

EXCESS OF INFECTIONS DUE TO A MULTI-DRUG SENSITIVE *SALMONELLA* ENTERICA SEROTYPE TYPHIMURIUM IN FRANCE IN JUNE 2008

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An unusually high number of cases of *Salmonella* Typhimurium was reported in France in June 2008. In the course of epidemiological investigations 112 cases were ascertained, of whom 75 were interviewed. Subtyping by PFGE and MLVA identified a strain named "majority profile". Subtyping results were available for 45 interviewed cases, 30 of whom (majority below 15 years of age) were found to be infected with the majority profile strain. Evidence suggested the occurrence of an outbreak due to a monoclonal *S. Typhimurium* strain with the single PFGE profile XTYM-50. Cases with identical PFGE profile were also detected in Switzerland but no link with outbreaks occurring in the same period in Denmark and in the Netherlands was found. Contamination of a product distributed nationally was suggested as the cause of the outbreak but investigations did not reveal any specific food source.

Introduction

In the middle of June 2008, several community-based medical laboratories reported an unusually high number of *Salmonella* Typhimurium infections to the French Institute for Public Health Surveillance (Institut de Veille Sanitaire). The laboratories were scattered throughout France and most cases were not linked to each other by a common meal. At that time, national and regional outbreak detection thresholds were not exceeded. Initial sub-typing at the French National Reference Centre for *Salmonella* (Centre National de Référence *Salmonella*, CNR *Salmonella*) revealed that several isolates recently received were susceptible to all antibiotics and exhibited an identical Pulsed Field Gel Electrophoresis (PFGE) and Multiple Loci Variable Number of Tandem Repeats Analysis

(MLVA) profile. During the investigation, this profile was then named "majority profile". In the same period, *S. Typhimurium* outbreaks were reported in Denmark [1,2], Switzerland [3] and the Netherlands [4].

We carried out an epidemiological and microbiological investigation in order to confirm the occurrence of an outbreak and, if so, to assess its extent, and to identify a potential link between cases in terms of food or other exposure. We also investigated possible links between notified French cases and the Danish and Swiss outbreaks.

Methods

A case was defined as a person from whom *S. Typhimurium* was isolated in June or July 2008. Cases were identified by contacting all major laboratories in districts where an increase of cases was reported. Patients were interviewed via telephone using a standardised trawling questionnaire on possible exposures including questions on food consumption (dairy, meat, fish, vegetable, pastry and chocolate products), occurrence of other cases in the family, meals in restaurants or other facilities, and animal contacts in the three days preceding the onset of symptoms. Medical laboratories were asked to send their isolates to the CNR *Salmonella* for PFGE [5] or MLVA sub-typing [6].

The French Food Safety Agency (Agence Française de Sécurité Sanitaire, AFSSA) sub-typed by PFGE the *S. Typhimurium* food isolates that were fully susceptible to all antibiotics and had been received through routine collection since January 2008.

We reviewed point-source food-borne outbreaks due to *S. Typhimurium* that were reported through the mandatory notification system during the period investigated.

We carried out a case-case comparison study among individuals who were interviewed and for whom the strain subtype was available. Cases were individuals infected with the *S. Typhimurium* majority profile strain. Controls were selected among individuals who, during the same period as the cases, were infected with a strain of *S. Typhimurium* with a non-majority profile. One individual for each non-majority profile strain was selected, in order to ensure the highest possible heterogeneity of strain profiles among controls [7]. Selected controls were therefore individuals infected with strains presenting different non-majority profiles.

Data were analysed using Stata 9.2 (College Station, Texas). We calculated univariate odds ratios and their exact 95% confidence intervals to examine the risk associated with each exposure. Differences in categorical variables were compared using the χ^2 Fischer exact test.

Results

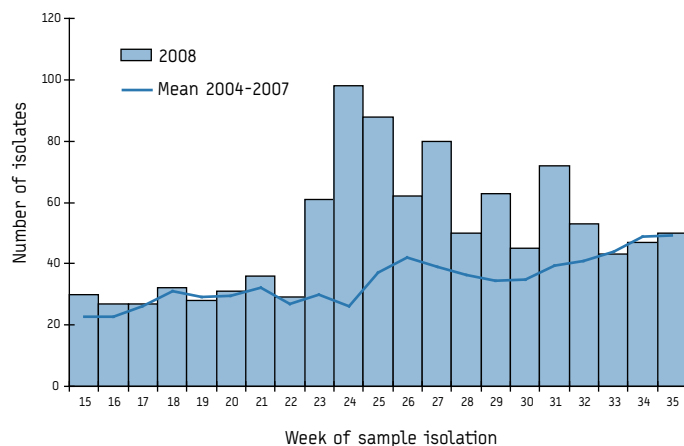
The number of *S. Typhimurium* isolates received by the CNR *Salmonella* in June 2008 was twice the mean number of those received in June of the previous four years (312 isolates versus 115 mean isolates in 2004-2007). With reference to the date of first laboratory diagnosis, the number of cases started increasing in the first week of June 2008, peaked (95 isolates) in the following week, and gradually returned to the expected seasonal values in the second week of July (Figure 1).

A total of 112 cases were ascertained in districts reporting an excess of cases between June and July 2008. Seventy-five were interviewed.

The CNR *Salmonella* sub-typed 90 isolates received between April and July 2008. Fifty-two isolates presented the MLVA "majority profile": 42 isolates with profile STTR3, number of repeats 11 (500 bp), STTR5, number of repeats 17 (282 bp), STTR6, number of repeats 9 (317 bp), STTR9, number of repeats 4 (171 bp),

FIGURE 1

Comparison of weekly number of *Salmonella Typhimurium* isolates received in 2008 with mean number for the years 2004-2007, by date of first isolation of the strain, CNR *Salmonella*, Pasteur Institute, Paris, France



STTR10, no amplification, and 10 isolates with a single difference either in the locus STTR5 or in the locus STTR6. Isolates with the "majority profile" were fully susceptible to the most commonly used antibiotics [5], showed a Xba-I PFGE profile XTYM-50 and had a different PFGE profile than the DT104 *S. Typhimurium* profile. The remaining 38 isolates presented 31 different MLVA profiles.

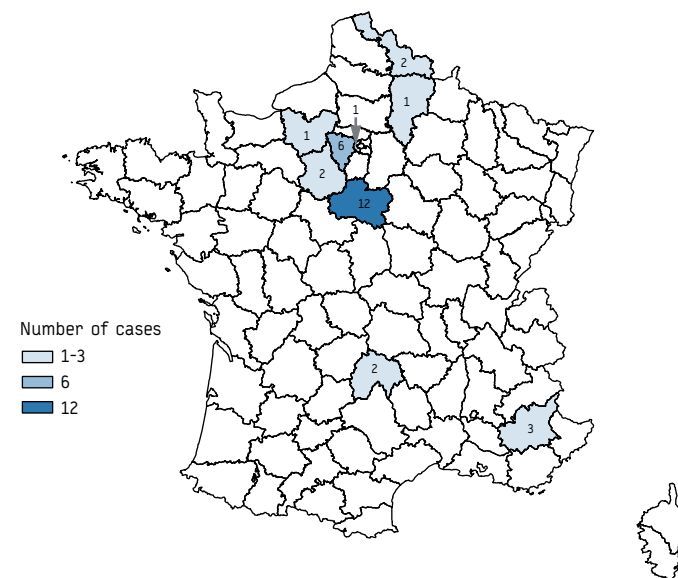
The isolated strain was sub-typed for 45 interviewed cases. Thirty cases were infected with the majority profile strain and diagnosed between 3 and 22 June 2008; 15 cases were infected with 13 different MLVA profile strains ("control cases") and diagnosed between 13 May and 21 June 2008.

Among the 30 majority profile strain cases, 24 (80%) were below 15 years of age, all, except one child of 1 month of age, were between 1 and 14 years. Age distribution below 15 years was higher in majority profile strain cases, when compared with *S. Typhimurium* cases recorded at the CNR *Salmonella* in the years 2004-2007 (62%), a difference that was very close to statistical significance ($p = 0.057$). Male/female ratio among the majority profile strain cases was 1.1. Twelve majority profile strain cases (34%) were residents in one district of region Centre. Two further cases were resident in another district of the same region, and eight cases were living in three neighbouring districts of regions Ile-de-France and Haute-Normandie. The other eight majority profile strain cases were scattered in four different districts of France (Figure 2).

The French majority profile strain corresponded to the dominant Swiss outbreak strain [3], but did not correspond to the Dutch outbreak strain in August 2008 [4]. Neither the majority profile strain nor any other non-majority profile strain sub-typed during this investigation matched with the Danish outbreak profile [1,2].

FIGURE 2

Cases infected with the *Salmonella Typhimurium* majority profile strain PFGE profile XTYM-50, by district of residence, France, June 2008 (n=30)



We identified one notified point source food-borne outbreak due to the *S. Typhimurium* majority profile strain involving two cousins. However, assessments of family food consumption did not permit identification of any exposure that could be incriminated as source of contamination.

The case-case comparison study was carried out on the 30 majority profile strain cases and 13 controls. Cases and controls did not significantly differ in age, symptoms and hospitalisation rate. No food product or other exposure was significantly associated with the majority profile strain infection.

AFSSA sub-typed 22 *S. Typhimurium* food isolates received through routine collection since January 2008. None of these corresponded to the PFGE profile XTYM-50 (majority profile strain) or to the Danish outbreak profile [1,2].

Discussion

Available information strongly suggested the occurrence of an outbreak due to a monoclonal *S. Typhimurium* strain with the single PFGE profile XTYM-50 in France in June 2008. This strain may have affected a younger than usual population. Although the majority of cases infected by this strain were concentrated in three regions, other cases were scattered in other French regions, suggesting the contamination of a product distributed nationally. Cases with identical PFGE profile were also found in Switzerland [3], but microbiological assays indicated no link with the outbreaks occurring in the same period in Denmark [1,2] and in the Netherlands [4].

Despite extensive epidemiological and microbiological investigations, we were not able to identify any specific food or other exposure as possible vehicle or way of contamination which could explain the occurrence of this outbreak. Hence no specific control measures could be proposed following this investigation. In July the number of human *S. Typhimurium* isolates reported at the CNR *Salmonella* returned within the expected values for the season.

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