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Nosocomial transmission of measles among healthcare workers, Bulgaria, 2010

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This report describes 326 cases of nosocomial transmission of measles with 286 cases among non-healthcare workers who acquired the disease in a hospital setting. Between October 2009 and April 2010, 40 healthcare workers from seven different regions in Bulgaria have contracted the disease.

Measles is a potentially severe highly contagious disease. However, at least 98% of those receiving two doses of measles-mumps-rubella vaccine (MMR) are protected against the disease. Preliminary reports for 2010 show that there were more than 30,000 measles cases in the Member States of the European Union (EU) / European Economic Area (EEA) – the highest number of measles reported in Europe in more than 10 years [1]. The highest number of cases was reported in Bulgaria, followed by France, Italy and Germany [1]. Measles continues to spread in 2011 with more than 4,000 cases reported in the EU/EEA in January and February [1].

Outbreak overview

The current outbreak in Bulgaria started in March 2009 following an imported case of measles from Germany [2]. It has been the largest outbreak ever reported in Bulgaria since the large outbreak which occurred in 1976, only a few years after the immunisation schedule with one dose of monovalent measles-containing vaccine starting with the age of 10 months had been implemented in the country. The second dose was introduced at four years of age in 1982. In 1993 the first dose of monovalent measles-containing vaccine was replaced by the MMR vaccine. Since 2001 the two-dose measles immunisation with MMR vaccine has been introduced with the first dose at 13 months and the second at 12 years of age [3].

In this outbreak, the total number of cases reached 24,253 during the two-year period, reached its peak in March 2010 and started gradually to subside in late summer [unpublished data]. Only a few cases were reported every week in September and October 2010 [3]. However, according to preliminary results, about 130 cases were notified in the first three months of 2011, some of them diagnosed in late December 2010 but notified in January 2011. This calls into question whether it is at all possible to control such a contagious disease in a short time and in the presence of many pockets of susceptible individuals.

Of the 24,137 cases with full epidemiological and clinical data available, 3,917 (16.2%) were laboratory-confirmed (measles IgM), 7,944 (32.9%) were epidemiologically linked and the remaining 12,276 (50.9%) were probable cases. The highest incidence rate was observed in children under one year of age (n=4,717; 6/100,000 population) who were not eligible for MMR vaccination. Despite the ongoing outbreak, the Bulgarian health authority did not change the recommendation regarding MMR vaccination, i.e. did not recommend the first dose to be given earlier, at the age of nine months. Of the 24,047 cases investigated, 89.3% belonged to the Roma ethnic community. The majority (86.8%) were hospitalised, mainly due to epidemiological considerations – patients from overcrowded households with poor living conditions and inadequate access to medical care. Twenty-four deaths were reported but no information on complications is available at the moment [4].

Transmission in medical settings

Transmission in medical settings was reported for 326 cases and the hospital was the most frequently reported setting. Of these 326 cases, 286 were not healthcare workers and acquired measles in hospital or primary care.

By April 2010, 40 healthcare workers (HCWs) (0.16% of all measles cases) in seven different regions in Bulgaria have contracted the disease. Most of them occurred during the peak of the outbreak, in March 2010. The measles case definition in Bulgaria is based on the EU case definition [5]. Twenty-three cases were classified as confirmed (presence of measles-specific IgM antibodies) and 17 as probable (not tested). Laboratory tests of all but two were performed at the National Reference laboratory of measles, mumps and rubella in Sofia. Thirty-four cases occurred in hospitals and six in primary care.

The mean age of the cases among HCWs was 38 years (range 24–48 years) and 28 of them were women. The largest group of measles cases among HCWs were physicians (n=19), followed by laboratory technicians (n=8), nurses (n=7), cleaning staff (n=4) and pharmacists (n=2). All but one are likely to have acquired the infection from patients and one physician from a colleague. Ten HCWs developed radiologically proven pneumonia and all recovered. Fifteen HCWs were hospitalised due to dehydration or pneumonia.

According to their age, the majority of cases should have been vaccinated with at least one dose of measles-containing vaccine, as one dose measles immunisation was introduced in Bulgaria in 1969 and in 1972 it became part of the immunisation schedule in the whole country. Nevertheless, only one case had a vaccination record of two doses of measles-containing vaccine; the rest did not know their vaccination status.

No secondary cases among other contact patients and family members were reported. Information about susceptibility status or post-exposure prophylaxis of the HCWs' contacts was not available.

Control measures

Two supplementary MMR vaccination campaigns were implemented. The first one started on 27 April 2009 and targeted all individuals aged between 13 months and 30 years in the affected regions (Razgrad, Shumen, Silistra and Dobrich), who had not undergone the full vaccination with two doses. Later, in order to increase the vaccine coverage, a second campaign was directed towards those older than 30 years without documented measles vaccination [4]. These measures were not very effective maybe because they were not implemented simultaneously for all 28 regions in Bulgaria. On the other hand, a large number of cases might have received a supplementary vaccine dose when already infected with measles virus. Post-exposure immunoglobulin for people at risk for a severe form of the disease was not routinely given. The full analysis of the outbreak is still in progress.

Discussion

Measles among HCWs accounts for a relatively small proportion of the reported cases but is important because of the potential for transmission of the disease to susceptible colleagues (thereby disrupting healthcare service), high-risk patients such as pregnant women, immunocompromised individuals, and family members. They have a nearly 19-fold higher risk of acquiring measles than the general population [6]. Transmission among HCWs was also reported in France in 2010 [7,8]. The Advisory Committee on Immunization Practice in the United States of America recommends all healthcare personnel to have presumptive evidence of immunity (positive serological test results or written evidence of appropriate (two doses) immunisation to mumps, measles and rubella or being born before 1957). For unvaccinated persons born after 1957 who lack evidence of mumps, measles and/or rubella immunity or laboratory confirmation of the disease, healthcare facilities should recommend two doses of MMR vaccine during an outbreak of mumps or measles and one dose during an outbreak of rubella [9]. European countries in general should recommend measles vaccine for HCWs who do not have documented vaccination record or history of the disease. This outbreak highlights the need for further activities with respect to vaccinating non-immune HCWs. Moreover, it illustrates that a high rate of hospitalisation for measles poses a risk for nosocomial infections that may have a detrimental effect on certain immunocompromised or non-immune patients and HCWs. Therefore, strict hygiene measures are important to prevent the spread in hospital settings.

The 40 cases of measles identified in HCWs in the course of this outbreak further highlights the need for such recommendations. Increased vaccine uptake among HCWs of other contagious diseases like varicella and influenza also needs to be considered in medical settings. Maintaining a high immunisation coverage and strengthening surveillance are essential if Europe is to meet the new elimination target of 2015.

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National outbreak of *Salmonella* Enteritidis phage type 14b in England, September to December 2009: case–control study

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We conducted an unmatched retrospective case–control study to investigate an upsurge of non-travel-related sporadic cases of infection with *Salmonella enterica* subsp. *enterica* serotype Enteritidis phage type 14b with antimicrobial resistance to nalidixic acid and partial resistance to ciprofloxacin (*S.* Enteritidis PT 14b $NxCp_L$) that was reported in England from 1 September to 31 December 2009. We analysed data from 63 cases and 108 controls to determine whether cases had the same sources of infection as those found through investigation of 16 concurrent local food-borne outbreaks in England and Wales. Multivariable logistic regression analysis adjusting for age and sex identified food consumption at restaurants serving Chinese or Thai cuisine (odds ratio (OR): 4.4; 95% CI: 1.3–14.8; p=0.02), egg consumed away from home (OR: 5.1; 95% CI: 1.3–21.2; p=0.02) and eating vegetarian foods away from home (OR: 14.6; 95% CI: 2.1–99; p=0.006) as significant risk factors for infection with *S.* Enteritidis PT 14b $NxCp_L$. These findings concurred with those from the investigation of the16 outbreaks, which identified the same *Salmonella* strain in eggs from a specified source outside the United Kingdom. The findings led to a prohibition of imports from this source, in order to control the outbreak.

Introduction

Infection with *Salmonella enterica* subsp. *enterica* serotype Enteritidis (*S.* Enteritidis) remains an important public health problem in Europe and other parts of the world [1-4]. Outbreaks caused by *Salmonella* infection have been associated with a variety of foods; however, outbreaks caused by *Salmonella* Enteritidis infection are closely associated with eggs and egg products [2,5,6]. In September 2009, the Department of Gastrointestinal, Emerging and Zoonotic Infections at the Health Protection Agency (HPA) reported a marked upsurge in the number of non-travel-related human cases of infection with *S.* Enteritidis phage type (PT) 14b with resistance to nalidixic acid and partial resistance to ciprofloxacin (*S.* Enteritidis PT 14b $NxCp_L$). Infectious diseases resulting from food poisoning are statutorily notifiable in England and Wales: cases are notified by registered medical practitioners and diagnostic laboratories to the HPA. In total, 572 cases of *S.* Enteritidis PT 14b $NxCp_L$ infection were reported between January and December 2009, compared with 141 in 2008. Between 1 September and 31 December 2009, there were 489 cases.

There were 14 recognised, discrete local outbreaks of *S.* Enteritidis PT 14b $NxCp_L$ infection in England and two in Wales between August and December 2009 (HPA unpublished data). All but one of these outbreaks were linked to food-service premises; the remaining outbreak was linked to a residential care home for the elderly. The total number of reported cases associated with these outbreaks was 152: six were hospitalised and two deaths were reported.

Preliminary investigations of these 16 outbreaks suggested putative links to infected eggs, with evidence of cross-contamination of *S.* Enteritidis PT 14b $NxCp_L$ to other foods, particularly ready-to-eat vegetarian foods. The outbreak strain was isolated from samples of eggs, egg mayonnaise, egg-fried rice, pooled liquid egg mix and work surfaces in the food-service premises investigated as part of the outbreak investigations. Eggs collected from these premises (five restaurants serving Chinese or Thai cuisine and two cafes) in seven of the outbreaks were from the same production establishment in Spain, as indicated by the stamp on the egg shells. We therefore conducted a case–control analysis to determine whether the likely source of infection in the apparently sporadic cases was the same as that for cases in the outbreaks.

Before the upsurge in *S.* Enteritidis PT 14b $NxCp_L$ infections in September 2009, there had been other sustained increases in the incidence of *S.* Enteritidis non-PT4 infections in England and Wales between 2000 and 2004 [7,8]. Epidemiological and microbiological investigations and a case–control study of primary sporadic indigenous cases found that consumption of eggs from food prepared outside the home was associated with being a case. The investigations identified eggs sourced from Spain used in the food-service sector as the main cause of the increase [1,2,7,8]. In the United Kingdom (UK), the predominant PT responsible for egg-borne *S.* Enteritidis infection had been PT 4 between 1992 and 2002 [5]. Following large epidemics of *S.* Enteritidis infection in the UK in the late 1980s, mainly due to PT 4, a decline in human S .Enteritidis PT 4 infection in England and Wales occurred from 1997, largely because of industry control programmes in the poultry sector, including vaccination of layer flocks [9]. Since 2000, egg-associated *S.* Enteritidis PTs other than PT 4 causing human infection have emerged, with the greatest increases occurring in *S.* Enteritidis PT 1- and PT 14b-related infections [7].

Surveillance of salmonellosis from 1998 to 2003 also showed upsurges in *S.* Enteritidis non-PT4 infections in other European countries [1]. Between 1998 and 2003, the proportion of PT4 infections fell from 61.8% in 1998 to 32.1% in 2003, with a concomitant increase in *S.* Enteritidis non-PT4 infections (including PT1, 8, 14b and 21) in Austria, Germany, Spain, Denmark, Finland, England, Wales and Northern Ireland, Scotland, the Netherlands and Sweden [1]. Major upsurges are thought to be associated with substantive changes in market supply: during this time, eggs were imported from producers in EU Member States where there was a lack of vaccination of layer flocks against *Salmonella* or controlled food industry assurance schemes were not in place [1,10,11]. From 2000 to 2008, the mean incidence rate for *S.* Enteritidis PT 14b $NxCp_L$ gradually increased from 0.01 per 100,000 population in England to 0.4 per 100,000 population, respectively. In 2009, this rate more than doubled, to 1.1 per 100,000 population (HPA unpublished data).

This evidence, along with the findings of the 16 food-borne outbreaks, was used to formulate a hypothesis that *S.* Enteritidis PT 14b $NxCp_L$ infection of cases who were not part of the outbreaks was associated with consumption of eggs outside the home, within five days before symptom onset, particularly at restaurants serving Chinese or Thai cuisine.

Table 1

Demographic characteristics of sporadic cases of *Salmonella* Enteritidis PT 14b $NxCp_L$ infection (n=63) and controls (n=108), England, October–December 2009

Characteristic	Number of cases	Number of controls
Sex		
Female	28	72
Male	35	36
Age group (years)		
<10	9	2
10–29	19	8
30–49	14	38
50–69	11	38
≥70	10	22
Total	**63**	**108**

$NxCp_L$: resistance to nalidixic acid and concomitant reduced susceptibility to ciprofloxacin; PT: phage type.

Methods

A unmatched case–control study was carried out to analyse the apparently sporadic cases, recruiting two controls per case, to determine associations between potential risk exposures and symptomatic infection with *S.* Enteritidis PT 14b $NxCp_L$. Cases from the 16 food-borne outbreaks were excluded from our study.

Sample size calculations indicated that having data for 60 cases and 120 controls would enable us to detect an odds ratio of 3 (for 50% of the controls exposed) to 4 (for 10% of the controls exposed) as being significant at the 5% level with around 90% power.

Case definition

A case of *S.* Enteritidis PT 14b $NxCp_L$ infection was defined as a person in England with abdominal symptoms (diarrhoea and/or vomiting), with an isolate from their stool sample positive for *S.* Enteritidis PT 14b with resistance to nalidixic acid and concomitant reduced susceptibility to ciprofloxacin, and the isolate received by the HPA Laboratory of Gastrointestinal Pathogens between 1 September and 31 December 2009.

Recruitment and investigation of cases

Recruitment of cases for the study took place between 1 October and 31 December 2009. Before the data collection period, 12 cases reported in September 2009 were reviewed using local authority food-poisoning questionnaires ('trawling' questionnaires) to assist in generating hypotheses for the possible source of infection. All cases interviewed with this questionnaire were excluded from the study. Cases associated with the 16 discrete food-borne outbreaks were also excluded from this study, as were cases who had travelled outside the United Kingdom within five days of symptom onset and cases who were contacts of other reported cases.

Standardised data were collected on all patients infected with *Salmonella* (i.e. before the serotype/subtype was known), so that cases and outbreaks could be identified and investigated rapidly. This involved the completion of a standardised questionnaire for each person with presumptive *S.* Enteritidis or laboratory-confirmed *Salmonella* infection (all serotypes) by the Health Protection Unit or local authority. The extensive questionnaire included captured data on basic demographics, occupation, details of gastrointestinal illness and any other symptoms, history of travel, and details of food consumption and contact with animals within the five days before symptom onset. Questions on food consumption gathered details of the type and brand of each food consumed, place of purchase, whether the food was consumed in or away from the home, and type of food-service premises visited. The completed questionnaires were sent to the HPA Department of Gastrointestinal, Emerging and Zoonotic Infections for data entry, validation and analysis. Isolates were sent to the *Salmonella* Reference Unit at the HPA Centre for Infections for further characterisation and antimicrobial susceptibility testing [12,13].

Recruitment and investigation of controls

We used cases' landline telephone numbers, which reflect the location of their domicile, as the basis of the selection of controls (cases who had been contacted by mobile telephone were asked for a landline number). For each case, two controls were recruited using random digit dialling [14]. Controls were therefore chosen from the same telephone exchange area and therefore lived in the same geographical area as the cases. Between 2 October and 2 December 2009, controls were recruited by telephone over five weekday evenings. The individual who picked up the telephone and who agreed to be interviewed was considered to be a control provided they were over the age of 18 years and they provided informed consent on the telephone before the interview.

All interviews were carried out using a standardised questionnaire for controls. This was similar to that used for cases, except that questions on contact with animals, travel history, food consumption and grocery-shopping habits related to the five days before the interview (rather than before symptom onset). Controls who had experienced any gastrointestinal symptoms in the two weeks before the interview were excluded from the study.

Data analysis

The data were analysed using STATA 11. For all exposures, estimated odds ratios and 95% confidence

Table 2

Single variable analysis of exposure variables for cases of *Salmonella* Enteritidis PT 14b NxCp$_L$ infection (n=63) and controls (n=108), adjusted for age and sex, England, October–December 2009

Exposure[a]	Odds ratio (95% CI)	P value
Eaten away from home		
Eaten away from home at any type of establishment	2.6 (1.1–5.9)	0.02
Eaten out at parties	1.5 (0.6–3.8)	0.4
Eaten foods from food-service premises		
Restaurants serving Chinese or Thai cuisine	4.1 (1.6–10.4)	0.002
Kebab houses	17.1 (1.7–172)	0.02
Restaurants serving Indian cuisine	2.7 (0.7–9.5)	0.1
Burger bars	0.5 (0.2–1.7)	0.3
Fried chicken bars	2.2 (0.3–17.4)	0.4
Public houses	0.6 (0.2–2.2)	0.5
Restaurants serving Italian cuisine	1.5 (0.4–5.0)	0.5
Food exposure		
Barbecued food	13.6 (1.4–129)	0.02
Eaten barbecued food at home	9.2 (0.9–93)	0.06
Eaten barbecued food away from home	ND	0.07
Pre-prepared sandwiches	2.5 (1.2–5.4)	0.02
Eaten pre-prepared sandwiches at home	1.5 (0.4–4.9)	0.5
Eaten pre-prepared sandwiches away from home	3.0 (1.3–7.2)	0.01
Vegetarian food	3.4 (1.3–9.2)	0.01
Eaten vegetarian food at home	1.7 (0.6–4.7)	0.3
Eaten vegetarian food away from home	13.6 (2.3–81)	0.004
Cold meats	1.9 (0.9–4.0)	0.08
Eaten cold meats at home	1.3 (0.6–2.5)	0.5
Eaten cold meats away from the home	8.0 (1.7–37)	0.008
Eggs	1.6 (0.7–3.6)	0.3
Eaten eggs eaten at home	1.0 0.5–2.1)	0.97
Eaten eggs eaten away from the home	7.0 2.0–24.8)	0.003
Environmental exposure		
Had contact with animals[b]	1.0 (0.5–2.0)	0.98
Lived on a farm or smallholding	4.4 (0.2–84)	0.3
Visited a farm	2.4 (0.5–11.5)	0.3

ND: not determined; NxCp$_L$: resistance to nalidixic acid and concomitant reduced susceptibility to ciprofloxacin; PT: phage type.

[a] The reference category for each exposure is having not eaten at the specified establishment or having not eaten the specified food, or having had the relevant environmental exposure.

[b] Occupational contact or contact with pets.

intervals were used as measures of association. In addition, all exposures were tested, singly, for association with the outcome variable (illness) using chi-square test or Fisher's exact test. Exposures exhibiting some evidence of an association ($p<0.2$) were deemed eligible for inclusion in the multivariable analysis. The $p<0.2$ cut-off was chosen so that important exposures would not be missed due to confounding effects. A logistic regression model was constructed using a forward selection procedure including the most significant exposure at each step (likelihood ratio test $p\leq 0.05$). Potential confounding variables – age and sex – were included in the multivariable analysis regardless of statistical significance.

Results

A total of 489 *S.* Enteritidis PT 14b $NxCp_L$ cases distributed across all regions of England were identified by the HPA Laboratory of Gastrointestinal Pathogens during the study period. Of these, 101 were associated with the discrete food-borne outbreaks and were therefore excluded. Some cases not associated with these discrete outbreaks were also not included because they were interviewed with the initial trawling questionnaire in September, before the investigation, and others were excluded because they were identified after our investigation had closed. In total, 81 sporadic cases of *S.* Enteritidis PT 14b $NxCp_L$ infection completed the questionnaire. Of these 81 cases, 63 were included in the analysis: four were excluded due to recent travel history and 14 were excluded because they were contacts of other cases (although the index cases were included). There were reports of people with *S.* Enteritidis PT 14b $NxCp_L$ infection after December 2009, but the number reported had fallen to background levels.

A total of 108 controls were recruited: a mean of 3.6 calls (range: 1–32 calls) was needed to successfully recruit a control. Table 1 compares the basic demographic characteristics of cases and controls. Controls were more likely to be female ($p=0.004$) and older (mean age: 52.5 versus 36.8 years, respectively, compared with cases, $p<0.0001$). Due to these differences between cases and controls, single variable analysis was performed using logistic regression analysis adjusting for potential confounding by age and sex.

The cases had dates of symptom onset between 26 August and 16 November 2009, and the mean duration of illness in those who had recovered was 7 days (median: 7 days; lower and upper quartiles: 3 and 10 days, respectively). The predominant symptoms were diarrhoea (in 59 of 60 cases), abdominal pain (49 of 56), fever, defined as body temperature of at least 38 °C (32 of 55), nausea (29 of 55), headaches (26 of 55) and vomiting (20 of 59). Of the 63 cases, 15 reported having blood in their stool. A total of 50 visited their general practitioner, while 13 attended hospital accident and emergency departments and 12 were admitted to hospital. No deaths were reported among the study cases.

As there could be a delay in reporting (i.e. date of symptom onset was not necessarily the date the cases were reported) and to allow time for isolates to be sent for typing, the cut-off date for receipt of isolates at the HPA Laboratory of Gastrointestinal Pathogens was 31 December 2009.

In single variable analysis there was an association between having eaten away from home and symptomatic infection with *S.* Enteritidis PT 14b $NxCp_L$, particularly in restaurants serving Chinese or Thai cuisine and kebab houses (Table 2). Having eaten barbecued foods either at home or away from home, and pre-prepared sandwiches obtained away from home, was also associated with a higher risk of becoming a case. There was a very strong association between having eaten eggs away from home and becoming a case (Table 2).

As both eating away from home at any type of establishment and eating foods from restaurants serving Chinese or Thai cuisine were found to be significantly associated with being a case, a three-level factor was generated to determine any association between being a case and (1) not eating out, (2) eating out at restaurants serving Chinese or Thai cuisine, and (3) eating out at other restaurants. The final multivariable logistic regression model including the implicated exposure variables (Table 3) demonstrated no significant association between having eaten away from home but not at restaurants serving Chinese or Thai cuisine and becoming a case. However, having eaten foods from restaurants serving Chinese or Thai cuisine (including takeaways) was significantly associated with becoming a case. Among food exposures, eggs eaten away

Table 3

Multivariable logistic regression model of implicated food exposures, adjusted for age and sex, England, October–December 2009 (n=63)

Food exposure	Odds ratio (95% CI)	P value	Number of cases exposed
Had not eaten away from home	Reference	–	15
Eaten away from home but not at a restaurant serving Chinese or Thai cuisine	1.5 (0.5–4.1)	0.5	24
Eaten foods from restaurants serving Chinese or Thai cuisine	4.4 (1.3–14.8)	0.02	25
Eaten eggs away from home	5.1 (1.2–21.2)	0.02	12
Eaten vegetarian food away from home	14.6 (2.1–99)	0.006	6

from home and vegetarian foods eaten away from home were also identified as significant risk factors for becoming a case.

Discussion and conclusion

The case–control study presented here provides evidence of significant associations between eating in restaurants serving Chinese or Thai cuisine and eating eggs and vegetarian food away from home with becoming a case of *S.* Enteritidis PT14b NxCp$_L$ infection in a large national outbreak in England in 2009. The association between eating vegetarian foods and becoming a case may be related to the fact that vegetarian foods may contain eggs (which could be infected). These findings corroborated evidence obtained from concurrent investigations of 16 local discrete food-borne outbreaks of *S.* Enteritidis PT14b NxCp$_L$ infection. Our results indicated that the source of infection for the sporadic cases was likely to be the same as that for cases associated with the outbreaks. Information on eggs collected from food-service premises in seven of the 16 outbreaks indicated a common origin (a single production establishment in Spain). *S.* Enteritidis PT14 NxCp$_L$ obtained from eggs from this establishment, and also from environmental and food samples from the food-service premises were indistinguishable by molecular diagnostic testing from isolates obtained from human cases of *S.* Enteritidis PT14 NxCp$_L$ infection (cases associated with the outbreaks and the sporadic cases). *S.* Enteritidis PT1 NxCp$_L$ was additionally detected in eggs produced by this establishment in Spain as part of the outbreak investigations [15] providing further evidence of *S.* Enteritidis contamination within the laying flock.

Control measures

The United Kingdom Food Standards Agency was informed of the findings both from the case–control study and the 16 outbreak investigations and notified the European Commission and other EU Member States in October 2009 through the Rapid Alert System for Food and Feed (RASFF) of the eggs contaminated with *S.* Enteritidis PT 14b NxCp$_L$ and also PT 1 NxCp$_L$ sourced from an approved establishment in Spain (one of the conditions of approval is compliance with all the relevant legislation set out by the relevant EU Member State competent authority). This led to Spanish authorities investigating and identifying the affected flock. Eggs from this flock were prohibited from entering the fresh table egg market and were sent for heat treatment (as required by EU regulations [15,16], which state that eggs from flocks testing positive for *S.* Enteritidis or *S.* Typhimurium need to be treated in a manner that guarantees the elimination of *Salmonella*). After this control measure was introduced in early December 2009, the number of cases in England and Wales fell from a mean of 20 confirmed cases per week in November to nine and three per week in December and January 2010, respectively.

A decreasing trend in the notification rate of salmonellosis cases in the EU, particularly those caused by *S.* Enteritidis, has been seen over recent years. This has largely been attributed to the implementation of *Salmonella* national control programmes in the laying flocks [17]. Nevertheless, most of the reported food-borne outbreaks reported in the EU are still caused by *Salmonella*, with the most important food source being eggs and egg products [17]. Eggs have continued to be implicated as a source of or vehicle for cross-contamination in outbreaks of salmonellosis chiefly associated with the food-service industry in the UK [5-8]. Food-poisoning risks associated with eggs and egg dishes in the food-service industry, especially those serving Chinese cuisine, have included high-risk practices such as breaking, pooling and mixing shelled eggs [18,19]. One *Salmonella*-contaminated egg is capable of contaminating the whole batch of raw shell egg mix, and large numbers of consumers may be exposed to this contaminated raw material. The risk is increased if the egg mix is stored in a warm kitchen for later use during the day, as this would allow growth of the pathogen. Cross-contamination through egg mix aerosolisation during whisking and transfer to utensils and food preparation areas is also of concern [19]. The rates of *Salmonella* contamination have been linked to the origin of the eggs [20]. The food-service sector and consumers still need to be aware of this continuing hazard and adopt appropriate control measures and follow advice provided by national food safety agencies, in order to reduce the risk of infection.

Study limitations

Our case–control study had a number of limitations. Firstly, because of the limited time and resources available to recruit the controls, the final number of controls was slightly below the required number, based on our sample-size calculation (108 recruited as opposed to 120). In some of our analyses, small numbers led to large confidence intervals

Secondly, for the recruitment of controls we interviewed the person who answered the telephone (provided they were aged over 18 years), which may have introduced further bias, as we found that those who were most likely to answer were more likely to be older and also female. We did not use a method such as the 'last birthday' method (in which the adult in the household with the most recent birthday is requested for interview during the telephone call) – such an approach might help to increase variation in the demographics of the controls. However, we took measures to try to minimise response bias by varying the days of the week and the times that controls were telephoned. To minimise any potential confounding by age and sex, these were adjusted for in the regression analysis.

Thirdly, recall bias was a potential problem, particularly for controls. When cases were interviewed, they were asked about their food consumption in the five days before becoming ill whereas controls were asked about their food consumption in the five days before the telephone interview.

Fourthly, the time period for recruitment of cases did not exactly mirror that for the recruitment of controls, as we recruited controls over five weekday evenings in October and December 2009, whereas cases were recruited over a continuous period throughout October and December 2009.

Finally, we recognise that there may have been further confounders relating to differences in occupation, socio-economic status and eating behaviours between cases and controls. We attempted to minimise these potential confounders by interviewing controls who were living in the same telephone exchange area as cases. We also note that cases were not over-representative of Chinese or Thai ethnic groups (data not shown), so this form of confounding is not relevant to our investigation.

Despite the limitations – most of which are common to case-control studies of outbreak investigations of gastrointestinal infection – the results of the study support our hypothesis.

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The proof of the pudding is in the eating: an outbreak of emetic syndrome after a kindergarten excursion, Berlin, Germany, December 2007

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An outbreak of food poisoning (emetic syndrome) occurred in three kindergartens (A, B and C) in Berlin, Germany, on 3 December 2007 after an excursion during which food was served. We conducted a retrospective cohort study among the kindergarten children and personnel who participated in the trip. The overall attack rate among the 155 participants was 30%. It was 31% among the 137 children (aged two to six years) and 17% among adults (n=18). The consumption of rice pudding was significantly associated with disease. Among those who ate rice pudding, the attack rate was 36%, compared with 0% for non-eaters (relative risk: infinite, p<0.001, aetiological fraction: 100%), but differed significantly between kindergartens A (43%), B (61%) and C (3%), probably because groups were served from different pots. *Bacillus cereus* sensu stricto was identified from one vomit sample. The clinical and epidemiological characteristics suggest that *B. cereus* emetic toxin (cereulide) was the causative agent, although it could not be proven in the single vomit isolate. Inadequate food handling most probably led to the outbreak. Single-portion ready-to-eat rice pudding was recommended for subsequent excursions and no further cases of food poisoning occurred.

Introduction

In some outbreaks of infectious gastroenteritis, emesis predominates. The emetic syndrome is characterised by acute-onset nausea and vomiting. The most common pathogens associated with emetic syndrome are enterotoxin-producing *Staphylococcus aureus* and emetic-toxin-producing *Bacillus cereus* [1-5]. Staphylococcal food poisoning results from the ingestion of enterotoxins preformed in food by enterotoxigenic strains of coagulase-positive staphylococci, mainly *S. aureus*. Several staphylococcal enterotoxins are heat-stable. The range of the incubation period is 0.5 to 8 hours. *B. cereus* is a spore-forming microorganism, which can cause both emetic and diarrhoeal types of disease. It occurs ubiquitously in the environment (e.g. in soil) and may also be found in various foodstuffs. The emetic type of disease is caused by a heat-stable peptide toxin (cereulide): the incubation period ranges from 0.5 to 6 hours. The illness usually does not persist longer than 24 hours but severe and fatal outcomes have been reported [6,7]. The toxin is produced in food when the organism multiplies at ambient temperature for several hours (e.g. if the food is inadequately stored after cooking) [5]. Emetic outbreaks due to *B. cereus* have mainly been linked to starchy foods such as rice, pasta and pastry [2].

Norovirus is also a common cause of outbreaks of acute gastroenteritis, with emesis as a prominent symptom. Infection can arise from contact with or airborne transmission from fomites, as well as faecal–oral and foodborne transmission.

Although outbreaks of acute gastroenteritis are notifiable in most countries, the number of toxin-related food poisoning outbreaks is largely underestimated because the disease is often mild and self-limiting, and laboratory detection (toxin testing) is not routinely performed.

On 3 December 2007, a kindergarten (A) reported cases of emesis among children and its personnel to the local health authority. In the morning of the same day they had been on an excursion on a local tram that included catering on the platform at the tram's final destination. Preliminary investigations by the local health authority confirmed the outbreak in this and two other participating kindergartens (B and C) from another Berlin district.

We conducted an investigation immediately after the outbreak had come to our attention, to assess its scope, to identify the causative agent, and to determine the risk factors and the vehicle of infection in order to prevent further outbreaks.

Methods

Case finding

The tram excursion took place on the morning of 3 December 2007 between 09:00 and 10:00. On the following day, cases among the kindergarten groups were identified by the local health authorities. On 6 December, we obtained the addresses and telephone numbers of the kindergartens from the local health authorities. Food safety authorities provided the address of the caterer and the list of food items served during the excursion.

Exploratory interviews at the kindergartens were conducted on 7 December and showed that the staff who had accompanied the excursion clearly remembered the relevant epidemiological details (e.g., disease status and food consumption) of the children. Therefore we interviewed the kindergarten personnel using a standardised questionnaire on the children's and their own clinical symptoms, time of disease onset, type and duration of symptoms, secondary spread among family members, food consumption and demographic data.

Case definition

We defined a case as a person who attended the excursion on 3 December 2007 between 09:00 and 10:00 and presented with vomiting, abdominal pain or diarrhoea within 24 hours after the excursion.

Cohort study

We conducted a retrospective cohort study among children and personnel of the three affected kindergartens. We described cases by date and time of disease onset. Age group-specific and kindergarten-specific attack rates were calculated. We also calculated food-specific attack rates, aetiological fractions, relative risks and 95% confidence intervals. Data were also stratified by kindergarten to compare the results between the kindergartens. We used EpiData for data entry and SPSS software, version 15.0, for statistical analysis.

Laboratory methods

Human samples

Stool samples (n=10) and one available vomit sample were tested (at the Institute for Food Safety, Drugs and Animal Health) for various enteric pathogens (*Salmonella, Campylobacter, Escherichia coli* and other enterobacteria, *Yersinia enterocolitica, S. aureus, B. cereus* and viruses such as norovirus, adenovirus, rotavirus and astrovirus). For detection of bacteria, routine culture methods were used, and for viruses, PCR and antigen tests were carried out. In the routine laboratory investigations of the stool and vomit samples, no tests for staphylococcal enterotoxins or *B. cereus* emetic toxin were performed.

An isolate of presumptive *B. cereus* from the vomit sample was tested for *B. cereus* cereulide production using liquid chromatography-tandem mass spectrometry (LC-MS/MS), and for the presence of the cereulide synthetase (*ces*) gene using PCR. For species differentiation, we used Fourier transform infrared spectroscopy [8].

For LC-MS/MS analysis of cereulide, bacteria were directly extracted with methanol during ultrasonification [8]. Chromatographic separation took place on a C8 column with a buffer/methanol gradient, a triple quadrupole mass spectrometer with positive electrospray ionisation run in multiple reaction monitoring mode (mass-to-charge ratio 1,170.7 $[M+NH_4]^+$ → 940.2; 1,170.7 → 741.4; 1,170.7 → 499.2; 1,170.7 → 357.2) was used for detection.

PCR to detect the *B. cereus ces* gene was performed using primers ces_TaqM_for and ces_TaqM_rev with probe ces_TaqM_probe (TIB-MolBiol, Berlin, Germany),

Table 1

Cohort characteristics with attack rates, outbreak of emetic syndrome following kindergarten excursion, Berlin, Germany, December 2007

Cohort characteristics	Number of participants (%)	Number of cases	Attack rate (%)
Sex			
Female	84 (54)	19	23
Male	71 (46)	27	38
Age group (years)			
2–6	137 (88)	43	31
≥18	18 (12)	3	17
Kindergarten			
A	96 (62)	34	35
B	23 (15)	11	48
C	36 (23)	1	3
Total	**155 (100)**	**46**	**30**

as described by Fricker et al. [9]. For more details, see Rau et al. [8].

Food leftovers

Two unopened tetrapaks of the rice pudding that had been used, and retain samples (obtained from the caterer) of spray cream, cinnamon–sugar mix, gingerbread and two opened bags of cocoa powder were tested for *Salmonella*, staphylococci, *B. cereus, Campylobacter, E. coli, Listeria monocytogenes, Clostridium perfringens*, Enterobacteriaceae, *Pseudomonas* and norovirus. Leftovers of heated rice pudding eaten on the tram platform were not available for testing.

Environmental investigation

Local health and food safety authorities inspected the caterer's facilities used on the tram platform and the cleaning facilities in the caterer's office. The caterer was interviewed regarding food purchase, transport and storage, the facilities on the tram platform during the excursion (stand, water and electricity supply), the preparation process of food items and drinks served during the excursions, and on the cleaning procedures of the cookware.

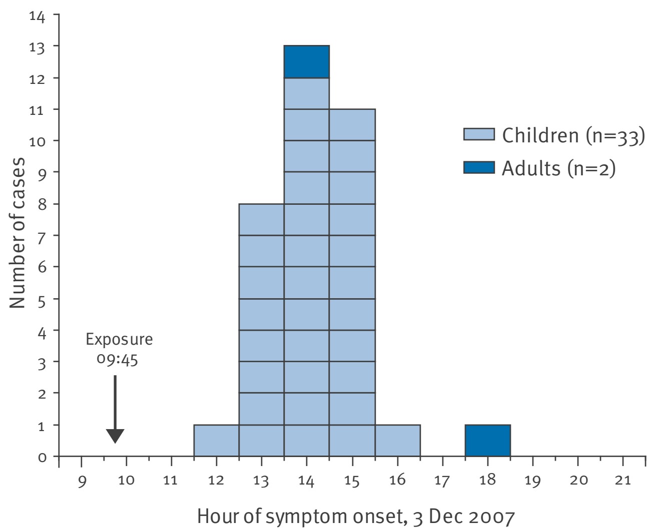
Results

Descriptive epidemiology

Overall, 155 persons (137 children, 17 kindergarten staff and one of the children's mother) from the three kindergartens participated in the excursion. The cohort characteristics are shown in Table 1. In total, 46 participants (43 children aged two to six years, and three adults) met the case definition (attack rate: 30%). The attack rate was higher among the children than among the adults, and differed significantly by kindergarten ($p<0.001$).

FIGURE

Cases by hour of symptom onset, outbreak of emetic syndrome following kindergarten excursion, Berlin, Germany, 3 December 2007 (n=35)



The predominant symptoms were vomiting (n=39), and abdominal pain (n=29). Diarrhoea was reported only in one person. Nobody was hospitalised and all cases recovered within one day. There were no secondary cases among household members.

The food items served during the excursion (at 09:45) were ready-to-eat rice pudding (from one-litre tetrapacks) that was heated before serving (served with cinnamon–sugar mix), cocoa drinks with and without whipped cream, and gingerbread. According to the personnel in Kindergarten C, the only person who became ill in this kindergarten recalled having been served from a different pot than that used for the other participants from this kindergarten. The participants had no other common meals before or after the excursion.

In all cases, symptoms started within a few hours after the end of the excursion. Detailed information about the time (hour) of symptom onset was available for 35 cases. Onset of symptoms began in the first case on 3 December, 2.5 hours after the meal had been served (Figure). The median time between the meal and symptom onset (the median incubation period) was four hours. No cases had onset of symptoms later than eight hours after the meal.

Cohort study

Of the food items served during the excursion, only consumption of rice pudding was significantly associated with illness in the cohort study. The relative risk was infinite (Table 2) with $p<0.001$, and all cases could be explained by the consumption of rice pudding (aetiological fraction: 100%). After stratifying by kindergarten (Table 3), the consumption of rice pudding remained associated with disease.

Laboratory results

One vomit sample was provided on the day of symptom onset (3 December 2007); 10 stool samples were provided after 6 December. 'Presumptive *B. cereus*' (collective name for *B. cereus* sensu strictu, *B. thuringiensis* and closely related bacilli), isolated from the culture of the vomit sample, was analysed by LC-MS/MS for cereulide production and for the presence of the *ces* gene by PCR: both analyses gave negative results [8]. No cereulide could be detected in the vomit sample itself. The isolate, initially described as presumptive *B. cereus*, was identified as *B. cereus* sensu stricto (non-cereulide producing) by Fourier transform infrared spectroscopy.

All stool samples taken within a few days after symptom onset and all food samples were negative for all tested pathogens.

Environmental results

All food items had been purchased by the caterer at the end of November 2007 and had been stored in the boot of the caterer's car until 1 December 2007. One similar excursion had taken place on 1 December 2007, with the same tram and the same catering company, but no outbreak occurred.

On both excursions, pots in an electric water-bath were used to heat the rice pudding and to keep it warm on the tram platform. The caterer stated that after the meal of the first excursion (on 1 December), rice pudding remnants had been scraped out of the pots and the pots were cleaned superficially in a wash-hand basin in an improvised kitchen in the caterer's office. According to the caterer, no food leftovers were served on 3 December. On that day, since there were more participants than in the previous excursion, the caterer used three additional cooking pots to heat up the rice pudding. The electricity supply was temporarily interrupted (due to a blown fuse) during the food preparation on 3 December.

Discussion

There is strong epidemiological evidence that the vehicle of the outbreak was rice pudding served during the excursion on 3 December 2007: the narrow epidemic curve indicated a common source of infection. All cases of emetic syndrome could be explained by the consumption of rice pudding from some of the pots used, while other food items were not associated with illness. Unfortunately, only one vomit sample was available for testing: no leftovers of the rice pudding portions served were available. This substantially hampered the laboratory investigations and no causative agent could be unambiguously identified. However, the clinical characteristics of this outbreak – including the short incubation period (of only a few hours), vomiting as the main symptom and the short self-limiting course of the disease – are typical for *B. cereus* emetic toxins or *S. aureus* enterotoxin. The fact that rice pudding was the likely vehicle suggests that this outbreak was caused by *B. cereus* cereulide. Starchy food products, including rice dishes, have been described as typical vehicles in *B. cereus* toxin outbreaks [2,5,10]. However, *S. aureus* cannot be ruled out as the responsible pathogen. In both scenarios of *B. cereus* or *S. aureus* having caused the outbreak, the food contamination must have occurred at least several hours before serving because this minimum time is required for pathogen multiplication or germination (in case of *B. cereus*) and for toxin production [2,5]. It is very unlikely that the unopened commercial ready-to-eat tetrapacks were contaminated: had they been, more outbreaks would have been expected, given the wide distribution of these products. Since the cinnamon–sugar mix was added to the rice pudding only

Table 2

Food-specific attack rates, aetiological fraction and relative risks with 95% confidence intervals, outbreak of emetic syndrome following kindergarten excursion, Berlin, Germany, December 2007

Food items served during the excursion	Eaten by the person	Number of participants who developed symptoms and with available information about food items consumed n=46	Overall number of participants with available information about food items consumed[a]	Attack rate (%)	Aetiological fraction (%)	Relative risk (95% CI)
Rice pudding	Yes	46	129	36	100	∞
	No	0	24	0	–	–
Cocoa drink	Yes	37	124	30	79	1.0 (0.5–1.9)
	No	7	23	30	–	–
Whipped cream	Yes	5	22	23	11	0.8 (0.3–1.8)
	No	32	109	29	–	–
Gingerbread	Yes	2	22	9	4	0.3 (0.1–1.1)
	No	34	105	32	–	–

[a] For rice pudding: n=153; cocoa drink: n=147; whipped cream: n=131; gingerbread: n=127.

Table 3

Stratified analysis by kindergarten for rice pudding-specific attack rates, aetiological fraction and relative risks, outbreak of emetic syndrome following kindergarten excursion, Berlin, Germany, December 2007

Kindergarten	Rice pudding eaten by the person	Number of cases who consumed rice pudding and developed symptoms n=46	Overall number of participants with available information about rice pudding consumption n=153	Attack rate (%)	Aetiological fraction (%)	Relative risk
A	Yes	34	79	43	100	∞
	No	0	16	0	–	–
B	Yes	11	18	61	100	∞
	No	0	4	0	–	–
C	Yes	1	32	3	100	∞
	No	0	4	0	–	–

shortly before consumption it can be ruled out as the vehicle of the outbreak.

Unfortunately, in the initial microbiological investigations the human and food samples had not been tested specifically for the presence of *B. cereus* toxins and *S. aureus* enterotoxins. In such outbreaks, human and food samples should be obtained and tested in a timely manner, not only for the usual pathogens (bacteria and viruses) but also for the relevant toxins, using the appropriate tests. The *B. cereus*-like strain isolated from the only vomit sample tested negative for cereulide or the *ces* gene. However, it is conceivable that emetic-toxin-producing *B. cereus* strains as well as non-toxin-producing strains were present in the rice pudding, but could not be detected in the vomit sample. The presence of *B. cereus* in the vomit sample and the absence of this agent from the unopened package of rice pudding is consistent with a scenario of *B. cereus* spores (including toxin-producing and non-toxin-producing strains) having contaminated the rice pudding after the tetrapacks were opened. The spores may have germinated and multiplied in remnants of the rice pudding left in the pots during an inadequate cleaning and storage process between the first and second excursion. This scenario is supported by the fact that not all of the pots appear to have contained contaminated rice pudding.

The fact that children from three kindergartens participated in the excursion and were affected by emetic syndrome shortly afterwards (although with attack rates differing by kindergarten) clearly pointed to a common source related to the excursion. This epidemiological pattern narrowed the spectrum of causative agents to toxin-producing agents. This shift of focus when patients from more than one setting are affected is an important epidemiological practice that is not always appreciated. If only one kindergarten had been involved, the investigation would have needed to also examine potential earlier sources of exposure to other pathogens such as norovirus and rotavirus. In this outbreak, the epidemiological investigation started shortly after the outbreak had been detected and the kindergarten staff clearly remembered the few food items consumed by the children. However, in other outbreak investigations, if substantial time elapses between symptom onset and epidemiological data collection (e.g. standardised interviews) or if many different food items had been served recall bias may be a major problem.

Although the environmental investigations did not determine the source of the food contamination, it revealed several breaches in food hygiene regarding cleaning of the cooking pots between the first and second excursion, as well as incorrect holding times and temperatures of food.

The epidemiological findings in this outbreak are consistent with other published *B. cereus*-associated food-borne outbreaks [11,12]. It should also be noted that food can be contaminated at the same time by different strains of presumptive *B. cereus* (*B. cereus* sensu stricto, *B. thuringiensis, B. weihenstephanensis*), which can be difficult to discern in some cases of food poisoning [13-15]. Also contamination with mixed cultures of emetic and non-emetic *B. cereus* sensu stricto can occur that can only be revealed by the testing of several isolates [8]. Detection of the *B. cereus* toxin as well as *S. aureus* enterotoxin in human and food samples is not straightforward and may require advanced methods in specialised laboratories [13-15].

Mobile caterers and persons responsible for such excursions should be aware of the potential risk of outbreaks caused by bacterial toxins. In order to prevent *B. cereus* spores from germinating and producing heat-stable cereulide, caterers need to ensure that food leftovers are discarded or refrigerated at a temperature below 10 °C and, if stored, that they are reheated thoroughly (at least 65 °C) before consumption.

In presumed food-poisoning outbreaks, stool and vomit samples from a substantial number of patients as well as relevant food leftovers and their ingredients should be obtained and investigated, not only for pathogens but also for the relevant toxins by appropriate tests. If *B. cereus* is identified, it is useful to further analyse several isolates from the culture to identify toxin-producing *B. cereus* strains.

In the light of our study, we recommended using single-portion, ready-to-eat rice pudding packs during future kindergarten field trips. No further food-borne outbreaks related to such excursions were reported to the local health authorities.

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Public health crises: the development of a consensus document on their management in Spain

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Several public health crises in Europe have led to sustained outbreaks, political problems, or have generated social alarm. For this reason, a nationwide study was conducted in Spain with the objective to determine which public health events provoke the most frequent crises, to reach a consensus regarding the appropriate actions to be taken when responding to public health crises, and to provide recommendations for their management. The events which had most frequently provoked crises between 1999 and 2004 were identified. A consensus was obtained by public health experts from the 17 Autonomous Regions of Spain and the National Epidemiological Centre using the *RAND/UCLA* method which combines the Nominal Groups and Delphi techniques. Legionellosis, foodborne diseases, severe acute respiratory syndrome (SARS), bovine spongiform encephalopathy (BSE), bioterrorism, meningococcal meningitis, tuberculosis, heat waves, and influenza epidemics were found to be cause for most public health crises. In Spain, 75% of the crises identified by senior public health experts from the Autonomous Regions involved infectious diseases. Factors triggering a crisis included the type of disease, social alarm, population affected, and the course of action taken by public institutions and reporting in the media. There was consensus that correct information, qualified personnel, availability of standardised protocols for investigation and control, information distribution, and setting up of 'crisis offices' were actions with a positive effect regarding crisis resolution. Appropriate management of outbreaks or other situations being perceived as a risk to health can mitigate or even contain the generation of public health crises.

Introduction

Each year, one of five World Health Organization (WHO) member states experiences some type of event (disease outbreak, environmental calamity, etc.) that threatens the health of its people [1]. It has been suggested that two billion people worldwide face health threats because they are at risk of, or exposed to, public health crises. Thus, preparation, mitigation, response, and control of such crises are public health priorities [1]. Nonetheless, decisions aimed at resolving them are often taken without the active participation of those responsible for the implementation of implicated programmes [2].

Spain has experienced several public health crises in recent years, some of which were solved rapidly and adequately, while others were not. The tardiness or failure to resolve some of them has lead to sustained outbreaks, difficult political situations, or inappropriate information by the press, and thus generated undue social alarm. Crises of public health require a rapid assessment of measures necessary for their resolution to accurately assign and manage resources [3]. When confronted with a crisis, many politicians are often rather concerned with its public consequences instead of investigating its causes. In response, pressure is put on epidemiologists to find causes and implement control measures rapidly that can complicate the investigation of an event.

In Spain, in 2005, a study involving public health experts from all Spanish Autonomous Regions was conducted with the intention to establish criteria for good practice in the management of epidemics (infectious diseases or not) or other emerging crisis situations in public health. The study objectives were (i) to determine which events provoke the most frequent public health crises, (ii) to reach a consensus regarding the appropriate actions to be taken when responding to events with an impact on public health, and (iii) to provide recommendations for their management.

Methods

For the purpose of the study, a public health crisis was defined as an event or a related series of events that overwhelm the capacity of the public health services to maintain the health of a community [4]. We identified events which had most often provoked health crises in Spain between 1999 and 2004 through expert consultation and a database search.

Study participants

A letter was sent to general directors of public health services in the 17 Autonomous Regions asking for information about the five largest or most frequent crises experienced in the study period. Furthermore, the Autonomous Regions and the National Epidemiological Centre (CNE, Centro Nacional de Epidemiología) were asked to nominate a technical expert for collaboration with the study leader to ensure reliable information and to achieve a consensus for actions at national level.

Database and other sources searched

Databases: Medline, Biblioteca Virtual en Salud (BVS), Scientific Electronic Library Online- (Scielo), Literatura Latinoamericana y del Caribe en Ciencias de la Salud (LILACS), Pan American Health Organization (PAHO) and the World Health Organization's library database (WHOLIS), Cochrane Library Plus and Embase.

Web pages: World Health Organization, *Eurosurveillance*, Morbidity and Mortality Weekly Report, Elsevier, and Scirus. Other: Google, Yahoo, Doyma Editors, online archives of important national newspapers (ABC, El Periódico de Catalunya, La Vanguardia, El País, El Mundo, Diario Médico), *Informe* Quiral [5], and other sources, such as Epidemiological Bulletins of the public health services of the Autonomous Regions.

Keywords used to identify crisis included: epidemic, outbreak, intoxication, foodborne disease, public health crisis, public health crisis management, heat wave, *Prestige* (the only oil-spill disaster in Spain during the study period), bovine spongiform encephalopathy (BSE) and mad cow disease. The selection of keywords was based on the most frequent crisis experienced by the 17 Autonomous Regions.

RAND/UCLA Appropriateness method

We implemented the *RAND/UCLA Appropriateness method*, which is based on scientific evidence and combines the Nominal Groups and Delphi techniques [6].

Nominal Group technique

According to the Nominal Group technique a group of experts discusses, and eliminates ideas to finally agree upon a prioritised list of ideas [7,8]. Our Nominal Group consisted of 17 experts responsible for epidemiological surveillance of epidemic outbreaks of transmissible and non-transmissible diseases in each of the respective Autonomous Regions and one expert from the CNE. In addition, the study coordinator and study leader were part of the group with a voting right. Consensus was considered as an agreement of at least 60% among the expert group members in line with the methodology described by Amezcua et al. [9].

Delphi qualitative evaluation technique

To reach a consensus on the most suitable actions for crisis management, the Delphi qualitative evaluation technique was considered as the most appropriate method [9,10]. This technique consists of interviewing a group of experts or panellists using a series of questionnaires to identify future topics of interest. In our study, experts participated in a series of interactive sessions, organised in rounds to eventually create a high level of consensus. The panellists were the same experts as in the initial Nominal Group and all participated in each round.

Based on the panellists' answers to the initial questionnaire, a new questionnaire was created for a second round. The order of items presented was based on the percentage of agreement achieved in the first round. The questionnaire was then sent to the panellists with a request to arrange the items numerically by order of perceived priority and a coincidence of at least 60% was considered a consensus [7]. After that, a final consensus list was created for the items for which consensus had been reached.

Email was used for the communication between panellists and the study leader for sending and receiving the questionnaires for each round, and for queries or feedback. In addition, telephone calls were used for clarification of remaining doubts. The role of the study coordinator was to supervise the work of the panellists

Table 1

Most frequent events/diseases provoking public health crises according to responses from senior public health experts from Autonomous Regions, Spain 2005

Public health crises aetiology	Number of autonomous regions
Legionellosis outbreaks	13
Foodborne diseases	10
SARS	9
BSE	6
Bioterrorism	6
Meningococcal meningitis	5
Drinking water contamination[a]	5
Tuberculosis	4
Heat waves	4
Brucellosis	3
Avian influenza	3
Hepatitis C[b]	3
Dioxins	2
Prestige oil-spill[c]	2
Tumours[d]	2
Pneumococcal pneumonia	1
Surgical aspergillosis[b]	1
Influenza	1
Chemical poisoning	1
Mumps	1
Measles	1
Rubella	1
Non-specific gastroenteritis	1
Hepatitis A	1

BSE: Bovine spongiform encephalopathy; SARS: Severe acute respiratory syndrome.

[a] Either by infectious pathogens such as norovirus, *Shighella*, and *Cryptosporidium* or toxins such as arsenic, and lead.

[b] Nosocomial infection.

[c] The only oil-spill disaster in Spain during the study period.

[d] Benign or malignant, due to proximity to magnetic fields.

and the study leader and to organise the meeting of the Nominal Group together with the latter.

Results

According to the representatives of the Autonomous Regions the most frequent diseases or events leading to public health crises involved outbreaks of legionellosis, foodborne diseases, SARS, BSE, bioterrorism, meningococcal meningitis, drinking water contamination (either by infectious pathogens such as norovirus, *Shighella*, and *Cryptosporidium* or toxins such as arsenic and lead), tuberculosis, and heat waves (Table 1). According to the results, 75% of the diseases or events provoking crisis in public health were of infectious aetiology, while 25% were due to other causes.

Our results show that events that cause or trigger public health crises vary considerably and that different bibliographic search strategies generate different results (Table 2).

The database search yielded a total of 106 articles; most frequently associated with public health crisis were: BSE (32 articles; 30%), foodborne diseases (14; 13%), influenza (8; 8%), meningococcal meningitis (6; 6%), SARS and nosocomial infections (5; 5%), for acquired immunodeficiency syndrome (AIDS), tuberculosis, legionellosis, bioterrorism, and avian influenza less than five articles were retrieved.

The search of online archives produced 3,454 reports mentioning most often the *Prestige* oil-spill (1,160; 34%), BSE (984; 29%), heat waves (332; 10%), legionellosis (307; 9%), foodborne diseases (197; 6%), SARS (128; 4%), influenza and AIDS (3% and 2% respectively) in connection with public health crisis.

The review of all issues of *Informe Quiral* yielded 18,448 reports on health. AIDS (2,638; 14%), smoking (2,177; 12%), legionellosis (1,826; 10%), BSE (1,660; 9%), drug abuse (1,550; 8%), eating conditions (particularly obesity) (1,513; 8%), cancer (1,457; 8%), foodborne diseases (1,291; 7%) and SARS (1,218; 7%) featured as most frequent topics, followed by bioterrorism, dioxin, tumours (benign or malignant) possibly from proximity to magnetic fields, the *Prestige* oil-spill, avian influenza and nosocomial infections which were mentioned in less than 5% of articles.

Table 2

Literature research on reported causes of public health crises from 1999-2004 by source, Spain 2005

Aetiology public health crises	Databases N(%)	Other on-line archives[a] N(%)	Informe Quiral N(%)
Legionellosis	3 (3)	307 (9)	1,826 (10)
Foodborne diseases	14 (13)	197 (6)	1,291 (7)
SARS	5 (5)	128 (4)	1,218 (7)
BSE	32 (30)	984 (29)	1,660 (9)
Influenza	8 (8)	93 (3)	-
AIDS	4 (4)	69 (2)	2,638 (14)
Bioterrorism	2 (2)	10 (0)	812 (4)
Prestige oil-spill[b]	-	1,160 (34)	277 (2)
Meningococcal meningitis	6 (6)	-	-
Nosocomial infections	5 (5)	-	203 (1)
Tuberculosis	4 (4)	-	-
Avian influenza	2 (2)	29 (1)	277 (2)
Heat waves	-	332 (10)	184 (1)
Hepatitis C[c]	-	24 (1)	-
Smoking	-	-	2,177 (12)
Drug abuse	-	-	1,550 (8)
Eating conditions[d]	-	-	1,513 (8)
Cancer	-	-	1,457 (8)
Dioxins	-	-	406 (2)
Tumor[e]	-	-	350 (2)
Other pathologies[f]	21 (20)	121 (4)	609 (3)
Total	**106 (100)**	**3,454 (100)**	**18,448 (100)**

AIDS: Acquired immunodeficiency syndrome; BSE: Bovine spongiform encephalopathy; SARS: Severe acute respiratory syndrome.

[a] Google, Yahoo, Doyma Editors, newpapers (ABC, El Periódico de Catalunya, La Vanguardia, El País, El Mundo and Diario Médico) and Epidemiological Bulletins.

[b] The only oil-spill disaster in Spain during the study period.

[c] Nosocomial infection.

[d] Particularly obesity.

[e] Benign or malignant, due to proximity to magnetic fields.

[f] Chickenpox, hepatitis B, chemical poisoning etc.

The factors which influence the development of a public health crisis according to the panellists in the first round are listed in Table 3. In the second round, the factors which influence in order of priority were: (i) the type of disease or risk, (ii) social alarm generated and the population's perception, (iii) the population affected, (iv) measures taken by public health authorities, and (v) attitudes of the mass media (Table 4).

Participants agreed on a number of points that are relevant for a fast resolution of public health crisis: correct information, adequate qualification of technical personnel, availability of standardised protocols for investigation and control, availability of channels for case notification, communication between surveillance experts and healthcare services and evaluation of progress during resolution and of the final outcome. However, delay in starting an investigation, lack of coordination, disagreement between experts and politicians, lack of resources, and lack good communication were seen as hindering crisis resolution (Table 5).

Discussion

Our findings and the resulting recommendations which are drawn from Spanish public health experts' consensus could be of particular interest to public health authorities and politicians involved in the management of epidemics or public health crises caused by both communicable and non-communicable diseases. Literature research did not reveal similar exercises attempting to reach consensus for recommendations on how to deal with public health crises. Thus the lack of comparison with similar research represents a limitation of our work. The selected keywords were based on the most frequent crises experienced by the 17 Autonomous Regions. This may have lead to an overrepresentation of the incidents included. However, we believe that the results are valid and can be generalised for the Spanish context because of our intensive literature research. Furthermore, our nominal group included 17 experts from all Autonomous Regions in Spain and one expert from the National Epidemiological Centre.

The Delphi technique is used to reach consensus in large population groups that cannot meet regularly, or when the consensus pertains to a sensitive topic that cannot be debated publicly [11]. We used the technique in our study considering the distance separating the panellists and the difficulty associated with face to face meetings of the Nominal Group. By combining two techniques (*RAND/UCLA Appropriateness method*) [6] however, it was possible for the experts to meet and discuss the proposals in a structured manner, and for us to facilitate consensus between disparate perspectives [9,10].

Early detection of an event that can lead to a crisis depends on standardised information systems available for health departments and clinical services to facilitate data management, investigation, and preparation of necessary responses [12,13]. A lack of coordination between departments and ministries concerned with their 'own interests' can aggravate a crisis [14].

Management of crisis situations consists of three recognised stages: prevention, preparation of measures to be implemented, and recovery [15]. Thus directors of public health authorities should estimate the impact of emergency situations, set up and implement appropriate actions, be persuasive, and employ organised management [16]. During an emergency situation, preparation and adequate operational capacity are fundamental for a rapid and appropriate response by the public health system [17,18]. For future improvement it is important to learn from the mistakes and successes of crisis response [19]. In our study, experts considered measures taken by the health authorities a priority for resolving public health crisis.

Recommendations for the management of public health crises resulting from our expert group consensus are as follows:

- To mitigate factors involved in crisis situations, it is necessary to create in advance guidelines with standardised protocols for investigation and control.
- For a better implementation of prevention and control measures and an appropriate response when facing a public health crisis, the coordination between public health departments and clinical services needs to be improved.
- Communication to the population should not be interrupted. Frequent contact between public health professionals and the media, is crucial.
- Evaluation of progress during crisis resolution and of the final crisis resolution is necessary. Evaluation (internal or external) should help avoid multiple, repetitive or unnecessary activities that could hinder adequate progress in crisis resolution.

Table 3

Factors influencing the occurrence of public health crises, according to senior public health experts from Autonomous Regions (questionnaire first round), Spain 2005

Factors which influence the occurrence of public health crises	Public health risks
	Social alarm
	Perception of the population
	Perception of the media
	Health of the population
	Public health actions
	Other[a]
Positive and negative aspects which have an influence in the resolution of public health crises	Intervention by public health experts
	Other factors[a]

[a] Discordant opinion, lack of coordination, new or limited knowledge of disease, outstanding relevance internationally.

Table 4

Factors influencing the occurrence of public health crises, according to senior public health experts from Autonomous Regions (questionnaire second round), Spain 2005

Type of disease or risk
Severity or lethality
Existence of effective treatment or a mechanism for eliminating the risk
Whether the disease or risk is new or not
Contagiousness
Incidence/prevalence
International repercussions
Social alarm and perceptions of the public
Alarmist messages via the media
Discrepancies in information from different social agents
Perception of imminence of danger or nearness of risk
Mistrust regarding the response of the administration
Saturation of the health system
Stigma
Population affected
Children, specifically if they are in settings like schools, nurseries, residences, hospitals, etc.
Low socioeconomic groups, tourists, healthy population
Deficits in public health organisation
Lack of communication or coordination between various organisations affected by the crisis
Lack of, delay in, or poor quality of information given to the public
Existence of standardised protocols for investigation and control allowing for rapid action with consistent criteria
Lack of training of experts
Politics of crises situations
Lack of resources
The media
Alarmist messages which provoke social upheaval
Contradictory messages, lack of transparency, or precipitated responses
Lack of skilled communication or poorly informed communicators
Existence of multiple spokesmen
Scarce information

Table 5

Consensus about appropriate actions for the resolution of public health crises, according to senior public health experts from Autonomous Regions, Spain 2005[a]

Positive actions
Correct, timely, and quality information for health professionals, affected populations, and the media
Qualified technical personnel, independent of political powers and with sufficient resources
Preparation of a standardised protocol for investigation and control
Established method of case notification, exchange of information and communication between public health experts and clinics
Arranging a crisis office or technical committee with a coordinator or leader (one or the other depending on type and severity of problem)
Existence of a single spokesman for the media
Evaluation of progress during resolution and of the final outcome
Negative actions
Delay in starting an investigation of the crisis
Lack of coordination among implicated institutions
Disagreement between experts and politicians in decision taking
Lack of technical or economic resources
Lack of knowledge about the related topics
Lack of good communication methods with de means; information excessively technical, lacking transparency, or contradictory

[a] In order of priority: highest priority on top, lowest on bottom.

- Health policy must establish priorities and directions which ensure the effectiveness and efficiency of interventions.

In conclusion, our study shows that a considerable number of public health crises in Spain involve infectious diseases and that various factors contribute to the occurrence or aggravation of such situations. However, backed up by the literature reviewed and the consensus in the group of senior experts, we believe that public health crises can be mitigated or contained by adequate management following consensus documents that take these factors into account. Public health crises management can be effective if: the information among parties involved (public health experts and clinicians) as well as between these parties and the media is correct, the qualification of technical personnel is adequate, standardised protocols for investigation and control are available, evaluation of progress during the public health crisis resolution and of the final outcome is performed and, finally, if responsibilities are specified and well understood.

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Influenza vaccine effectiveness, 2010/11

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To the editor: The editorial [1] and the articles related to it published on 17 March 2011 in *Eurosurveillance* provide important information on preliminary mid-season influenza vaccine effectiveness (VE) estimates for the 2010/11 season. Reliable VE estimates are essential for effective communication and planning of scarce resources. It is important to assess concordance between pooled European data [2] and national estimates, to evaluate on the one hand whether pooling indeed provides more robust estimates, and on the other hand, to explore potential geographical variation in such estimates.

In the Netherlands, we have been estimating effectiveness of the influenza vaccine in preventing medically attended laboratory-confirmed influenza-like illness (ILI) using the test-negative case-control approach for several years. While incorporating this in the routine ILI/influenza surveillance in primary care limits the possibility to optimise the design, to avoid bias, and to adjust for potential confounding, it ensures sustainability and assessment of annual variation. Unfortunately, our limited sample sizes do not allow strain-specific estimates, result in large confidence intervals, and make adjustment for age and underlying conditions challenging. Therefore, to increase power and obtain more valid VE estimates, we very much support pooled European analysis [2].

We estimated the VE using logistic regression on all medically attended ILI patients in the sentinel surveillance system with disease onset between the week in which influenza virus was encountered for the first time in the season and the end of April, the following year. For the current season, we included cases up to 21 March 2011. For 2009/10 and 2010/11, we excluded cases if the period between disease onset and date of swabbing was greater than seven days.

The crude effectiveness of the trivalent seasonal influenza vaccine in 2006/07, 2007/08 [3], 2008/09 [4], and of the monovalent 2009 influenza A(H1N1) pandemic vaccine in 2009/10 ranged from 20% to 60%. Adjustment for age lowered the VE estimates and widened the confidence intervals (Table).

The crude VE estimate for the 2010/11 vaccine was 46% (95% confidence interval: 9–67), which is similar to what has been reported in other European studies [2]. The 2010/11 VE estimate was lower when only individuals with an indication for vaccination (underlying condition or aged 60 years or older) were included.

It is worrying that patterns similar to those observed in the Netherlands are observed on a European scale. In particular, the consistent pattern of reduced VE estimates following correction for potential confounding by age or underlying conditions warrant further studies to develop methodologies for robust, non-biased VE estimates.

Table

Influenza vaccine effectiveness estimates per season, the Netherlands, 2006/07 – 2010/11

Influenza season	Vaccinated / total positive	Vaccinated / total negative	Crude VE (95% CI)	Age-adjusted VE (95% CI)
2006/07	9/72	25/144	32% (-55 to 70)	6% (-132 to 62)
2007/08	10/141	38/236	60% (17 to 81)	59% (7 to 82)
2008/09	20/167	45/311	20% (-41 to 54)	19% (-56 to 58)
2009/10[a]	6/36	72/258	48% (-29 to 79)	35% (-76 to 76)
2010/11	26/217	52/260	46% (9 to 67)	5% (-80 to 49)

CI: confidence interval; VE: vaccine effectiveness.
[a] Vaccine effectiveness calculated for the adjuvanted MF-59TM 2009 influenza A(H1N1) pandemic vaccine.

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