

Nationwide outbreak of multidrug-resistant *Salmonella* Heidelberg infections associated with ground turkey: United States, 2011

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SUMMARY

On 23 May 2011, CDC identified a multistate cluster of *Salmonella* Heidelberg infections and two multidrug-resistant (MDR) isolates from ground turkey retail samples with indistinguishable pulsed-field gel electrophoresis patterns. We defined cases as isolation of outbreak strains in persons with illness onset between 27 February 2011 and 10 November 2011. Investigators collected hypothesis-generating questionnaires and shopper-card information. Food samples from homes and retail outlets were collected and cultured. We identified 136 cases of *S. Heidelberg* infection in 34 states. Shopper-card information, leftover ground turkey from a patient's home containing the outbreak strain and identical antimicrobial resistance profiles of clinical and retail samples pointed to plant A as the source. On 3 August, plant A recalled 36 million pounds of ground turkey. This outbreak increased consumer interest in MDR *Salmonella* infections acquired through United States-produced poultry and played a vital role in strengthening food safety policies related to *Salmonella* and raw ground poultry.

Key words: Food-borne infections, food safety, outbreaks, *Salmonella*, salmonellosis.

INTRODUCTION

Salmonella continues to be a major public health problem in the United States. It is the most common bacterial cause of foodborne disease in the United States, causing an estimated 1 million illnesses and

400 deaths annually [1]. The National Antimicrobial Resistance Monitoring System (NARMS) defines multidrug-resistant (MDR) as resistance to ≥ 3 antimicrobial classes as described by the Clinical and Laboratory Standards Institute (CLSI) [2]. MDR strains of *Salmonella* are associated with increased risk of hospitalization, invasive disease, and antimicrobial treatment failure [3–5].

In 2011, *Salmonella* Heidelberg ranked ninth among the most common sources of human salmonellosis in the United States [6]. This strain appears to

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cause more invasive disease than most other non-Typhi *Salmonella* [3, 7]. *S. Heidelberg* is often found in poultry and ground turkey [8] and is the third most common *Salmonella* serotype in retail meat and food animal isolates [9, 10]. Antimicrobial resistance is an emergent problem within this serotype, including strains that are resistant to multiple antimicrobial agents [10–12]. Particularly concerning are strains that carry resistance to third-generation cephalosporins, used to treat bloodstream infections.

As a growing proportion of the United States consumes poultry products for their perceived health advantages [13], vigilant surveillance for *Salmonella* and strict control practices are increasingly important. At the time of this investigation, *Salmonella* was not considered an adulterant in raw poultry [14], but continued outbreaks of human illness and growing rates of antimicrobial resistance in poultry-specific strains of *Salmonella* called this policy into question [15, 16]. This report describes the multistate *S. Heidelberg* outbreak investigation which led to one of the largest U.S. Department of Agriculture's Food Safety and Inspection Service (USDA-FSIS) Class I recalls in history. The USDA-FSIS defines a Class I recall as 'a health hazard situation where there is a reasonable probability that the use of the product will cause serious, adverse health consequences or death' [17]. The results of this investigation led the USDA-FSIS to issue a Federal Register Notice in December 2012 to inform establishments producing raw ground poultry that they must reassess their Hazard Analysis and Critical Control Points (HACCP) plans for these products to take into account recent *Salmonella* outbreaks. The notice also describes FSIS's policy on how it determines whether raw meat or poultry products associated with an outbreak are adulterated [18].

METHODS

Outbreak identification

On 23 May 2011, PulseNet, the national molecular subtyping network for foodborne disease surveillance, identified a cluster of *S. Heidelberg* illnesses with pulsed-field gel electrophoresis (PFGE) *Xba*I pattern JF6X01.0058 [19]. At this time, identical PFGE patterns from 30 ill persons had been reported to PulseNet from 17 states since 1 March 2011. Additionally, two retail ground turkey isolates with the same PFGE pattern were uploaded to the PulseNet database from Minnesota and New Mexico in April and May 2011. These samples

were collected as part of routine retail meat surveillance conducted by the Food and Drug Administration Center for Veterinary Medicine (FDA-CVM). PFGE pattern JF6X01.0058 was the sixth most common pattern of *S. Heidelberg*, comprising 2.7% of the PulseNet Heidelberg database at the beginning of this investigation [20]. Based on a comparison of uploads to PulseNet in the previous 5 years, about 6–10 illnesses with this PFGE pattern would have been expected during this 3-month time-frame; however, in 2011, PulseNet had recorded 30 uploads since 23 May.

Case definition

In the early stages of this investigation, a case was defined as illness in a person with a culture-confirmed *S. Heidelberg* infection in the United States, with illness onset on or after 27 February 2011 and *Xba*I restriction enzyme PFGE pattern JF6X01.0058. Based on information obtained later in the investigation, the case definition was expanded on 1 August 2011 to also include illness in a person with a culture-confirmed *S. Heidelberg* infection with *Xba*I restriction enzyme PFGE pattern JF6X01.0032. These patterns differ by one band.

Hypothesis generation

During 26 May to 7 July 2011, cases were interviewed with a standard questionnaire developed in collaboration with local, state, and federal partners. This questionnaire included more than 200 food and environmental exposures that occurred in the 7 days before illness onset, ensuring that similar exposures are ascertained across many jurisdictions and allowing for rapid pooling of data to improve the timeliness of hypothesis-generating analyses. Early in the investigation, several patients reported ground turkey consumption, and the outbreak strain was isolated from ground turkey samples collected from retail settings; subsequently, we focused the investigation on ground turkey. A poultry-specific supplemental questionnaire was developed that included questions about exposures to all types of chicken, turkey, eggs and other poultry. State and local health departments were encouraged to interview past and present patients from whom the outbreak strain was isolated with this new questionnaire.

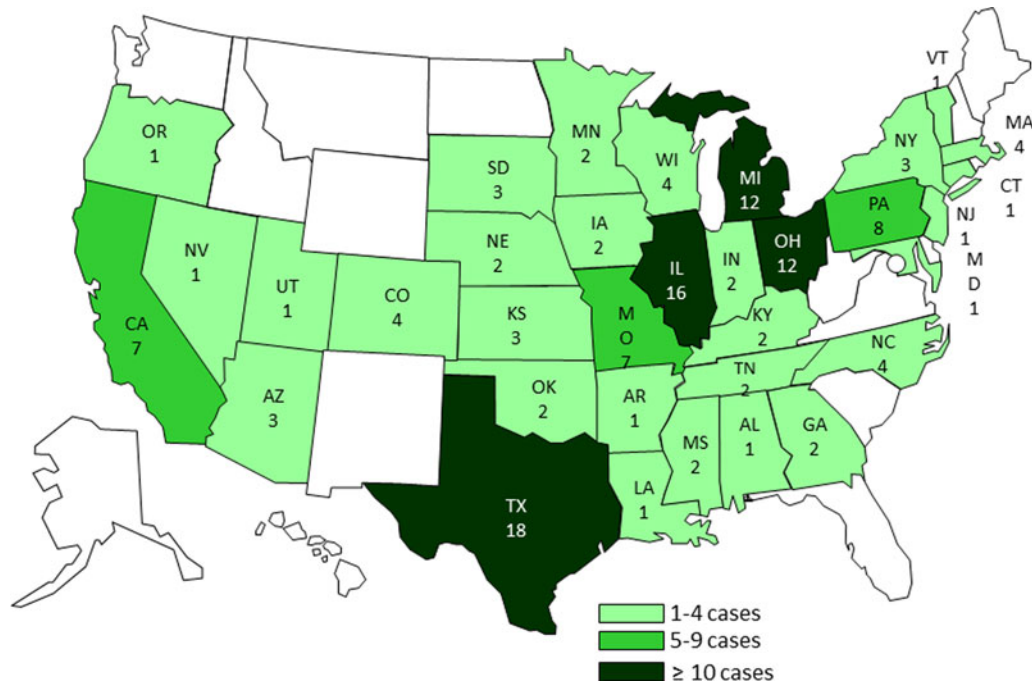


Fig. 1. Infections with *Salmonella* Heidelberg, by state, February–November, 2011 ($N = 136$).

Traceback and environmental investigation

State and local health departments and USDA-FSIS conducted traceback investigation of epidemiologically implicated food items. Traceback efforts began in Ohio on 19 July 2011 through information obtained from patients' purchases collected from grocery store shopper cards. Product information (such as date and location of purchase of ground turkey) was collected from ill persons.

Laboratory investigation

Salmonella isolates from patients' clinical samples and leftover ground turkey samples were serotyped and subtyped by PFGE at state public health laboratories, and the results were uploaded into PulseNet. As part of routine FDA-CVM *Salmonella* surveillance activity, retail meat samples were tested, analysed, and the results uploaded to PulseNet. CDC-NARMS performed antimicrobial susceptibility testing on selected patients' clinical isolates and leftover ground turkey samples using broth microdilution and resistance was determined by CLSI interpretive standards, when available [21]. Product and environmental samples obtained during USDA-FSIS's investigation of plant A were cultured for *Salmonella* at FSIS laboratories.

Statistical analysis

Data were analysed with SAS v. 9.2 software (SAS Institute Inc., USA). The proportion of patients reporting exposure to specific food items in the week prior to becoming ill was compared to the proportion reported in interviews of healthy persons in the FoodNet population survey, a population-based survey of the US population that includes questions about food consumption in the week prior to interview [22]. A binomial probability distribution was used to determine whether food exposures reported by patients were significantly more common than those reported in the FoodNet population survey.

RESULTS

Case-finding

We identified 136 cases of *S. Heidelberg* infection in 34 states (Fig. 1); interview and/or questionnaire information was available for 103 cases (76%). Dates of illness onset ranged from 27 February to 17 October 2011 (Fig. 2). The median age of patients was 23 years (range 6 months–90 years); 63/136 (46%) were female. Of the 96 ill persons with information available, 35 (36%) were hospitalized, and one death was reported.

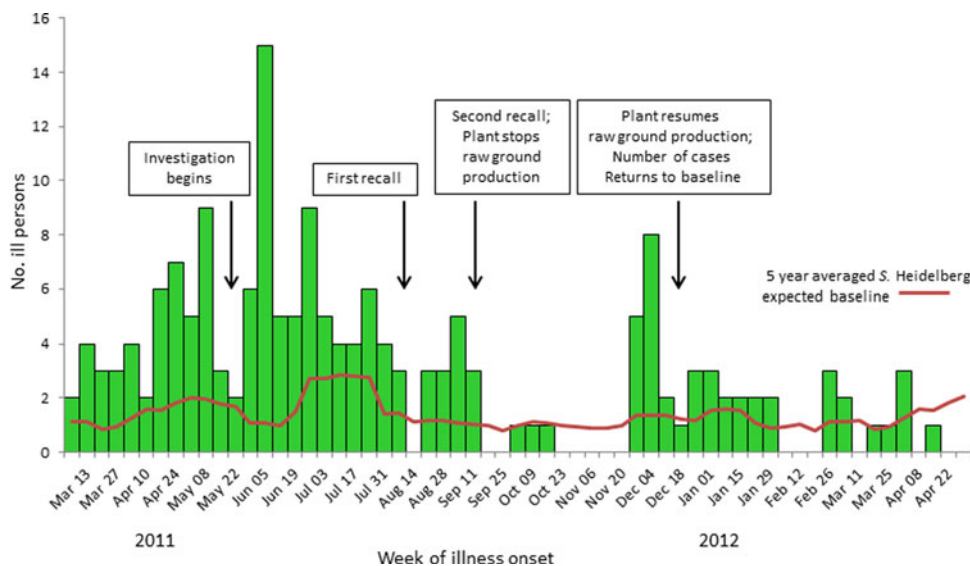


Fig. 2. Infections with the outbreak strain of *Salmonella* Heidelberg reported to PulseNet, March 2011–April 2012.

Table 1. Frequency of selected food exposures in patients with outbreak-associated illnesses vs. 2006 FoodNet population survey as of 7 July 2011

Exposure	Cases (N = 34) n/N (%)*	FoodNet population survey, %†	P value
Ground turkey	12/34 (35.3)	10.8	<0.001
Whole chicken	32/34 (94.1)	51.9	<0.001
Breaded chicken	13/34 (38.2)	21.1	0.01
Bologna	9/34 (26.5)	13.9	0.03
Eggs	28/34 (82.4)	75.4	0.11
Milk	28/34 (82.4)	78.5	0.15
Ground beef	7/34 (20.0)	39.8	–
Iceberg lettuce	11/34 (33.3)	45.7	–
Pre-packaged salad greens	11/34 (33.3)	39.1	–

* Any consumption in the 7 days prior to illness onset.
 † Foodborne Diseases Active Surveillance Network (FoodNet) Population Survey Atlas of Exposures, 2006–2007 [22].

Early in the investigation, we interviewed 34 patients, and 12 (35%) reported eating ground turkey in the 7 days prior to illness. This proportion was significantly higher than in the 2006 FoodNet population survey, in which 11% of healthy persons interviewed reported consuming ground turkey in the 7 days before they were interviewed ($P < 0.001$) [22] (Table 1). Patients were also significantly more likely than the FoodNet survey population to report having eaten whole chicken, breaded chicken, or bologna. Based on this initial information, we implemented a poultry-

specific questionnaire to ask in-depth questions about poultry consumption. From 7 July to 3 August 2011, we interviewed additional patients, and 17/28 (61%) reported ground turkey consumption. Overall, for the patients with *S. Heidelberg* infection interviewed during the outbreak 51/95 (54%) recalled consumption of ground turkey products in the week before illness onset.

Traceback and environmental investigation

The Ohio and Michigan state health departments discovered three patients with available shopper-card information who had purchased the same brand of ground turkey. This information was used to trace back the ground turkey to its source. USDA-FSIS traced this brand to a single production plant, plant A. Additionally, four ground turkey samples, representing this brand and a different brand, purchased as part of routine environmental NARMS FDA-CVM sampling between 7 March and 27 June 2011 yielded *S. Heidelberg* matching the outbreak strain PFGE pattern. All four samples originated from plant A. In total, eight different ground turkey brands reported by patients were traced back to plant A.

On 29 July 2011, a sample of leftover ground turkey from an Ohio patient’s home yielded the outbreak strain of *S. Heidelberg*, a second *S. Heidelberg* strain with a closely related PFGE pattern that differed by one restriction enzyme band (JF6X01.0032), and *Salmonella* serotypes Uganda and Saintpaul. Although packaging information was not available,

shopper-card information indicated that plant A was the likely source. A review of the PulseNet database showed 27 isolates with pattern JF6X01.0032 had been reported to PulseNet since 27 February 2011. Of patients who were interviewed with pattern JF6X01.0032, 12/13 (92%) reported consumption of ground turkey in the 7 days before their illness began. A retail sample of ground turkey collected on 23 May 2011 as part of routine environmental NARMS FDA-CVM sampling yielded an isolate with pattern JF6X01.0032. This retail sample originated from plant A. Based on these findings, the outbreak and case definition was expanded to include these 27 ill persons.

Laboratory investigation

Nineteen outbreak isolates from patients' samples or leftover ground turkey samples were sent to CDC NARMS for antimicrobial susceptibility testing. All isolates were MDR with the same pattern of resistance to ampicillin, gentamicin, streptomycin, and tetracycline [21].

Control measures

On 29 July 2011, USDA-FSIS released a public health alert for frozen or fresh ground turkey products [23]. This alert reminded consumers of the critical importance of following package cooking instructions for frozen or fresh ground turkey products and general food safety guidelines when handling and preparing any raw meat or poultry. On 3 August 2011, plant A recalled over 36 million pounds of raw ground turkey products, one of the largest USDA-FSIS Class I recalls in history [24]. Between 22 August and 5 October 2011, USDA-FSIS conducted a food safety assessment and incident investigation team (IIT) review at plant A. USDA-FSIS issued a Notice of Intended Enforcement (NOIE) to plant A on 7 September. An NOIE is issued to a plant for non-compliance that does not pose an imminent threat to public health. On 11 September 2011, as a result of isolation of the outbreak strain from ground turkey samples collected during the IIT, plant A recalled approximately 185 000 pounds of raw ground turkey products. On 13 September 2011, plant A ceased production of raw comminuted ground turkey products until corrective actions could be identified and implemented. The establishment reassessed and made changes to its *Salmonella* control programme, in

addition to performing strict ongoing assessments, to ensure that it is achieving *Salmonella* levels well below the *Salmonella* USDA-FSIS performance standard for ground turkey [14]. After the second recall, the number of cases dropped substantially (Fig. 2). In November, the number of cases with the outbreak strains reported to PulseNet returned to the previously observed levels.

DISCUSSION

Epidemiological, laboratory, traceback, and environmental investigations indicated that the likely source of this nationwide outbreak of *S. Heidelberg* was ground turkey products produced at plant A. Results from this investigation led USDA-FSIS to implement measures to better address *Salmonella* and raw ground poultry. Because the contaminated ground turkey was sold under different brand names, detailed information obtained from interviews with patients and grocery store shopper cards was vital to determine a link to plant A products. Use of NARMS FDA-CVM routine antimicrobial resistance surveillance data provided initial clues on possible food sources by uploading matching retail ground turkey PFGE patterns to PulseNet. NARMS then confirmed that resistance patterns of clinical and retail meat isolates were identical, further validating the link between illness and ground turkey. The clear link between the product and human illnesses was a key factor in prompting the recall.

MDR *Salmonella* remains an especially important threat to the US food supply. In 2011, 9.1% (213/2344) of non-typhoidal *Salmonella* human isolates were resistant to ≥ 3 CLSI antimicrobial classes. The serotype with the highest proportion of isolates with MDR was Heidelberg (30%, 21/70) [25]. Because MDR strains can be associated with increased morbidity and mortality, the high hospital rate of 36% (35/96) was an important factor motivating plant A to issue a recall. By comparison, hospitalization rates for non-MDR salmonellosis average approximately 24–27% [26, 27]. The use of antibiotics in food animals, including those used for growth promotion, is a possible contributing factor to the development of MDR bacteria. According to data published by FDA, there are more kilograms of antibiotics sold in the United States for food-producing animals than for people [28]. Recently, FDA-CVM issued new regulatory guidelines concerning the judicious use of medically important antimicrobials in livestock production [29, 30]. These guidelines (1)

allow animal pharmaceutical companies to voluntarily re-label antimicrobials for therapeutic use only and not for production purposes (e.g. promoting animal growth or feed efficiency), and (2) change the over-the-counter status of certain antimicrobials to bring them under veterinary oversight to treat, control, or prevent disease in livestock. Currently the new guidelines are voluntary, and FDA will allow a 3-year transition period for animal pharmaceutical companies to fully implement the plan. Such an approach could help reduce MDR *Salmonella* in the food supply, since resistance genes to multiple classes of drugs are commonly encoded on a single mobile element, such as a plasmid. In this case, resistance to ampicillin, gentamycin, streptomycin and tetracycline found in the outbreak strain were due to genes encoded on a single plasmid [21].

Two aspects of this investigation beyond those discussed above are noteworthy. First, we compared food exposures in patients to those reported by healthy persons in the 2006 FoodNet population survey, which was conducted 5 years before the outbreak. To the extent that poultry consumption in general and ground turkey consumption in particular may have increased over that time, this comparison could have overestimated the association between ground turkey and illness. An updated FoodNet survey would more accurately mirror current dietary preferences; however, it is doubtful that ground turkey consumption changed so markedly over these 5 years to weaken our conclusion, which is supported by multiple lines of evidence including the epidemiological associations, traceback investigations and laboratory profiles. Second, almost 6 months elapsed between 27 February 2011, when the first patient became ill and 4 August 2011, when the product was removed from commerce. Despite the indistinguishable clinical and NARMS isolates, no direct epidemiological link between illness and consumption of ground turkey was observed early in the investigation. An epidemiological link consists of finding the identical illness-causing organism in a patient's sample and in a sample of product recovered from the patient's home in its original packaging. Only in late July, through coordinated traceback efforts, interviews with patients, and the presence of the outbreak strain in leftover product, was enough evidence accumulated to implicate both a specific product and the production establishment.

Despite these limitations, this large outbreak played a vital role in strengthening USDA-FSIS food safety policies related to *Salmonella* and raw ground poultry.

Salmonella is not considered an adulterant in raw poultry products. In 2011, USDA-FSIS performance standards for ground turkey establishments allowed no more than 49.9% of the samples to test positive for *Salmonella*. In addition, up to 15% of ground turkey sampled at retail establishments were found to contain one or more strains of *Salmonella* [12, 14]. Under the notice informing establishments producing not-ready-to eat ground poultry to reassess their HACCP plan released by USDA-FSIS on 6 December 2012, FSIS explained that when poultry or meat products that are not ready-to-eat are associated with an illness outbreak and contain pathogens that are not considered adulterants (e.g. *Salmonella*), FSIS likely will consider the product linked to the illness outbreak to be adulterated because the product is unsound, unhealthful, unwholesome or otherwise unfit for human food [18]. In such cases, FSIS would request that the establishment recall the product if it is still in commerce, thereby facilitating a quick regulatory response to prevent additional human illness in future outbreaks. Combined with the FDA-CVM livestock antimicrobial use guidelines, this policy will continue to help reduce the public health burden of MDR salmonellosis and its attendant excessive morbidity and high hospitalization rates.

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DECLARATION OF INTEREST

None.

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