Dose–response in an outbreak of non-bacterial food poisoning traced to a mixed seafood cocktail

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SUMMARY

An outbreak of non-bacterial food poisoning presumed due to small round, structured viruses (SRSV) occurred at a national conference.

A detailed postal survey of all conference attenders was carried out to ascertain the cause of the outbreak and 355 questionnaires were returned.

Univariate analysis showed that mussels in the seafood cocktail were the likely vehicle of infection. A dose–response relationship between the amount of seafood cocktail consumed and the risk of illness was demonstrated. Dose–response has not previously been documented in a food-borne outbreak due to small round structured virus.

Detailed quantitative food histories can be useful in eliciting dose-response relationships and may be crucial in establishing the vehicle of infection when investigating food poisoning following consumption of a set-menu meal. Their use should be considered in other outbreak situations.

INTRODUCTION

Reports that a number of people at a national conference of the Association of Continence Advisors had suffered from a gastro-intestinal illness reached Cardiff Environmental Services on 12 April 1991 just as delegates were dispersing home.

The conference, which had been held on 10–12 April 1991, was attended by 265 delegates from all over the UK plus a large number of exhibitors from 40 different companies. Delegates and exhibitors stayed at a number of different hotels in the city, but main meals were provided at the conference. In all, four meals prepared by two different caterers were served. Eight local guests were invited to the first evening meal on 10 April.

Initial investigation by means of a telephone survey of 118 conference attenders strongly implicated the evening meal consumed on 10 April, a set meal of five

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courses, as the cause of the outbreak. This association was subsequently investigated in more detail by a postal survey.

METHODS

A list of the names, addresses and telephone numbers of all delegates and exhibitors, and of the eight evening dinner guests, was obtained from the conference organizer. Details of meals served at the conference were obtained from the caterers.

A case was defined as a person attending the conference who reported that they had suffered from a gastro-intestinal illness (one or more symptoms of diarrhoea, nausea, vomiting or abdominal pain) with an onset date between 10 and 14 April 1991.

As many people as could be contacted by telephone on the 16 and 17 of April were interviewed by Environmental Health Officers and Public Health Physicians using a structured questionnaire. This included details of occupation, illness, food consumed at the conference, and accommodation.

A postal survey was conducted subsequently using a revised questionnaire which sought supplementary details including a quantitative food history for the suspect meal served on the evening of 10 April. Respondents were asked to indicate if they had consumed none, a mouthful, half, all or an extra portion of each of the food items available and allocated an estimated exposure score of 0, 0.25, 0.5, 1 or 2 accordingly. This questionnaire was sent to all registered delegates (including those previously contacted by telephone), and to the catering and waitressing staff who had prepared or served the suspect meal. No comprehensive list of exhibitors attending was available, so forms were sent to each company known to be represented, with a request that they be distributed to the people who had attended. No follow-up letter was sent.

Analysis of the data was done using Epi Info Version 5 [1]. The Mantel-Haenzel $\chi^2$ test and $\chi^2$ test for trend were applied where appropriate. Responses from conference attenders previously contacted in the telephone survey were included in the analysis of the postal questionnaire since this had elicited additional detail on food consumption histories.

Environmental investigations included interviews of the caterers and food suppliers, and inspection of the premises and facilities used for food preparation. Microbiological investigation was problematic by virtue of the wide geographic spread of delegates, but faecal specimens were sought from conference attenders who lived locally.

RESULTS

Telephone survey

One hundred and eighteen people attending the conference were contacted. It is estimated that attempts were made to telephone at least twice this number, so the response rate was approximately 50%. Contact was made with 99/265 (37.4%) registered delegates. 15 exhibitors and 4 of the 8 guests invited to the meal on 10 April. Forty-five (38.1%) people met the case definition. Of these,
Dose–response with food poisoning

Fig. 1. Non-bacterial food poisoning at a national conference of continence advisors.
Epidemic curve for 114 cases.

Table 1. Symptoms of illness. Postal survey (n = 355)

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. ill</td>
<td>114</td>
<td>—</td>
</tr>
<tr>
<td>Of those ill</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>33</td>
<td>(28.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>89</td>
<td>(78.1)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>90</td>
<td>(78.9)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>60</td>
<td>(52.6)</td>
</tr>
<tr>
<td>Fever</td>
<td>34</td>
<td>(29.8)</td>
</tr>
</tbody>
</table>

14/45 (97.8%) had eaten the evening meal on 10 April compared to 52/73 (71.2%) of those who were not ill (odds ratio 17.8, \( P < 0.001 \), Yates corrected). Two of the guests who had only attended the evening meal on 10 April reported illness. It was not possible to identify with certainty which food was the likely vehicle of infection.

Postal questionnaire

Replies were received from 234/265 (88.3%) of registered delegates, 105 exhibitors (total unknown), 11 waitressing and 5 catering staff. Three hundred and fifty-five questionnaires were returned in total. Two hundred and ninety-six people ate the evening meal on 10 April. There was no definitive list of people attending this meal, but as food had been prepared for exactly 400 people, it is estimated that over 70% of those attending were contacted.

One hundred and fourteen people (32.1%) reported that they had suffered a gastro-intestinal illness with a median onset of 34 h (range 4–80 h) after the meal. The epidemic curve is shown in Fig. 1. The mean age of the cases was 40 years and 85% were female. The predominant symptoms were nausea and abdominal pain (Table 1) and the median duration of illness was 36 h (range 1–96 h).

Of the 296 people attending the meal on 10 April, 112 (37.8%) were ill, compared to 2/59 (3.4%) of those not eating the meal (relative risk 11.2, 95% CI
Table 2. *Analysis of consumption of individual components of seafood cocktail*

<table>
<thead>
<tr>
<th>Food item</th>
<th>Number ill</th>
<th>Number eating</th>
<th>Attack rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seafood cocktail</td>
<td>112</td>
<td>262</td>
<td>42.4</td>
</tr>
<tr>
<td>Prawns</td>
<td>107</td>
<td>261</td>
<td>41.0</td>
</tr>
<tr>
<td>Mussels</td>
<td>92</td>
<td>196</td>
<td>40.9</td>
</tr>
<tr>
<td>Cockles</td>
<td>92</td>
<td>205</td>
<td>44.9</td>
</tr>
<tr>
<td>Prawns only</td>
<td>12</td>
<td>52</td>
<td>23.0</td>
</tr>
<tr>
<td>Mussels only</td>
<td>1</td>
<td>2</td>
<td>50.0</td>
</tr>
<tr>
<td>Cockles and mussels</td>
<td>4</td>
<td>15</td>
<td>26.7</td>
</tr>
<tr>
<td>Mussels and prawns</td>
<td>3</td>
<td>4</td>
<td>75.0</td>
</tr>
</tbody>
</table>

Mantel-Haenzel summary relative risk

- Mussels: 2.4 (95% CI 1.1-4.0), $\chi^2$ 5.43, $P = 0.002$
- Prawns: 1.7 (95% CI 0.7-4.1), $\chi^2$ 0.84, $P = 0.35$
- Cockles: 0.9 (95% CI 0.5-1.6), $\chi^2$ 0.01, $P = 0.9$

Table 3. *Consumption of seafood cocktail and risk of illness (n = 296)*

<table>
<thead>
<tr>
<th>Amount eaten</th>
<th>Exposure score</th>
<th>Ill Yes</th>
<th>Ill No</th>
<th>Attack rate (%)</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0.0</td>
<td>4</td>
<td>28</td>
<td>12.5</td>
<td>1.0</td>
</tr>
<tr>
<td>A mouthful</td>
<td>0.25</td>
<td>2</td>
<td>9</td>
<td>18.2</td>
<td>1.6</td>
</tr>
<tr>
<td>Half</td>
<td>0.5</td>
<td>20</td>
<td>31</td>
<td>39.2</td>
<td>3.1</td>
</tr>
<tr>
<td>All</td>
<td>1.0</td>
<td>76</td>
<td>102</td>
<td>42.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Extra portion</td>
<td>2.0</td>
<td>10</td>
<td>12</td>
<td>45.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Not recorded</td>
<td>0.0</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>184</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\chi^2$ test for linear trend 7.9, $P = 0.005$

2.8-43.9, $P \leq 0.0001$, Yates corrected). None of the catering or waitressing staff were ill. Detailed food histories indicated that 108/262 (41.2%) people who ate the seafood cocktail were ill compared with 4/32 (12.5%) of those who did not (relative risk 3.3, 95% CI 1.3-8.3, $P = 0.003$, Yates corrected). Two people could not recall if they had eaten seafood cocktail or not.

The seafood cocktail consisted of pre-cooked mussels, prawns and cockles, a commercially prepared sauce, a prawn garnish, lettuce and a slice of lemon. Every component of the seafood cocktail except lettuce and the lemon garnish was significantly associated with illness. The closest correlation was with mussels which were demonstrated by univariate analysis to be independently related to illness after allowance for prawns, cockles and both prawns and cockles (Table 2). Neither prawns nor cockles were independently associated with illness.

There was a dose–response relationship between the risk of illness and the amount of seafood cocktail eaten (Table 3). There was considerable individual variation in duration of illness, but median duration increased with quantity of seafood cocktail consumed – 23 h in those eating a mouthful, 27 h (half portion), 36 h (full portion) and 48 h (extra portion) – though this was not statistically significant. There was no clear relationship between the amount of seafood cocktail consumed and the incubation period or the severity of illness (as measured by number of symptoms).
Microbiological and environmental investigations

No organisms were isolated from three faecal samples known to have been submitted for microbiological testing, and no food was available for analysis. None of the faecal samples were examined by electron microscopy. The catering premises were satisfactory and food handling methods were not considered to have contributed to the outbreak. The source of each ingredient of the seafood cocktail was traced and the mussels found to have come from Eire. Details of the investigation were forwarded to the PHLS Communicable Disease Surveillance Centre.

DISCUSSION

This investigation of an outbreak of food poisoning illustrates how a detailed quantitative food history was used to convincingly demonstrate a dose–response relationship between the risk of illness and the vehicle of infection. The incubation period and short median duration of symptoms were consistent with an illness caused by small round, structured virus (SRSV), and the epidemiological investigation implicated mussels in the mixed seafood cocktail as the most likely vehicle of infection.

Shellfish, specifically bivalve molluscs such as oysters, cockles, mussels and clams, are well recognised as a cause of viral gastroenteritis [2–4]. These provide ideal conditions for primary contamination because they filter large quantities of water through their gills during feeding. Depuration and re-laying considerably reduce contamination from bacteria, but are much less effective in dealing with viral contamination [5], and several outbreaks of SRSV occurring after consumption of depurated raw oysters have been described [6, 7].

Adequate heat treatment is the only sure way to eliminate viruses [8, 9]. In the case of hepatitis A, studies on heat inactivation have shown that the internal temperature of shellfish meat must be raised to 85–90 °C and maintained for 1.5 min to ensure that virus is killed [10]. A standard heat treatment process for hepatitis A has consequently been recommended by the Ministry of Agriculture, Fisheries and Food and implemented within the UK shellfish industry since early 1988. Although it is not known whether this regimen is adequate for killing SRSV, there has been a subsequent reduction in reported outbreaks of viral gastroenteritis from treated bivalve molluscs, whilst shellfish that have not been heat treated continue to be associated with illness [11].

The mussels implicated in this outbreak were supplied pre-cooked. However, as heat processing is frequently done at the quayside or aboard ship, conditions may be less than optimal. Until effective heat treatment processes are assured, outbreaks are likely to continue to occur even from ostensibly heat-treated shellfish. The Report of the Committee on the Microbiological Safety of Food has recommended that all processors of bivalve molluscs should provide an effective heat process and avoid subsequent cross-contamination [12]. Accurate identification of the vehicle of infection and its source in shellfish-associated outbreaks are imperative if the effectiveness of changes in food processing techniques are to be monitored.

Dose–response has not to our knowledge been previously reported in an
outbreak of food poisoning presumed due to SRSV, though has been well-documented in bacterial food poisoning. A comprehensive review of the infective dose of salmonella from 11 food poisoning outbreaks indicated that illness could occur with very low ingested doses, and that higher doses resulted in higher attack rates and shorter incubation periods [13]. Similarly, in a large outbreak of staphylococcal food poisoning at a school in the USA, the attack rate was shown to increase with the number of cartons of contaminated chocolate milk consumed [14].

More recently, dose–response has been demonstrated in outbreaks of hepatitis A. A clear relationship was shown between frequency of raw shellfish consumption and risk of hepatitis A in a recurrent epidemic in northern Italy [15], whilst in one large outbreak of 290,000 cases in China, risk of illness was shown to increase with both the frequency and quantity of contaminated clam consumption [16]. A multi-state outbreak of hepatitis A associated with raw oysters reported from the USA has also shown risk of illness to be dose-dependent, but with no apparent relationship between dose and incubation period, duration or severity of illness [17].

Existing knowledge on the relationship between infecting dose of SRSVs and time of onset, severity and duration of illness derives from early volunteer studies on the Norwalk agent [18, 19]. These indicated an incubation period of 18–48 h which might be dose-dependent, and a duration of illness of 24–48 h. Experimental studies on other Norwalk-like viruses have demonstrated similar characteristics [20]. In one UK outbreak of SRSV related to eating raw oysters, no association between dose and incubation period was found, but the relationship between dose and risk of illness was not examined [6]. The clearest demonstration of dose–response in an outbreak of SRSV occurred during a large waterborne outbreak of Norwalk virus in Arizona, USA in which risk of illness increased significantly with the number of glasses of water consumed [21].

In this outbreak, both attack rate and duration of illness increased stepwise with increase in exposure dose, and the former was significantly associated. However, there was no apparent relationship with incubation period or severity of illness.

It can be difficult to investigate a food poisoning outbreak where there has been universal exposure to a suspected source [22], as in consumption of a set-menu meal. However, we have shown that if estimates of the quantity of food consumed are ascertained, a convincing dose–response relationship between consumption of suspect food and risk of illness can be demonstrated, allowing identification of the vehicle of transmission. The questions used to obtain a detailed quantitative food history appeared to be acceptable and achieved a good response rate. We have also shown that provided sufficient detail is collected, univariate analysis can be used to identify the individual component of a mixed dish as the vehicle of infection.

Outbreaks of food poisoning are common and rapid epidemiological investigation is needed to determine their extent and cause. Accurate identification of the vehicle of transmission is important if surveillance of foodborne infections is to be effective. An association between illness and consumption of a particular foodstuff is frequently found, but demonstration of dose–response can provide powerful additional evidence to support the existence of a cause and effect relationship.
between the two. This may be particularly valuable in the investigation of outbreaks where there is a dearth of microbiological or other evidence as occurs commonly with SRSV due to inherent difficulties in the detection methods used at present. We therefore recommend that the use of self-reported quantitative food histories should be considered in every outbreak investigation.

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REFERENCES