Five patients with cardiac failure showed no appreciable difference in theophylline plasma levels from asthmatics receiving the same compound.

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SALM. THOMPSON GASTRO-ENTERITIS REPORT OF TWO OUTBREAKS

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Since the end of the war *Salmonella thompson* has been one of the commoner causes of human salmonellosis in England and Wales (Wilson and Miles, 1955; Public Health Laboratory Service Reports, 1954, 1955), but until 1956 had been rarely encountered in Edinburgh. In the University Laboratory which serves the City of Edinburgh and much of the South-East of Scotland, *Salm. thompson* was not isolated from any cases in 1950-1-2, from only one in 1953, from another in 1954, and from two in 1955. In the summer of 1956, however, two apparently unrelated outbreaks of *Salm. thompson* infection came to our notice, and these seem to be of sufficient interest to be put on record.

First Outbreak

The first outbreak occurred in May, 1956, when *Salm. thompson* was isolated from faecal specimens in 10 cases of acute gastro-enteritis within a fortnight. The patients were all children (aged 10 months to 7 years); and, except for two brothers, were from different households widely distributed throughout the city. *Salm. thompson* was also isolated about this time from the faeces of three adults who frequently travelled into Edinburgh from surrounding districts; three more cases were admitted direct to the Edinburgh City Hospital for Infectious Diseases; another was found in a private nursing-home, and two more were found in the wards

of a general hospital. (One of these patients had undergone an operation for hernia two days before the onset of diarrhoea.) Food-poisoning was not notifiable in Edinburgh at this time, and other cases may have occurred which did not come to our notice.

The condition varied from comparatively mild diarrhoea and vomiting, which cleared clinically and bacteriologically in a few days, to a more severe type of illness which required hospital treatment (in one case for six weeks), and in two cases with *Salm. thompson* persisting in the faeces for four to eight weeks respectively.

Owing to the unexplosive character of the outbreak and the scattered distribution of the cases, there was inevitable delay in arriving at any facts to indicate a common source of infection, for often the housewife could not recall where or what foodstuffs she had bought at the relevant time. Suspicion, however, focused on a city bakery and restaurant. One patient had eaten "trifle" from this firm 24 hours before the onset of illness; two of the patients lunched daily in this restaurant; another had had tea and cream cakes there two days before symptoms appeared, and in six instances this firm supplied goods to the household. Therefore, some two weeks after the first case was diagnosed it was decided to visit this bakery.

It was found that a good standard of general cleanliness of premises and equipment was being maintained, and all meringues, cream cakes, sponges, and similar products were being made in a separate department. From our own previous observations of samples of imported whole egg and egg albumen, and from reports from other parts of the country (Newell *et al.*, 1955), imported egg was thought to be the most likely vehicle of the infection; but at this time the bakery in question was using home-produced, hen shell-eggs instead of imported liquid egg. Egg albumen, which was being used in large quantities mainly for meringues, was, however, an imported product. Two days before this inquiry Chinese albumen crystals had been in use for meringues, but this stock of albumen had been exhausted and frozen Argentine egg albumen brought into use.

The method of handling this was to defrost a 22-lb. (10-kg.) tin and to pour the contents into a "reservoir" container from which the albumen could be ladled. The favourite container used as a "reservoir" was a round three-gallon (13.6-litre) "synthetic cream" tin, which after removal of the cream was washed in warm water and then used for the egg. It was alleged that a different tin was obtained daily for this purpose or at least every second day. However, at the time of the inspection this seemed doubtful, as deposits of dried albumen were found encrusting both the inside and the outside of the rather dented tin.

Samples for bacteriological examination were taken from (1) stock tins of frozen Argentine egg albumen; (2) tins of synthetic cream; (3) the albumen encrusted on the sides of the "reservoir" tin; and (4) fluid albumen from the ladle. *Salm. thompson* was isolated both from the dried albumen on the sides and from the fluid albumen in the centre of the container, but was not isolated from the stock tins of albumen or synthetic cream.

Immediately after obtaining the samples the reservoir container and its contents were discarded, and the firm undertook to use for this purpose special containers constructed of stouter metal which could be more effectively cleansed with boiling water. Otherwise no change was made: the stocks from which the synthetic cream and egg albumen were drawn were still the same; the shell-eggs (manipulated in another part of the building) were obtained from the same source; and no change was made in personnel. Repeated samples of cream and albumen were examined during the next few days, always with negative results; and no further clinical cases came to our notice after the infected "reservoir" tin was put out of use. No cases of *Salm. thompson* infection did, in fact, come to our notice until some ten weeks later, when this organism was isolated in the second group of cases about to be described and the infection traced to an entirely different source.

Attempts were made to trace the batch of Chinese egg albumen used before the Argentine albumen. Unfortunately, owing to the sudden death of the head of the firm which had supplied it, no exact information was obtainable and none of their stock was left; but we found from information supplied by the bakery firm that the date on which this Chinese egg albumen had been put into use could be related to the incidence of the cases.

The precise source of the contamination of the albumen in the container must remain a matter for conjecture. After the inspection of the bakery the conditions were unchanged except for the use of a different "reservoir" for the albumen; but cases ceased. This would seem to rule out the Argentine albumen and the synthetic cream as the source of contamination, and also the shell-eggs, and the likelihood of contamination by a healthy carrier among the workers. It seems, therefore, that the Chinese albumen in use before the Argentine product must have been the real source of contamination; and that, owing to the continued use of the same "reservoir," the contamination continued. The danger to the consumer must have been at least lessened by the bactericidal effect of heating the meringue; and one must conclude that casual contamination of meringues and cakes after baking, by the hands of the workers or by contaminated implements, must have constituted the main danger to the consumers. The fact that in several instances the victims had eaten cream cakes and not meringues lends emphasis to this.

Second Outbreak

The second outbreak occurred two and a half months later. On August 16 a medical practitioner in an outlying district of Edinburgh notified the medical officer of health that his own 9-months-old child had acute salmonella infection and that his elder child was also ill with gastro-enteritis. He strongly suspected that the household milk supply, which came from a near-by farm and which was not heat-treated, was the vehicle of the infection. Within an hour of this notification another practitioner in the same district informed the medical officer of health that the byreman on the same farm had acute gastro-enteritis.

This farm supplied tuberculin-tested unpasteurized milk to households in the surrounding district. As a result of the notifications, the farm was immediately visited and information obtained about the byreman's illness and the health of the other farm workers. A veterinary inspection was also made and a sick cow found amongst the twenty-four dairy cows. This cow was removed from the herd, her milk was ordered to be destroyed, and arrangements were made for the milk of the herd to be pasteurized before distribution pending further investigations. The byreman's wife, whose work it was to wash the dairy utensils, was sent off duty. Faecal specimens were obtained for bacteriological examination from the farm workers and their relatives; also dung from the sick cow, a specimen of her milk taken with aseptic precautions, and the samples of the bulk milk before pasteurization. No pathogenic organisms were isolated from the bulk milk on this and numerous subsequent occasions, but *Salm. thompson* was isolated from the dung and milk of the sick cow, both on this occasion and from specimens taken on August 21. Five symptomless excretors of *Salm. thompson* were found among the farm workers and their relatives. These were the wife of the byreman, his 14-year-old daughter and 9-year-old grandson, the farm manager, and a worker employed mainly as a vanman. These were all suitably treated and excluded from the dairy until judged bacteriologically negative.

As well as the byreman, whose symptoms appeared on August 14, altogether five persons supplied with milk from this farm are known to have been acutely affected. The first became ill on August 10 and the last on August 17. Two were infants of less than a year, one was a 2-year-old child, and the others were adults. Clinically, all rapidly responded to treatment; but one man, a fishmonger who was eventually admitted to hospital, was found to be carrying the organism

eleven weeks after the onset of the illness. *Salm. thompson* was again isolated from the doctor's baby after seventeen weeks, when there was a recurrence of symptoms. Specimens of dung and milk from the infected cow were consistently negative by the end of August, but she was not returned to the dairy herd.

The sick cow had been in the herd for two years. She had produced a healthy calf at the beginning of August, but had developed "milk fever" (a calcium deficiency) on August 3. She responded to calcium injections, but remained listless and did not feed well, and when seen on August 17 seemed very ill. There were obvious signs of dehydration, the abdomen seemed tender, the dung was soft, dark, and foul-smelling. The udder was, however, normal and the milk free from clots. So far as could be ascertained, the byreman had been excluding this cow's milk from the milk for distribution, though a milking-machine unit had been used on her after the other cows had been milked; but after the byreman had fallen ill the sick cow's milk had actually been distributed with the rest on two occasions.

It seems, then, reasonable to conclude that this cow's infection was the cause of the human cases. These ceased to occur as soon as she was removed from the herd. Although her milk is thought to have been included in the milk for distribution on only two occasions since calving, there was sufficient opportunity for contamination of the whole supply from the milking-machine. The machine and other dairy utensils were sterilized after the morning milking; but, following the usual custom in dairy farms, the apparatus was merely rinsed after the afternoon milking. Thus bacterial contamination from the milk of the sick cow could readily be carried over to the milk for distribution at the subsequent milking. Although it is not known how long the byreman's wife had been a symptomless excretor of *Salm. thompson*, she too may have contaminated the dairy utensils and, in turn, the milk from the healthy cows.

The actual source of the cow's infection was not determined. The farm was within an urban area with a water-borne sewage system which made any human source of infection highly improbable. No faecal carrier of *Salm. thompson* was found among the other cattle on the farm and none of them was known to have been sick. Serological examination of the hens, which had no access to the byre but were housed in a building adjacent to it, proved negative. No other poultry were kept and the pig-sties were well removed from the byre. The cows grazed in a near-by field and drank from a stream below a housing estate, but no case of *Salm. thompson* infection was known in the district before this outbreak, although cases of *Salm. typhimurium* enteritis had occurred in Edinburgh during the summer.

Two theories might reasonably be advanced regarding the cause of the septicaemic infection in the cow. The first is that the cattle cake (a well-known brand of compound feeding-stuffs) was infected and this cow, unlike the others in the herd, was unable to combat the infection, or, secondly, that this animal was a carrier of *Salm. thompson* and the strain of calving activated the infection. An analogous human case of latent *Salm. typhimurium* infection which flared up into fatal septicaemia after childbirth is known (Riddell, 1954).

Discussion

Although enteritis due to *Salm. thompson* had been almost unknown in the Edinburgh district for years, and these two outbreaks occurred within four months, we have been unable to find any link between them. Numerically they were comparatively trivial—some nineteen cases in the first and six in the second. Probably the most important limiting factor was the low atmospheric temperatures in both May and August in 1956, which would not encourage rapid multiplication of bacteria even in such excellent media as cakes and milk. There were several other fortunate circumstances: the incriminated egg albumen was used mainly for meringues and therefore heated, and also the bakery was owned by a reputable firm who employed a good type of worker; and

in the milk-borne outbreak the ready co-operation of the general practitioners in notifying the cases made it possible to find and eliminate the source of infection with the minimum delay. Even so, it seems unnecessary to stress the personal annoyance and economic waste of an infection of this kind and its potential danger, especially to young children and to the old or debilitated; and, as apparently *Salm. thompson* readily leads to the convalescent carrier state, there is a real danger that this type of salmonella infection may become endemic if the sources of infection are not eliminated.

One such source is known to be frozen imported egg (Ministry of Health, 1956). In 1956 we ourselves examined 350 tins of this product and found that 5% were infected with salmonellae. Of this number, seven were found to contain *Salm. thompson*. Newell *et al.* (1955) found *Salm. thompson* in 20 out of 153 tins examined. It is true that, even although the constituents may have been contaminated, cakes which have been adequately heated are made safe for the consumer; but the presence of any contaminated commodity in a bakery must always constitute a risk too grave to be countenanced. The handling of infected material by workers who are largely ignorant of aseptic techniques must remain difficult to control; and sooner or later, through pressure of work or carelessness, regulations, however strict, will be disregarded. Contamination will then be conveyed from the raw ingredient to the finished article, and it only remains for conditions such as atmospheric temperature and humidity to combine to favour bacterial growth, and cakes and confections which are in effect lively cultures of pathogenic organisms will be distributed to the public.

The heat treatment of egg albumen crystals at present being carried out—that is, 127–130° F. (52.8–54.5° C.) for 10 days—seems to be satisfactory, but the evolution of an efficient pasteurizing process for whole-egg products, which at present presents great practical difficulties (Murdoch, 1956), seems really essential.

The main interest of the second outbreak is that the infection was milk-borne and due to a septicaemic type of *Salm. thompson* infection in a cow. *Salm. typhimurium* and *Salm. dublin* are the types of salmonella which most commonly infect cattle in this country (Taylor *et al.*, 1953). In adult cattle the acute infection usually takes the form of an enteritis with the likelihood of faecal contamination of the milk; but the disease may also become septicaemic, with actual excretion of the infecting organism in the milk. Thus two epidemics in Dundee in 1926 and 1927 were traced to cows with *Salm. dublin* septicaemia which were excreting the organism in the milk (Tulloch, 1939); and similarly, in an outbreak in County Durham involving 252 persons, *Salm. typhimurium* was isolated from the faeces and milk of a sick cow in a herd supplying tuberculin-tested milk (Norton and Armstrong, 1954); also Henderson *et al.* (1948) described an outbreak of milk-borne infection in Aberdeenshire traced to *Salm. dublin* enteritis in a bovine animal.

On the other hand, *Salm. thompson* infection of cattle is apparently rare. *Salm. dublin* was isolated from the faeces of 8.6% of 1,000 healthy cattle in Belfast, but *Salm. thompson* was isolated from only two animals (Murdoch and Gordon, 1953); and from England and Wales only two strains of *Salm. thompson* in 1955 and one to the middle of November, 1956, had come to the notice of the Veterinary Laboratory of the Ministry of Agriculture, Weybridge (personal communication). So far as we are aware, there is no record of any previous outbreak of milk-borne *Salm. thompson* infection, or of the generalized type of the disease in cattle.

The method of disposal of infected imported egg should be carefully considered. The finding of a bovine case of generalized infection, with resultant infection of a milk supply, presents, in our opinion, a warning against the possible disposal of rejected imported egg by its inclusion in the manufacture of animal feeding-stuffs.

Summary

Two outbreaks of *Salm. thompson* gastro-enteritis are described.

The infections are attributed to (1) Chinese egg albumen used in a bakery, and (2) a septicaemic type of disease in a cow producing infected milk.

Attention is drawn to this type of bovine disease as a source of milk-borne infection.

The importance of excluding bacteriologically contaminated commodities from bakeries is stressed.

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THE HOUSSAY SYNDROME

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Houssay and Biasotti (1930, 1931) and Houssay (1936) demonstrated that hypophysectomy relieved the diabetes mellitus of depancreatized animals. The Houssay animal exhibited diminished glycosuria, negligible ketosis, increased insulin sensitivity, survival for months without insulin treatment, widely fluctuant glycaemia, and a tendency to progressive undernutrition and to hypoglycaemic episodes. The clinical counterpart due to natural disease, conveniently termed the Houssay syndrome, is apparently rare. Indeed, Balfour and Sprague (1949) found no true example in the records of a 15-year period at the Mayo Clinic. Apart from the sporadic literature prior to Houssay's observations, 17 well-documented cases (listed in the discussion) have since been recorded.

The varied clinical patterns of hypopituitary coma (Sheehan, 1955) include three standard types—namely,