RELATIONSHIP OF PARATYPHOID FEVER TO FOOD POISONING OUTBREAKS

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OWING, in our opinion, to faulty classification and terminology of bacterial types, it is very common, especially on the Continent and, to a lesser extent, in U.S.A., to ascribe outbreaks of food poisoning to *B. paratyphosus* B, the common cause of paratyphoid fever. If such a conception is true, it is obvious that *B. paratyphosus* B can at one time cause paratyphoid fever, at another an outbreak of food poisoning. Further, one would expect in outbreaks of either condition that some cases would be of the one clinical type while others would exhibit the other. In particular in outbreaks of paratyphoid fever in which the vehicle of infection was some form of food, it is to be anticipated, on this view, that a considerable proportion of the cases would be of acute food poisoning type.

This conception is one with which we entirely disagree and we think that a comparison of the two conditions from a number of aspects will be valuable.

Symptomatology of paratyphoid fever.

The incubation period in food poisoning of the gastro-intestinal type is invariably short. When both living bacilli and toxins are ingested it is usually from 6 to 24 hours and very rarely more than 36 hours. In paratyphoid fever it is much longer. The information in recorded outbreaks is rarely definite, but 10–14 days are frequent periods, although it may be much shorter, such as 4–5 days or even less according to some writers.

As regards the symptoms of paratyphoid fever, while the usual form is an insidious onset with long continued fever of enteric type, the main interest from the present point of view is as to the extent to which outbreaks or individual cases occur in which the disease is of the acute food poisoning type with its classical and almost invariably present symptoms of acute abdominal pain, severe acute diarrhoea and extensive vomiting.

A study of the literature does show that in a small proportion of cases the onset is sudden, while also acute diarrhoea and vomiting may be met with. Detailed study of the individual cases shows however (when care is taken to exclude genuine food poisoning outbreaks) that it is with extreme rarity for all the symptoms of acute food poisoning to be present at the same time, and that when such a type of onset does occur the subsequent history is one of prolonged fever with the other enteric type of symptoms. This, for example, is brought out in the interesting discussion on paratyphoid fever at the Royal Society of Medicine (Medical Section) in 1915¹.

¹ *Proc. Roy. Soc. Med.* 1915, ix. Medical Section, p. 1.

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The elaborate study of paratyphoid fever by Rathery, Ambard, Vansteenberghe and Michel¹ of 1088 cases from 1914–1916, includes a bewildering variety of clinical types, but none of them resemble the food poisoning type.

A most valuable study is that of Torrens and Whittington². Their paper includes an analysis of the different symptoms as regards their frequency. Vomiting occurred in only 17, abdominal pain in 35, diarrhoea in 55 per cent. of their cases. They remark that vomiting in association with severe abdominal pain and severe diarrhoea, *i.e.* that type of paratyphoid fever which simulates food poisoning in its onset, occurred in only about 3 per cent. of their cases. These cases seemingly always pass on subsequently to the ordinary enteric type.

This clear distinction is confused by so many continental investigators by their failure to distinguish between true paratyphoid fever and acute gastro-enteritis due to food poisoning bacilli, owing to the prevailing continental plan of grouping the causal organisms as all *B. paratyphosus* B. Paratyphoid fever is taken as the disease caused by this organism, a terminology which includes several types which in this country are recognised as entirely distinct.

The paper of Stolkind³, the article by Kutscher⁴ and the monograph of Mallié⁵ may be cited as examples of this point of view.

Further light is thrown upon the subject by a study of the symptomatology in the light of the vehicle of infection. The view has been advanced that the clinical type is conditioned by the nature of the vehicle. It is a possible hypothesis that when the bacilli are introduced in small numbers, as is usually the case in outbreaks spread by direct case-to-case infection or by water, then an onset of insidious type is to be anticipated with slowly developing symptoms of enteric type, but that when the infection is massive, such as results when the vehicle is milk or some other form of contaminated food, the type of onset would be sudden and the grouping of symptoms identical with or in close approximation to those which occur in acute food poisoning. We have been at some pains to look up the facts in a number of genuine paratyphoid fever outbreaks in which the vehicle has been some type of food.

We have particulars of eight such recent outbreaks, two in U.S.A., five in England and one in Germany. All of these were definitely due to *B. paratyphosus* B. In an outbreak in Iowa⁶ in 1916 spread by milk and involving ten cases, all were of the paratyphoid fever type and there were no acute cases of food poisoning type.

In an outbreak in 1918 at a Public School Boarding House⁷ including

¹ *Les Fièvres paratyphoïdes B. à l'hôpital mixte de Zuydroote*, 1916. Published by F. Alcan. Paris.

² *Brit. Med. Journ.* 1915, ii, Nov. 13, p. 697.

³ *Proc. Roy. Soc. Med.* 1915, ix. Medical Section, p. 34.

⁴ *Handbuch der Pathogenen Microorganismen*. Kolle und Wassermann, 1907. *Ergänzungsband* II. 655. Article "Paratyphus."

⁵ *Les infections paratyphoïdes et Gaertneriennes*, 1923. Paris: A. Maloine et Fils.

⁶ *Journ. Infect. Dis.* 1916, xviii. 143.

⁷ *Local Government Board Report of Medical Depart. for 1918–19*. p. 172. Report by Dr Candler (and personal communication).

24 cases, the exact food implicated was not ascertained with certainty, but Candler, who investigated it with great care, was of opinion that the outbreak was spread by food. The first few cases were notified as "enteric" and all were of the typhoidal type and none resembled acute food poisoning.

In February to April, 1923, an outbreak of paratyphoid fever occurred in Sutton and Wallington¹. The vehicle of infection was confectionery (fancy cakes) probably infected by a human carrier, but the proof of this was incomplete. The symptoms varied in intensity from an intermittent pyrexia unaccompanied by any other manifestations of illness to a severe enteric infection indistinguishable clinically from true enteric fever. None of the cases were of the food poisoning type.

An outbreak of paratyphoid fever at Lowestoft in August, September and November, 1923, is of much interest. This was worked out with great care by Dr Stott (M.O.H.) and Dr Hutchinson, the bacteriological work being done partly by us and partly by Stott. In all there were 22 cases, two being secondary attacks. Inquiries showed that the probable source of infection, for at least some of the cases, was due to confectionery and the outbreak was evidently of food origin. The first two cases had eaten oysters the night before they were attacked but there is no evidence that these oysters were the vehicle of infection. *B. paratyphosus* B was isolated by us from both of these two persons and this organism was established as the cause in a number of the other cases.

Through the courtesy of Dr Stott we were able to examine the clinical records in these cases. In only two instances did the symptoms in any way resemble those met with in food poisoning outbreaks. These were the two women who were taken ill in the early hours of the morning after having had an oyster supper together the previous night. The onset was sudden with diarrhoea, vomiting and severe abdominal pain. The acute symptoms gradually subsided and the attacks passed on to the typical typhoid fever picture including prolonged temperature, rose spots and splenic enlargement. One of the two died from haemorrhage and perforation. This was the only fatal case in the outbreak. The other facts excluded any infectivity in the oysters and it is evident that the oysters merely precipitated an attack of acute gastro-enteritis in cases already infected, probably ten days earlier.

None of the other cases showed any resemblance to food poisoning. All were of the ordinary enteric type with long continued temperatures.

In one case the incubation period could be determined with precision and it was 14 or 15 days.

The precipitation of an acute attack after the oysters is of considerable interest. The oysters were eaten by dozens of people but only these two were attacked. Presumably they reacted pathologically as direct irritants upon an already damaged and infected gastro-intestinal tract and in turn this irritative action caused the attacks of paratyphoid fever to be very severe, for both suffered from severe haemorrhage and one died. Dr Stott (personal com-

¹ *Special Report to Ministry of Health.*

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munication) mentions two other cases of paratyphoid fever in 1924 with typical prolonged enteric type attacks, in one of which the onset was acute with severe abdominal pain and diarrhoea, both of whom had eaten shrimps (from the same source), in one case the night before the onset.

Another outbreak, described as an outbreak of paratyphoid fever, in Cascade, Montana, caused by head cheese¹ is of great interest, but there is not complete evidence that it was due to genuine *B. paratyphosus* B bacteriologically differentiated. The incubation period was 2 to 13 days with an average of 7 days. The onset was very sudden with practically no prodromal symptoms. It was manifested by severe headache, chills and chilliness, pains in the limbs and joints, backache, and, in a number of the more severe cases, stiffness of the neck associated with excruciating pain on moving the head was noticed. The temperature in practically all cases rose rapidly to 102° F., to 104° F. and in a few instances to 105° F. The temperature remained high with only slight morning remission for the first 10 days, when it fell by lysis, reaching normal about the 17th day of the disease. A noticeable feature was the absence of leucocytosis. There were 44 cases in all and 11 showed vomiting and 10 diarrhoea at onset. In 38 the onset was sudden, 19 had abdominal pain. Forty out of 44 showed rose spots and in general there seems no doubt the outbreak was paratyphoid fever. The "head cheese" was seemingly a form of brawn but its composition is not set out definitely.

In general the symptoms were of enteric type but with acute onset in many cases. While the prominent symptoms of food poisoning were present in a number of cases it does not appear that all of them were present in any or at least many cases. In all the earlier cases the onset is given as similar and consisting of sudden onset of headache, chills, pains in joints, etc. and the cases were described as simulating severe influenza. No question of diagnosis from acute gastro-enteritis seems to have arisen.

In an outbreak of 88 cases of paratyphoid fever in 1923 at Leamington, described by Goldie and Ward², 80 per cent. of the cases were associated with a particular confectioner and in some cases the only possible connection was in relation to cakes having been eaten from this shop. There was some, but incomplete, evidence of a carrier on the staff of this confectioner. The outbreak was definite paratyphoid fever with positive blood agglutination to this bacillus alone and there is strong presumptive evidence that it was spread by cakes, etc. from this shop. Clinically the cases were, with a very few exceptions, of an extremely mild type and free from complications. The rash was nearly always well marked and the cases were clinically paratyphoid and none were of the acute gastro-enteritis type.

An outbreak in October 1924 in Chorley³ involved 52 cases of paratyphoid

¹ *Public Health Reports*. New York, Vol. xxxvi. Sept. 1921, No. 35, p. 2095.

² *The Medical Officer*, Jan. 5, 1924, p. 5.

³ "Report on an outbreak of Paratyphoid Fever," by Dr W. V. Shaw, *Ministry of Health Report*, No. 30, 1925.

fever, two of which ended fatally, was spread by milk infected with *B. paratyphosus* B. None of the cases were of food poisoning type although a few showed a definite onset with some abdominal pain.

Amongst Continental outbreaks due to food it is easier to find records of more acute symptoms of gastro-enteritis but great care has to be taken to ascertain that they really refer to paratyphoid fever as most are examples of food poisoning with a different bacterial origin. One of the most interesting from this point of view is that described by Hamburger and Rosenthal¹. In this outbreak in Germany there were 65 cases and the vehicle was also a sweetmeat eaten on two separate occasions as cold rice pudding and as cream puff pastry. Both were prepared by the same baker who was shown to be a *B. paratyphosus* B carrier. The authors group their cases into three clinical groups, *i.e.* 41 showing the clinical picture of paratyphoid fever, 14 cases of acute gastro-enteritis and 10 cases which were very mild and were only definitely diagnosed by the bacteriological findings. A consideration of all the facts leaves no doubt that the outbreak was one of paratyphoid fever, so chief interest from the present point of view centres in the 14 cases of acute gastro-enteritis. Five of them are described as slight diarrhoea of no characteristic character and only identified bacteriologically. The other nine showed high fever with general toxic symptoms and continued intestinal catarrh which cleared up after a few days and was followed by constipation. These nine cases are not described in detail but there is no reference to vomiting or abdominal pain and they do not seem to be of acute food poisoning type.

These outbreaks definitely negative the hypothesis that the type of the disease is conditioned by the vehicle. They do, however, suggest that when the disease is conveyed by food massively infected with *B. paratyphosus* B some of the cases show a more sudden onset, and at times preliminary symptoms superficially resembling the acute food poisoning symptomatology which, nevertheless, almost invariably pass on to the long continued fever type characteristic of paratyphoid fever. This is what might be anticipated.

Is the ordinary type of food poisoning ever caused by B. paratyphosus B?

The term *B. paratyphosus* B is often used to include not only the Schotmüller type isolated from man but also *B. aertrycke*, *B. suipestifer*, etc. This is an unsatisfactory method of classification with nothing to recommend it. To use the same name as both a type and a group designation obviously must cause confusion and, indeed, is responsible for much of the present confusion in the literature.

We use the term *B. paratyphosus* B to refer to the perfectly well-defined type of the Salmonella group as met with in paratyphoid fever. All strains, *whatever their source*, which possess its cultural and serological properties, would be included as this organism.

¹ *Deutsches Arch. f. klin. Med.* 1918, cxxv. 415.

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An uncritical student of the subject would at once answer the question raised and state that this organism is a common cause and that there are very numerous outbreaks of food poisoning ascribed in the literature to *B. paratyphosus* B. We have obtained numerous strains from such sources and labelled *B. paratyphosus* B and in no single instance has such a strain been that organism when adequate serological tests have been applied. This matter is discussed at some length in a Report dealing with the serological types of the Salmonella group and their distribution, which is published elsewhere¹, and it is unnecessary to retrace the ground. We content ourselves here by stating that so far as we can ascertain there is no evidence that genuine *B. paratyphosus* B has ever caused an outbreak of food poisoning of the ordinary gastro-intestinal type. It causes paratyphoid fever and nothing else.

Paratyphoid fever is a definite disease caused by *B. paratyphosus* B, *B. paratyphosus* A and possibly by *B. paratyphosus* C. It is never caused by the Salmonella strains, such as *B. aertrycke* or *B. enteritidis*, which are responsible for the great majority of food poisoning outbreaks. Whether some of the other types, such as the Newport, Derby or Stanley strains, at present known only in association with animals or food poisoning outbreaks, can cause a continued fever of enteric type is one upon which we are not in a position to give a definite opinion, as our knowledge of the distribution and pathogenic properties of these types is most incomplete. We have had one outbreak of a disease of paratyphoid symptomatology from which we isolated an organism of "Reading" type, so it is unwise to be dogmatic. Most of our available evidence is against such an association. While this is common ground to many English bacteriologists, the converse that *B. paratyphosus* B never causes the ordinary outbreaks of acute food poisoning is not accepted generally, although we believe it to be equally true.

As we are unaware of any outbreaks of paratyphoid fever due to a Reading type organism, a short description of this outbreak will be of interest:

Bristol, January, 1923. A very interesting outbreak in regard to which the epidemiological details are unfortunately incomplete. A maid-servant in the household of a member of the Bristol University staff returned from a holiday in Liverpool and three or four days after her return suffered from headache and diarrhoea, but not at first sufficient to necessitate a stay in bed. She subsequently became much worse and remained in bed for three weeks with fever, diarrhoea and abdominal pain, but no vomiting. Her blood showed definite leucopenia with decrease in polynuclears. It agglutinated several strains of *B. paratyphosus* B, the titre increasing gradually up to 1/2000. It agglutinated similarly a Salmonella strain isolated from the faeces. Eight days after the re-entry of the maid into the house the master had an attack of acute diarrhoea. The following day her mistress had severe headache followed by three days' diarrhoea and some temperature. Positive agglutination reactions with *B. paratyphosus* B. were obtained and the same Salmonella strain was isolated. All three recovered. This strain, when serologically worked out, was found to be of the Reading type. No food could be implicated or definite source of infection traced, but during her holiday the maid had visited many families in a district where there were some cases of

¹ An investigation of the Salmonella group with Special Reference to Food-poisoning. *Med. Research Council, Report No. 91* (1925).

so-called "gastric flu." This is the only example in which definite paratyphoid fever has been caused by this type and the point is of great scientific interest.

Can these clinical differences be explained by differences in the pathological behaviour of the bacilli?

The commonest Salmonella group strain associated with food poisoning outbreaks is *B. aertrycke* (i.e. *B. aertrycke* (mutton)). This organism, in its cultural characters is practically identical with *B. paratyphosus* B and in the non-specific phase is so closely related to this serologically that absorption tests have to be employed to effect a discrimination. If our contention is true, we have the very interesting fact that two strains which are nearly identical exhibit a remarkably different functional activity in man and, as we shall show later, in the lower animals. It is important to consider critically whether there are any differences in their pathological behaviour which explain and elucidate these differences of action.

From our own studies we have been able to show very important differences some of which have been described by other workers, but others are new, so far as we are aware. In the paper already quoted we have set our results in some detail. It is only necessary here to give those of our conclusions which bear upon this aspect for the sake of completeness and to emphasise how they serve to explain the differences in the clinical type of disease caused by the two strains.

Tabular comparison of the two types.

Pathological action	<i>B. paratyphosus</i> B	<i>B. aertrycke</i>
A. <i>Living cultures:</i>		
1. Parenteral introduction into laboratory animals	A fatal septicaemia	A fatal septicaemia
2. Feeding of laboratory animals	No infection: bacilli rapidly die out	Varies with the animal and dose but in general causes a fatal septicaemia. Bacilli may survive in the intestinal canal for many weeks
3. Feeding of man	Paratyphoid fever. Invasion of blood and persistence of the bacilli	Acute food poisoning. Shorter persistence of bacilli. Successful tissue invasion rare
B. <i>Dead but not heated cultures:</i>		
1. Parenteral introduction into laboratory animals	Toxic symptoms or none. (?) No agglutinins	Toxic symptoms or none; + agglutinins
2. Feeding of laboratory animals	—	—
3. Feeding of man	No symptoms*	Not tested
C. <i>Boiled cultures:</i>		
1. Parenteral introduction into laboratory animals (mice used)	No effect usually, but can cause death insufficiently large doses	May exhibit diarrhoea and other symptoms and may die
2. Feeding of laboratory animals (rabbits, guinea pigs, kittens)	At most a transitory irritation	Marked gastro-intestinal irritation
3. Feeding of man	Headache but no gastro-intestinal symptoms*	Diarrhoea, vomiting and abdominal pain

* Direct personal experiment upon one of us.

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We suggest that the differences of toxigenic and infective properties shown by these two types are adequate to explain why they produce such different diseases in man. *B. paratyphosus* B is an organism which behaves like *B. typhosus* as regards its reaction to man and laboratory animals. Both are incapable of setting up disease in laboratory animals when introduced by the natural channel but both are "virulent" to laboratory animals in the sense that they can induce a fatal septicaemia when injected direct into the tissues. We have the striking and definite fact that *B. paratyphosus* B introduced in enormous numbers into the alimentary tract of these animals regularly dies out after a few days and shows no ability to penetrate the mucous membrane and gain access to the blood stream. In man the conditions are more favourable and they may persist after infection (probably reinforced from the gall bladder) for long periods. The comparative absence of a heat resistant (or heat produced) irritant substance in the bacilli explains the insidious onset and long incubation period in man. The bacilli have first to establish themselves in the small intestine. The absence of this irritant may favour this since otherwise the resultant diarrhoea may sweep them out. When the vehicle is food and large masses of bacilli are introduced at once, a few cases may have an acute onset, probably associated with the slight irritant action of the bacilli which we have been able to demonstrate in laboratory animals and to which man is no doubt more sensitive. This is a transient initial phenomenon and the cases pass on to the enteric type with foci in the lymphatic nodules of the small intestine and in some of the internal organs.

The closely allied *B. aertrycke* acts differently because of the presence of this toxic irritant heat resistant substance in the bacilli, the action of which dominates the clinical type produced in man. It causes the symptoms of acute gastro-enteritis which sweep out the bacilli, and which quickly pass off. General infection is rare and as we show elsewhere¹ this seems conditioned mainly either by excessive dose or more usually in relation to some specially favourable intestinal condition.

In man the toxic action of *B. aertrycke* is the predominant one, with *B. paratyphosus* B the invasive. In animals their behaviour is very different and in some respects opposite. The different reactions of animal hosts to these two types is of great interest and suggests many possibilities, some of which we hope to study.

This paper is in connection with extended studies upon food poisoning and allied problems which we have been conducting under the aegis of the Medical Research Council and with the co-operation of the Ministry of Health.

¹ "Food-Poisoning: a Study of 100 Recent Outbreaks," *Medical Research Council*, Report No. 22 (1925).