8) The demonstration of flagellar antibodies in patients' sera provided a more reliable means of diagnosis than did demonstration of somatic antibodies.

(9) An outbreak of infection due to *Bact. potsdam* coincided with that of paratyphoid fever. It was probably derived from the same source and propagated by the same vehicle.

(10) Synthetic cream substitutes are dangerous products unless handled carefully as instanced directly by the small outbreak of (*aertrycke*) bacillary food infection traced to that product. The large number of *Bact. coli* which are sustained by this material constitute indirect evidence corroborating this view.

(11) A variety of Salmonellas can be recovered from the faeces of apparently healthy people.

(12) In the investigation of faeces, the 'tetrathionate-brilliant green eosin agar' technique is eminently suitable especially in isolating *Bact. paratyphosum* B and other Salmonellas.

(13) Direct plating of urine on brilliant green eosin agar yields satisfactory results both for *Bact. paratyphosum* B and other Salmonellas.

(14) 'Slide agglutinations' using specific antisera prepared by absorption of heterologous antibodies allow of preliminary reports being issued, resulting in earlier isolation of cases.

We wish to thank Dr Burgess and Prof. Tulloch for their guidance and criticism and for consenting to the publication of the foregoing details; we would also record our indebtedness to their staffs and our colleagues for clinical, bacteriological and clerical help during the epidemic.

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(MS. received for publication 2. I. 43.—Ed.)