Large outbreak of *Salmonella enterica* serotype *paratyphi B* infection caused by a goats' milk cheese, France, 1993: a case finding and epidemiological study

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See editorial by Rampling

Abstract

***Objective*—To assess the magnitude of a nationwide outbreak of infection with *Salmonella enterica* serotype *paratyphi B* and identify the vehicle and source of infection.**

***Design*—A case finding study of *S paratyphi B* infection between 15 August and 30 November 1993; a pair matched case-control study; an environmental investigation at a processing plant that produced a raw goats' milk cheese incriminated in the outbreak; phage typing and genotyping of food and human *S paratyphi B* isolates.**

***Setting*—France, 15 August to 30 November 1993.**

***Subjects*—273 patients with *S paratyphi B* infection; 59 pairs of cases and controls matched for age, sex, and city of residence.**

***Main outcome measures*—Numbers of cases and incidence rates by region of residence and age; matched odds ratios for dairy food preferences.**

***Results*—Among the 273 cases there was one death; 203 (78%) strains belonged to phage type 1 var 3. The incidence of infection was greatest in the region where goats' milk cheese is commonly produced. Comparison of cases and controls showed a 12-fold greater risk of illness (95% confidence interval 1·6 to 92·3) from eating brand A unpasteurised goats' milk cheese. *S paratyphi B* isolates of phage type 1 var 3 were recovered from cheese A, goats' milk at the plant processing cheese A, and goats' milk supplied to the plant by a single farm. Genotypic IS 200 typing of food and human 1 var 3 phage type isolates showed a common IS 200 pattern.**

***Conclusion*—This outbreak emphasises the potential health hazards of widely distributed unpasteurised milk products in France and the need for their close bacterial monitoring.**

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BMJ 1996;312:91-4

Introduction

Salmonella enterica serotype *paratyphi B* causes sporadic gastroenteritis and, less frequently, paratyphoid fever.[1] Few foodborne outbreaks of *S paratyphi B* infection have been reported. In France two or more outbreaks have occurred in the past 10 years.[2,3] An outbreak in 1990 (277 cases) was possibly related to contaminated goats' milk cheese.[3] Unpasteurised dairy products have caused outbreaks of salmonellosis, campylobacteriosis, listeriosis, and the haemolytic-uraemic syndrome.[1,4-10] In France large amounts of many different types of raw milk cheeses are consumed, yet raw milk cheese has only rarely been incriminated in foodborne outbreaks.[3,10]

We describe a large nationwide outbreak of *S paratyphi B* infection caused by unpasteurised goats' milk cheese.

Subjects and methods

SALMONELLA SURVEILLANCE

In France surveillance for salmonellosis is carried out by the National Reference Centre for Salmonella and Shigella, which receives isolates for serotyping from one third of the 4000 microbiology laboratories. For the past 12 years monthly trends have been computed for each serotype of *Salmonella* isolated. During the third week of October 1993 a nationwide increase in the number of *S paratyphi B* isolates submitted for typing was observed.

EPIDEMIOLOGICAL INVESTIGATION

A case was defined as a resident of France from whom a specimen (stools, blood, or other body tissue) had been culture positive for *S paratyphi B* between 1 August and 30 November 1993. Cases were identified by reviewing isolates received by the National Reference Centre. Multiple isolates from the same patient were excluded. Additional cases were sought by district public health officers from local laboratories. For each case identified, the patient's sex and age (<1, 1-5, 6-14, 15-64, and ≥ 65 years) and the date, site, region, and laboratory were recorded. Missing data were obtained by contacting the relevant laboratory.

After the outbreak was recognised a food questionnaire given to a few patients indicated that most had consumed brand A medium size round goats' milk cheese. Because a relation with a similar cheese had been suggested in the 1990 outbreak[3] we hypothesised that this cheese was the vehicle of infection in the present outbreak. To test this hypothesis we conducted a case-control study. Patients were included as cases if they had *S paratyphi B* gastroenteritis (more than three loose stools daily) or septicaemia. For each case investigated a community control matched for age (within the ranges <1, 1-4, 5-14, 15-34, 35-44, 45-54, 55-64, and ≥ 65 years), sex (for cases aged >5 only), and city of residence was sought from the telephone directory. People whose names (different spelling from the case name) came after the case name in the directory were called alphabetically until one was located who met the matching criteria. Potential controls who reported diarrhoea (more than three loose stools daily) in the previous three months were excluded.

Cases and matched controls (or their mothers if under 18) were interviewed by telephone by district public health physicians or a medical epidemiologist from the National Public Health Network using a standardised questionnaire. This was mainly targeted at milk products, particularly cow and goats' milk cheeses, and included questions on names and types of cheeses. Cases and controls were interviewed two to 12 weeks after the illness. Hence rather than ask them to try to recall the foods actually eaten during the three days before the illness we aimed at ascertaining their food preferences. Interviewers were not blinded to the subjects' case or control status.

ENVIRONMENTAL INVESTIGATION

In early November the processing plant (plant A) that produced the suspect cheese was inspected by a district veterinarian from the Ministry of Agriculture and one of us (EBL). Goats' milk sources, cheese production and storage, and the microbiological

monitoring of milk and cheese produced at the plant between June and November 1993 were reviewed. In addition, stool specimens were obtained from goats, cows, dogs, a cat, and workers from a farm that had supplied plant A with milk found to be contaminated by *Salmonella*.

LABORATORY INVESTIGATIONS

Salmonella serotype *paratyphi B* isolates (human, milk, and cheese) were phage typed at the National Reference Centre for Enteric Molecular Typing by using Felix and Callow's international system.[11] Human and food isolates were also subjected to genotypic IS 200 typing.[12]

STATISTICAL ANALYSIS

Isolation rates were calculated by age group and administrative region by using data from the 1990 French census as denominators.[13] Data from the case-control study were analysed by calculating univariate matched odds ratios and 95% confidence intervals.[14]

Results

EPIDEMIOLOGY

Two hundred and seventy three cases (4·3/million residents) were recorded (259 by the National Reference Centre, 14 by other laboratories). In 240 cases (88%) *S paratyphi B* was isolated from stools, in 15 (5·5%) it was isolated from blood, and in 14 (5%) it was isolated from other tissue (site unknown for four isolates). Clinical details were obtained for 97 (36%) patients by telephone interview. Thirty six (37%) had been admitted to hospital and one died. Gastroenteritis was characterised by diarrhoea (three to over 20 stools daily, median 6) that lasted from three to 27 days (median 5 days), fever (>38°C; 80 cases), abdominal cramp (76 cases), nausea (33 cases), and vomiting (30 cases). Of the 259 isolates phage typed, 203 (78%) belonged to phage type 1 var 3.

The outbreak began during the second week of August 1993 and continued till the second week of November (fig 1). Most of the infections were due to phage type 1 var 3. Cases were distributed nationally; however, the incidence was greatest in Poitou-Charentes (a traditional area of goats' milk cheese production) and the surrounding regions (fig 2). The isolation rate was highest among infants and children aged 1 to 5 years (table 1).

Food questionnaires were completed for 72 pairs of cases and controls. Because most of the infections in the outbreak were attributed to phage type 1 var 3 the analysis was restricted to the 59 (82%) pairs in which that phage type was isolated. The 59 cases did not differ from the total series of 203 patients infected with phage type 1 var 3 in age (P=0·9), sex (P=0·9), or region of isolation (P=0·2). There was a trend towards an increased risk in the presence of an underlying illness (for example, diabetes, malignancy, treatment with corticosteroids, chemotherapy; odds ratio 2.0 (95% confidence interval 0·6 to 6·7)). Analysis of the consumption of milk products showed a 3·8-fold greater risk of illness among people who ate goats' milk cheese (table 2). For the subsequent analysis cheeses were categorised as brand A goats' milk cheese (a medium size round cheese), medium size round goats' milk cheese of unspecified brand, other types of goats' milk cheese, and non-goats' milk cheese. Compared with the risk of illness among people who did not eat goats' milk cheese, there was a 12-fold greater risk among those who ate brand A and a sixfold greater risk among those who ate medium size round goats' milk cheese of unspecified brand. There was no substantially increased risk of illness among people who ate other goats' milk cheeses (table 2).

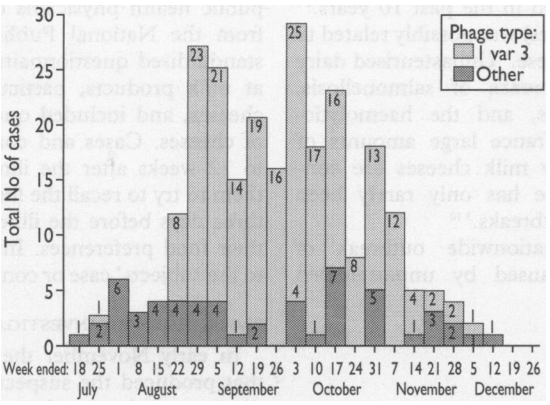

Fig 1—*Numbers of cases of Salmonella enterica serotype paratyphi B infection by week of isolation and phagetype, France, 1993*

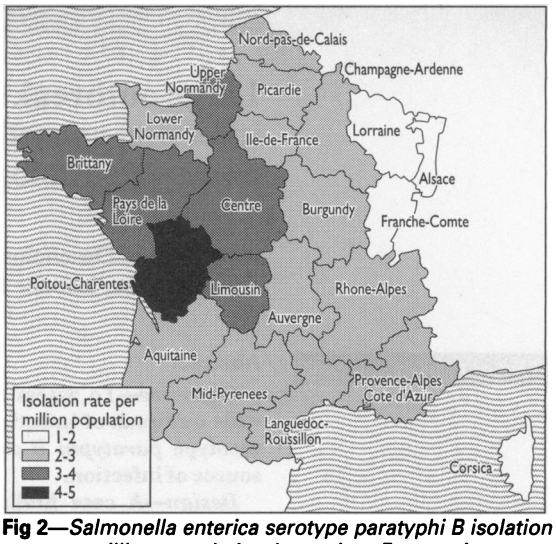

Fig 2—*Salmonella enterica serotype paratyphi B isolation rate per million population by region, France, August to November 1993*

Table 1—*Cases of Salmonella enterica serotype paratyphi B infection by age, France, August to November 1993*

Age (years)	No (%) of cases†	Rate per million population
<1	16 (6·0)	21·0
1-5	77 (29·1)	20·3
6-14	53 (20·0)	7·7
15-64	94 (35·5)	2·5
≥65	25 (9·4)	3·0

†Age missing for eight patients.

ENVIRONMENTAL AND MICROBIOLOGICAL INVESTIGATIONS

Cheese A is made from raw goats' milk at a single plant and distributed to food stores and supermarkets nationally. Every other day two batches of cheese A are made (11 000 to 15 000 cheeses (200 g each) per batch), each corresponding to a pool of 40 farms supplying goats' milk. Cheeses are stored for 11 days at the plant for maturation before distribution. The "use by" date is 45 days after the cheeses leave the plant.

Before October 1993 internal control for *Salmonella* at the plant consisted of a weekly culture on five cheeses picked from a single batch. Then, on 6 October, one brand A cheese grew *Salmonella*, later typed as *paratyphi B*. Subsequently, from 7 October, all batches of cheese stored at the plant, milk pools, and milk from all the farms that supplied each pool were

Table 2—*Cases of Salmonella enterica serotype paratyphi B infection (phage type 1 var 3) and controls by dairy food and type of goats' milk cheeses eaten, France, August to November 1993*

Dairy food	No (%) of cases (total=59)	No (%) of controls (total=59)	Matched odds ratio	95% Confidence interval
Milk	45 (76·3)	53 (89·8)	0·2	0·04 to 0·9
Cream	25 (42·4)	33 (55·9)	0·6	0·3 to 1·2
Cheese (any)	57 (96·6)	55 (93·2)	2·0	0·4 to 10·9
White cheese†	31 (52·5)	29 (50·9)	1·2	0·6 to 2·4
Cows' milk cheese	49 (83·1)	53 (89·8)	0·6	0·2 to 1·7
Goats' milk cheese	46 (78·0)	29 (49·2)	3·8	1·6 to 9·4
Type of goats' milk cheese‡§:				
Brand A	32 (54·2)	10 (17·2)	12·0	1·6 to 92·3
Medium size round of unspecified brand	9 (15·3)	8 (13·8)	6·0	0·7 to 49·8
Other	5 (8·5)	10 (17·2)	1·7	0·4 to 7·0
None	13 (22·0)	30 (51·7)	1·0 (reference)	Reference

†Data missing for two controls.
‡Matched odds ratios refer to no goats' milk cheese.
§Data missing for one control.

sampled daily for *Salmonella*. The district public health authorities remained unaware of these matters until 8 November, when the district public health physician contacted the district veterinarian's office about a possible link of the outbreak with cheese A. The milk pool corresponding to the batch that grew *S paratyphi B* on 6 October was also positive for *S paratyphi B* on 9 October but negative on the 7th, 11th, and 13th.

S paratyphi B was recovered from the milk of only one of the 40 suppliers. No salmonella was found in stool specimens from workers, cows, goats, and pets at the farm. Cheese A and goats' milk isolates belonged to the epidemic phage type (1 var 3). IS 200 genotypic typing was done on three human and four cheese A 1 var 3 isolates. All seven strains exhibited a common IS 200 pattern (profile 2·7).

Around 30 tonnes of cheese, corresponding to the batches stored at the plant between 21 September and 6 October, were destroyed after the isolation of *S paratyphi B* from cheese A, and cheese production from the relevant milk pool was pasteurised until daily *Salmonella* control of each batch was implemented. Subsequently all batches produced have been tested for *Salmonella* on day 1 (milk pool), on days 2 and 6 of the maturation process, and on days 9 and 12 (packaging and distribution, respectively).

Discussion

This large nationwide outbreak of salmonellosis was caused by unpasteurised goats' milk cheese made in a single plant. Evidence comes from the results of the case-control study and the isolation from cheese A and goats' milk of an *S paratyphi B* strain of the same phage type and IS 200 pattern as the epidemic strain. The increased risk suggested in the case-control study for medium size round goats' milk cheese of unspecified brand may reflect consumption of cheese A, because this exposure category may have included people who ate cheese A but could not recall the brand name.

Contamination of the milk pool from which one of the two batches was made originated from a single farm. However, the precise source of infection (human, animal, or environmental) was not identified. The duration of the outbreak (three months) indicated that cheese A had been contaminated for a similar period, probably from mid-June (date of onset of the epidemic minus three days for the incubation period, 11 days for cheese maturation, and 45 days before the use by date). The outbreak was detected during the third week of October, when contamination had gone unnoticed for almost three months. Detection of contamination at the plant in early October was not notified to the authorities and so did not contribute to faster recognition of the outbreak. (Routine microbiological control programmes in food processing plants are carried out voluntarily by producers to reduce the risk of foodborne infections; however, the results are not required to be notified to public health authorities.) Routine daily control of each batch for *Salmonella* would have detected the contamination much earlier.

In France only one third of laboratories send isolates of *Salmonella* for typing. Furthermore, only about 6% of patients with diarrhoea have a stool culture[15] and some patients with diarrhoea do not see a doctor at all. Hence the true size of the epidemic was probably much underestimated. Several thousands of cases may have occurred because of contamination of the cheese.

Despite the amount of raw milk cheese consumed daily in France outbreaks of infection remain comparatively rare.[3,10] In France pasteurisation of raw milk cheeses is not feasible for cultural, social, and economic reasons. Strategies for preventing infection by raw milk cheeses should therefore be aimed at both producers and consumers. Strict and carefully planned hazard analysis critical control point procedures should be developed and implemented for unpasteurised dairy products.[16] As part of this procedure any batch of cheese made from raw milk should be closely monitored for *Salmonella* and not be distributed until known to be clear. Producers should also report positive results of end production internal

Key messages

- Contaminated raw goats' milk cheese produced by a single processing plant caused a three month nationwide outbreak of *Salmonella paratyphi B* infection in France in 1993
- Though the cheese was probably contaminated for more than two months, the outbreak continued undetected for a further two months
- The source of the infection was goats' milk from one of the 40 farms that supplied the cheese processing plant
- Internal microbiological monitoring at the plant was not sensitive enough to detect the salmonella contamination initially
- Any batch of unpasteurised cheese or milk product should be closely monitored for *Salmonella* and should not be distributed until known to be clear

sampling to public health authorities. Consumers—particularly those susceptible to infectious diseases (for example, infants, elderly people, immunocompromised patients)—should also be warned that a nil risk cannot be warranted for raw milk products.

We thank the following public health physicians who participated: M Andrillon, A Armangaud, C Barbier, F Belingard, D Bousquet, E Boutin, V Bleuzè, B Cabo, C Cazenave, F Charlet, M Charron, M J Communal, M Cunnac, M Desvaux, M C Dubois, M L Ferial, M Feltin, J Y Goarant, L Gossel, A Hetru, M Juge, A Meunier, J Patureau, C Piau, E Pons, F Quittançon, and P Rogez (Directions Départementales de l'Action Sanitaire et Sociale); V Goulet, B Hubert, N Lacan, E Laurent, I Mehl-Augier, R Pinget, and E Sariot (Réseau National de Santé Publique); A Lepoutre and C Moyse (Direction Générale de la Santé). We also thank public health veterinarian F Peyre (Direction des Services Vétérinaires des Deux-Sèvres).

Funding: This study was conducted as part of routine activities in the institutions concerned. The Réseau National de Santé Publique is funded by the Ministère de la Santé et de l'Assurance Maladie; the Centre National de Référence des Salmonella-Shigella and the Centre National de Référence de Typage Moléculaire Entérique are funded by the Ministère de la Santé et de l'Assurance Maladie and the Pasteur Institute; the Direction Départementale des Affaires Sanitaires et Sociales des Deux-Sèvres is funded by the Ministère de la Santé et de l'Assurance Maladie.

Conflict of interest: None.

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(Accepted 2 November 1995)

Ethnic differences in the outcome of serum screening for Down's syndrome

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BMJ 1996;312:94-5

Serum screening for Down's syndrome was introduced in Oldham health district in January 1991 to reduce the false positive rate associated with screening based on age alone and to improve the detection rate.[1] A retrospective analysis was undertaken to evaluate whether these objectives were achieved throughout the entire obstetric population in Oldham.

Subjects, methods, and results

All women booked at the Royal Oldham Hospital and the community clinic before 18 weeks' gestation are counselled and offered serum screening by the booking midwife, who also records their ethnic origin. The gestation is confirmed by an ultrasound scan. α Fetoprotein and intact human chorionic gondatrophin values are measured by enzyme immunoassay. The risk for Down's syndrome is calculated from the two analyte results (adjusted for weight) and the maternal age.[2] Women who have a positive result (estimated risk of 1 in 300 or higher of a fetus with Down's syndrome) are counselled by a senior obstetrician and offered an amniocentesis. A trained interpreter is used if necessary.

Between 1 February 1991 and 31 October 1993, of the 9217 women offered serum screening 1655 (18%) were classified as "Indian Asians"—that is, from the Indian subcontinent. Pakistani and Bangladeshi women formed the largest subgroups, 956 (10·3%) and 605 (6·5%) respectively, with Indians and East African Indians accounting for the rest. Other ethnic minorities were counted together with the white population because of their small numbers: West Indian 51 (0·5%), Chinese 22 (0·2%), African 6 (<0·1%), Arab 9 (<0·1%), Mediterranean 6 (<0·1%). The outcomes of the pregnancies in the study population were determined from the obstetric, paediatric, and regional cytogenetics databases; the last includes all antenatal and postnatal karyotyping carried out in the North West region. In addition, all children with Down's syndrome known to social workers were identified. Proportions within ethnic groups were compared by using χ^2 tests and 95% confidence intervals[3] calculated for proportions and for the relative risks of positive screening.

Among the white and other women, serum screening improved the detection rate for Down's syndrome from a maximum of 25% (3/12) for a 7·8% amniocentesis rate if selection for amniocentesis had been based on age alone to 42% (5/12) for a 3·5% amniocentesis rate (table). It also extended the opportunity for screening to women under 35, in whom 80% of Down's pregnancies in these women occurred. In women of Asian origin, however, there was a significantly higher false positive screening rate (12·3% *v* 3·4%), seen both in those aged 35 and over and in those aged under 35, with no evidence of a higher incidence of Down's syndrome or an improved detection rate. The failure to detect either of the two babies with Down's syndrome born to serum screened Asian women was not due to their significantly lower uptake of amniocentesis. Both babies were born to women who gave a negative result on screening.

Comment

The apparent failure of serum screening in the Asian population may be due to ethnic influences (cultural and religious beliefs, uncertainty about age) as well as racial differences. The age specific risk estimates and