Use of sequential case-control studies to investigate a community salmonella outbreak in Wales

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Abstract

Study objective—To establish the source of a community outbreak of Salmonella typhimurium definitive type 124.

Design—Three districts in south east Wales.

Subjects—Cases of salmonella food poisoning and community controls.

Main results—An initial case-control study identified an association between illness and eating ham (odds ratio 4.50, 95% confidence intervals 1.10, 21.8) and also found a possible association between illness and food bought from delicatessen stores (odds ratio 5.03, 95% confidence intervals 1.01, 32.3). However, only after a second stage case-control study was a single common ham producer identified as the source (odds ratio 25.0, 95% confidence intervals 2.33, 1155).

Conclusion—Sequential case-control studies are an important and underused tool in the investigation of community outbreaks.

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Public health investigations of foodborne disease outbreaks are often unsuccessful: the vehicle of infection was traced in only 170 of 342 (50%) of salmonella outbreaks in the US between 1983–1987, and in only 124 of 272 (46%) salmonella outbreaks in England and Wales between 1992–93. Several aspects of foodborne disease outbreaks present difficulties in investigation. Firstly, cluster identification and outbreak recognition may be delayed because the pathogen is a common isolate. Secondly, the vehicle of infection may be a food commonly eaten by both cases and controls and the source not easily identified unless precise details (for example, brand, batch number, supplier) are elicited. Thirdly, cases may be geographically scattered hampering both early cluster identification and coordination of investigation and finally, delay in investigation may lead to recall bias and problems obtaining food for microbiological examination.

Case-control studies are particularly suited for investigating outbreaks and where they have been used routinely, success rates have been high. This is because they are efficient; they can be used where the population at risk cannot be clearly defined; they allow multiple aetiological hypotheses to be tested concurrently; and they permit interim data analysis.

Sometimes, however, sequential case-control studies may be necessary to clarify and refine the hypothesis. The case-control method allows case definitions to be refined to improve specificity, and hypotheses about risk factors to be formulated and tested in an adaptive and sequential process.

In 1992, a geographically scattered outbreak of Salmonella typhimurium definitive type (DT) 124 occurred in south east Wales. We highlight the value of a sequential case-control study method in tracking down the source to a single ham producer and bringing the investigation to a successful conclusion.

Methods

In mid June 1992, the Laboratory of Enteric Pathogens of the Public Health Laboratory Service reported a cluster of isolates of Salmonella typhimurium definitive type (DT) 124 identified through its total laboratory surveillance system. Eighteen reports were from laboratories in south east Wales, including 16 recorded during May, compared with only one other isolate from the remainder of the United Kingdom during the previous six months. S. typhimurium DT 124 is rare in the United Kingdom and only one outbreak has ever been reported, resulting from contaminated imported salami sticks.

All microbiology laboratories in Wales were alerted to the incident using the electronic network EPINET, and requested to report all suspected S. typhimurium isolates to the outbreak control team. Preliminary face to face interviews were conducted with 12 cases using a trawling questionnaire and information sought on date of onset of illness, foods eaten in the three days before illness, and general food preferences. Any history of recent foreign travel was also noted. Two sequential case-controls studies were subsequently performed—the first during the final week of June and the second during the initial fortnight of July.

The first case-control study was undertaken to test the hypothesis generated by the initial investigation that illness was associated with the consumption of ham from a local store. A case was defined as a person living in south east Wales with a faecal isolate of S. typhimurium DT 124 since 1 April 1992. Secondary cases (household contacts in whom the onset of illness was 24 hours after the onset of illness in the first household case) were excluded from the case-control study. For each case, two people registered with the same general practitioner were selected as controls from each
Outbreak investigation by sequential case-control studies

performance of the second stage can be extremely powerful.

Table 1 Case-control study 1. Association between illness and foods eaten by cases and controls in a salmonella outbreak in southeast Wales, 1992

<table>
<thead>
<tr>
<th>Food item</th>
<th>Case (n=20)</th>
<th>Control (n=34)</th>
<th>Odds ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home cooked chicken</td>
<td>11</td>
<td>9</td>
<td>0.67 (0.19, 2.40)</td>
<td>0.68</td>
</tr>
<tr>
<td>Any cold meat product</td>
<td>18</td>
<td>12</td>
<td>7.11 (1.30, 70.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Sliced ham</td>
<td>16</td>
<td>18</td>
<td>4.50 (1.10, 21.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Sliced turkey</td>
<td>4</td>
<td>16</td>
<td>1.81 (0.29, 11.1)</td>
<td>0.46*</td>
</tr>
<tr>
<td>Corned beef</td>
<td>2</td>
<td>18</td>
<td>0.26 (0.02, 1.46)</td>
<td>0.10*</td>
</tr>
<tr>
<td>Sliced chicken</td>
<td>3</td>
<td>17</td>
<td>1.28 (0.18, 8.55)</td>
<td>1.00</td>
</tr>
<tr>
<td>Salami</td>
<td>0</td>
<td>20</td>
<td>0.00 (0.00, 8.82)</td>
<td>0.52*</td>
</tr>
<tr>
<td>Any delicatessen</td>
<td>14</td>
<td>13</td>
<td>5.03 (1.01, 32.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Meat pie</td>
<td>2</td>
<td>18</td>
<td>0.23 (0.02, 1.30)</td>
<td>0.10*</td>
</tr>
<tr>
<td>Meat partie</td>
<td>2</td>
<td>18</td>
<td>0.36 (0.03, 2.15)</td>
<td>0.29*</td>
</tr>
<tr>
<td>Sausage roll</td>
<td>2</td>
<td>18</td>
<td>0.36 (0.03, 2.15)</td>
<td>0.29*</td>
</tr>
<tr>
<td>Eggs</td>
<td>9</td>
<td>11</td>
<td>0.25 (0.07, 0.96)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>8</td>
<td>12</td>
<td>1.60 (0.42, 5.90)</td>
<td>0.62</td>
</tr>
<tr>
<td>Ice cream</td>
<td>6</td>
<td>14</td>
<td>0.11 (0.03, 0.46)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Yoghurt</td>
<td>9</td>
<td>11</td>
<td>0.92 (0.26, 3.20)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Two tailed Fisher’s exact test.

Results

Preliminary interviews were completed for six men and six women aged from 14 months to 58 years, all of whom had become ill during May. Although cases were scattered throughout southeast Wales, there was some geographical clustering. None of the cases had recently been abroad. All 11 primary cases had eaten cold meats and 10 had eaten sliced, pre-cooked ham purchased from local retail stores.

STAGE 1 CASE-CONTROL STUDY

Twenty of 28 confirmed cases were interviewed. Three cases could not be contacted, one case had died, and the remaining four were secondary cases. Dates of onset of symptoms ranged from 3 to 24 May (fig 1). Thirteen cases were men and mean age was 31.9 years (range 1–77). The most common symptoms described by cases were diarrhoea (19 of 20 cases), abdominal pain (18 of 20 cases), and...
facer (14 of 20 cases). Other symptoms included nausea (10 of 20), vomiting (5 of 20), and drowsiness (3 of 20). Two cases required hospital admission, of whom one died (salmonella septicaemia and a cerebrovascular accident).

Thirty four controls were interviewed, the remainder could not be contacted despite several attempts. Because of the shortfall in matched pairs the matching was not preserved in the analysis and data handled as group matched rather than individually matched. Consumption of any cold sliced meat, cold sliced ham, and shopping at a delicatessen were all associated with increased risk of illness (table 1). Sixteen of 20 cases compared with 16 of 34 controls had eaten ham within three days of onset of illness (odds ratio (OR) = 4.50, 95% CI 1.10, 21.8).

### STAGE 2 CASE-CONTROL STUDY

Of the 16 cases and 16 controls who had eaten ham, 12 cases compared with four controls had bought the ham from a small, local store (rather than a large supermarket) (OR = 9.00, 95% CI 1.46, 60.6, p = 0.012). The 12 cases who had eaten ham bought from a local store identified 20 different stores from which ham had been purchased. However, 10 of 12 cases had bought ham from stores supplied by a common wholesaler—producer A. By contrast, only one of four controls had eaten ham from a local store supplied by this producer (table 2). The association between illness and the consumption of ham originating from producer A was highly significant (OR = 25.0, 95% CI 2.33, 1155, p = 0.002).

Producer A was a small combined distributor and retailer. The premises comprised a retail store at the front with a food preparation room behind. None of the staff involved in ham preparation had undertaken any food hygiene training. Raw pork joints, imported from Europe, were delivered to the premises three times a week. Joints were boned and mechanically injected with curing solution before being placed in tanks of brine for three days. Curing tanks were hosed down between use but seldom disinfected. Cured joints weighing around 7 kg were sealed in cooking bags using metal ties, steam cooked for eight hours at a temperature of 86°C, and cooled using cold water showers. Batches of around 70 ham joints were cooked at a time. After cooking, the ham was placed on a meat preparation table to remove the cooking bag, jelly, and fat. It was then vacuum packed and stored in a refrigerator room before distribution by refrigerated van. The ham had a shelf life of several weeks.

Repeated close questioning of producer A failed to identify any oven or refrigerator breakdown problems. However, after several visits by investigators, the producer admitted changing his usual ham cooking procedure as an economy measure after receiving a large bill for water supplies in April. Instead of cooling hams in the usual way, the joints had been removed from the oven while still hot and placed overnight in cold water in two tanks normally reserved for curing raw pork. This cooling method had been used on only one occasion as it was not deemed a success, as the ham took too long to cool. No residual ham from the implicated batch was available for microbiological analysis, but all ham samples obtained from retail stores and samples of recently cooked ham and drain swabs from producer A tested negative.

### Discussion

This outbreak investigation shows the value of a sequential case-control study method for establishing the source of a community salmonella outbreak caused by a common food item even when some time after the incident has elapsed. After confirming the initial hypothesis that sliced cooked ham was the vehicle of infection, the source was traced to a single distributor. Detailed environmental investigation then identified a breakdown in ham preparation procedures, which probably allowed cross contamination between raw pork and cooked ham and incubation of contaminated ham in a warm water bath overnight. The staged approach permitted gradual refining of the hypothesis and avoided the need for a cumbersome and inefficient investigation to obtain multiple details on all possible hypotheses at the outset.

Several forms of bias can affect the results of a case-control study of which the most pertinent in the context of outbreak investigation are selection bias (for example, non-participation bias), interviewer bias, and recall bias. Non-participation bias was limited in this study by making strenuous efforts to contact all cases and controls, although the participation rate for controls was less than that for cases. It is also important to minimise the influence of the interviewer on answers elicited from both cases and controls although it is seldom possible to use blind interviewers in field investigations. In this study, experienced interviewers used the same structured questionnaire for all subjects to ensure compatibility of information collected. Recall bias is a particular problem in outbreak investigation because considerable time may elapse between onset of

### Table 2  Case-control study 2. Association between illness and type of ham consumed by cases and controls in a salmonella outbreak in south east Wales, 1992

<table>
<thead>
<tr>
<th>Food item</th>
<th>Case (n=16)</th>
<th>Control (n=16)</th>
<th>Odds ratio (95% CI)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sliced ham from local store</td>
<td>12</td>
<td>4</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Sliced ham from store supplied by</td>
<td>10</td>
<td>6</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>producer A</td>
<td>6</td>
<td></td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9.00 (1.46, 60.6)</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25.00 (2.33, 1155)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*Two tailed Fisher’s exact test.
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The case-control design is the most efficient in circumstances where multiple hypotheses require evaluation as new hypotheses may be advanced during the course of the investigation and the study adapted as necessary. It is particularly appropriate in the absence of microbiological evidence of food contamination when a highly specific hypothesis is necessary to provide satisfactory, plausible, epidemiological evidence of causation. The precision of the second stage can be extremely powerful but depends on collecting data on the source of foods eaten by both cases and controls, a principle not always appreciated by the regulatory authorities who may be involved in the traceback process. The outbreak investigation we describe shows that even when primary microbiological methods cannot be used, the case-control method can still be successful. It is also an example of consequential epidemiology. By defining the most probable sequence of events leading to the outbreak, a
poor practice was identified at producer level that could be prevented in future.

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