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Multi-drug Resistant *Salmonella* Hadar Infections Associated with Turkey Burger Consumption

ABSTRACT

In mid-January 2011, the Minnesota Department of Agriculture's (MDA) retail food sampling program detected *Salmonella* Hadar in a turkey product produced by a corporation with nationwide distribution. Enhanced surveillance led the Wisconsin Department of Health Services (WDHS) to notify the United States Department of Agriculture Food Safety and Inspection Service (FSIS) of three clinical cases of *Salmonella* Hadar infection from January. The case-patient isolates were indistinguishable by Pulsed-Field Gel Electrophoresis (PFGE) from the MDA sample. All samples had resistance to five antimicrobials on the Wisconsin State Laboratory of Hygiene (WSLH) clinical test panel. The WSLH determined that *Salmonella* isolated from intact turkey product from a case-patient's home was indistinguishable from the outbreak strain by PFGE and antimicrobial susceptibility testing. The Food Safety Inspection Service tworked with additional states with illnesses in the cluster to determine exposures. This report describes the investigation that resulted in the first FSIS raw poultry recall due to contamination with multi-drug resistant *Salmonella* in the United States.

INTRODUCTION

Multi-drug resistant (MDR) foodborne salmonellosis is an ongoing concern in the public health community *(13)*. Clinical human salmonellosis is generally a self-limiting illness characterized by fever, abdominal pain, diarrhea, nausea, and vomiting. Severe cases, which are characterized by dehydration or septicemia, require effective antimicrobials. For adults, fluoroquinolones are generally regarded as the optimal treatment, while cephalosporins are often used in children with serious infections. Alternative treatments include ampicillin, amoxicillin, chloramphenicol, and trimethoprim sulfamethoxazole *(2)*.
Salmonella Hadar is a serotype commonly associated with poultry *(15)*. In 2008, *Salmonella* Hadar accounted for nearly 14.7% (72/491) of *Salmonella* isolated from retail meats, a notable increase from the average of 6.6% seen from 2002 to 2006. S. Hadar has become the most common sterotype

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in ground turkey *(14)*. Antimicrobial-resistant *Salmonella* strains may be more virulent than antimicrobial-sensitive salmonellae *(4, 6, 9)*, though this is still a topic of debate. In 2008, 51% of all *Salmonella* isolates were MDR *(14)*. From 2002 to 2007, MDR *Salmonella* (resistant to three or more antimicrobial classes) ranged from 20.3% to 42.6% among isolates in ground turkey *(14)*. Importantly, fluoroquinolone resistance has rarely been reported in *Salmonella* Hadar in the United States *(14)* as well as in *Salmonella* Hadar isolated from turkey meat in Denmark *(3)*. Fluoroquinolone resistance also is an emerging issue in *Salmonella* Kentucky, another serotype common in poultry *(11)*.

The United States Department of Agriculture, Food Safety and Inspection Service (FSIS) has recalled products because of contamination with MDR *Salmonella* associated with human illness. In 2009, a cluster of 42 MDR *Salmonella* Newport illnesses in 11 states was linked to consumption of ground beef; the investigation resulted in a recall of 825,769 lbs of ground beef *(7)*. Also in 2009, a cluster of 15 MDR *Salmonella* Typhimurium illnesses in Colorado was linked to consumption of ground beef, which resulted in a recall of 466,236 pounds of ground beef *(8)*. This report describes the investigation that resulted in the first FSIS raw poultry recall due to contamination with MDR *Salmonella*.

MATERIALS AND METHODS

Clinical laboratories send *Salmonella* isolates from case-patients to state public health laboratories for serotyping and Pulsed-Field Gel Electrophorsis (PFGE) subtyping *(18)*. State public health laboratories submit PFGE subtyping results to the national molecular subtyping network for foodborne disease surveillance (PulseNet) database for rapid detection of disease clusters. In this investigation, the Wisconsin State Laboratory of Hygiene (WSLH) additionally performed antimicrobial susceptibility testing on the *Salmonella* Hadar clinical isolates, using Clinical and Laboratory Standards Institute (CLSI) protocols. Also using CLSI automated protocols, but testing a different panel of antimicrobials, a Colorado hospital laboratory performed antimicrobial susceptibility testing on a single *Salmonella* Hadar clinical isolate.

A case was defined as a in a person with laboratory-confirmed *Salmonella* Hadar infection with PFGE XbaI pattern indistinguishable from the outbreak strain isolated between December 27, 2010 and March 29, 2011. FSIS worked with 10 health departments in states with cases in the cluster. State and local health departments conducted case-patient interviews concerning poultry consumption in the seven days prior to diarrheal onset, including type of product and brand. Case-patients (or their families) also were asked about hospitalization. Findings from these interviews were provided to FSIS.

The Wisconsin Department of Agriculture Trade and Consumer Protection—Bureau of Laboratory Services (DATCP-BLS) conducted culture and isolation from the product purchased in Wisconsin. The product isolate was sent to the WSLH for serotyping, PFGE subtyping, and susceptibility testing (using Clinical and Laboratory Standards Institute (CLSI) protocols). The Colorado Department of Public Health and Environment Laboratory Services Division (CDPHE) performed culture, isolation, serotyping, and PFGE subtyping from the product consumed by the Colorado case-patient. Susceptibility testing was performed at USDA Agricultural Research Service (ARS) using National Antimicrobial Resistance Monitoring System (NARMS) sensititre methods for the Colorado and Wisconsin product isolates.

FSIS reviewed historic *Salmonella* Pathogen Reduction/ Hazard Analysis and Critical Control Points (HACCP) verification sampling results for *Salmonella* Hadar at the Company A processing establishment and at the slaughter establishments that supplied the source products. Establishments use PR/HACCP to identify where potential hazards are likely to occur and take steps to prevent, eliminate, or mitigate these hazards to ensure product safety. FSIS verifies that establishments are operating effectively under their PR/HACCP plan. In addition, FSIS requested PFGE and NARMS data from the USDA Agricultural Research Service, Bacterial Epidemiology and Antimicrobial Resistance research unit (ARS-BEAR) to determine historic *Salmonella* trends at Company A.

RESULTS

In mid-January 2011, the Minnesota Department of Agriculture's retail food sampling program detected *Salmonella* Hadar in a turkey and gravy product produced by Company A, a corporation with nationwide distribution. A Minnesota case-patient with infection of the same serotype and indistinguishable PFGE pattern reported turkey consumption; however, the product had been purchased and then frozen six months prior to consumption. Additional product traceback information was not available from this case-patient. At approximately the same time, two clinical *Salmonella* Hadar isolates with indistinguishable PFGE results were uploaded in Wisconsin. FSIS asked the Wisconsin Department of Health Services (WDHS) for the dietary histories of the case-patients; one case-patient was lost to follow-up and a reliable food history could not be obtained from the other case-patient.

On February 11, 2011, WDHS notified FSIS of another case-patient with *Salmonella* Hadar infection with an indistinguishable PFGE pattern. The case-patient reported consuming Company A turkey burgers in the seven days prior to illness onset. During a follow-up interview, the case-patient reported having unopened, individually wrapped Company A turkey burger product that was from the same box as the product that had been consumed prior to illness. The case-patient's family was willing to have it tested. WDHS

also reported that all three Wisconsin *Salmonella* Hadar case-patients with indistinguishable PFGE patterns collected during 2011 had similar antibiograms, with resistance to five antimicrobials on the WSLH test panel. One of the three case-patients was hospitalized overnight.

On February 20, 2011, the DATCP-BLS reported that *Salmonella* Hadar had been recovered from the unopened turkey burger product from the third case-patient's home. The isolate was submitted to the WSLH for PFGE subtyping. On February 22, 2011, WSLS found the isolate to be indistinguishable from the outbreak strain by PFGE and antimicrobial susceptibility testing. FSIS worked with other state health departments with isolates matching the cluster to determine additional case-patient exposures.

On March 3, 2011, the CDPHE notified FSIS of a hospitalized case-patient with MDR *Salmonella* Hadar who had consumed Company A turkey burgers prior to illness onset. Leftover product collected from the case-patient's home tested positive for *Salmonella* Hadar, with a PFGE pattern indistinguishable from that of the outbreak strain. FSIS assisted the CDPHE in obtaining shopper card information, which was consistent with purchase of brand A turkey burger product on January 3, 2011.

On March 14, 2011, the Ohio Department of Health notified FSIS of a case-patient who was hospitalized with *Salmonella* Hadar infection and who had a history of consuming Company A turkey burgers. Additional information was not available.

On March 18, 2011, the New Mexico Department of Health uploaded the PFGE pattern for an unopened product with the outbreak strain of *Salmonella* Hadar to PulseNet as part of NARMS retail sampling.

Nineteen case-patients in 13 states were infected with the outbreak strain of *Salmonella* Hadar. Of the 13 case-patients interviewed, 4 (30.8%) reported consuming Company A turkey burgers, and 4 (30.8%) reported consuming other turkey or chicken products (one of these reported exposures also involved a different turkey product produced by Company A). Two case-patients did not report any known poultry exposure; one of these also did not report any symptoms of diarrheal illness.

Of the 12 interviewed case-patients with diarrhea, 4 (33.3%) were hospitalized overnight, and 1 (8.3%) required an emergency room visit. Hospital stays ranged from two to six nights. Data on whether antimicrobials were given during treatment was not available. Three of the hospitalized case-patients (75.0%) had consumed Company A turkey burgers. Two (50.0%) of these case-patients had leftover product to test.

Investigation of multiple establishments owned by Company A revealed an extensive history of *Salmonella* samples collected during PR/HACCP testing that were positive for *Salmonella* Hadar with PFGE patterns indistinguishable from that of the outbreak strain. Of 23 *Salmonella* Hadar isolates with this pattern collected during 2008 to 2011 from three Company A establishments, 73.9% (17/23) were MDR via NARMS testing. Three samples were resistant to four antimicrobials (ampicillin, kanamycin, streptomycin, and tetracycline), 14 samples were resistant to three of the aforementioned antimicrobials, four samples were resistant to two antimicrobials, and two samples were resistant to a single antimicrobial.

The Wisconsin turkey burger isolate expressed intermediate resistance to amoxicillin-clavulanate (MIC = 24 g/ml) and resistance to ampicillin (MIC > 64 g/ml), cephalothin (MIC=32 g/ml), streptomycin (MIC > 96 g/ml), and tetracycline (MIC > 32 g/ml). The three Wisconsin clinical isolates had similar patterns. One expressed intermediate resistance to amoxicillin-clavulanate; the other two were resistant to all five of the antimicrobials just listed. The product isolate tested by ARS expressed intermediate resistance to amoxicillin-clavulanate (MIC=16 g/ml) and resistance to ampicillin (MIC > 32 g/ml) and tetracycline (MIC > 32 g/ml). Cephalothin was not included in the NARMS panel used by ARS. Resistance to streptomycin was not detected (MIC <= 32).

The Colorado case-patient's clinical isolate expressed resistance to ampicillin (MIC >= 32 g/ml), ampicillin/sulbactam (MIC >= 32 g/ml), piperacillin/tazobactam (MIC >= 128 g/ml), and amikacin (MIC <= 2 g/ml). The Colorado turkey burger isolate tested by ARS expressed intermediate resistance to amoxicillin-clavulanate (MIC=16 g/ml) and resistance to ampicillin (MIC >32 g/ml) and tetracycline (MIC = 32 g/ml).

The implicated product was produced at a large, integrated corporation. Lot codes from product collected at the Wisconsin case-patient's home and shopper information from the Colorado case-patient were used to trace production dates. Lot codes from product collected at the Wisconsin case-patient's home traced production back to a single shift during a single day. Likewise, Colorado shopper card information identified the product purchased as having originated from the same establishment and production day. FSIS does not classify *Salmonella* as an adulterant in raw poultry, because proper cooking and handling should eliminate the potential for illness from this pathogen. However, in light of the illnesses and hospitalizations that occurred in conjunction with consumption of this product, combined with laboratory, epidemiological, and establishment traceback findings, the product was determined to be injurious to health. Notably, only one of the twelve symptomatic case-patients mentioned the possibility of having consumed undercooked product. Proper cooking and handling of raw comminuted poultry products is of particular concern *(10)*.

On April 1, 2011, Company A recalled nearly 55,000 pounds of frozen raw turkey burger products. FSIS traced records back to two production lot ranges (products produced during a particular day and production shift); one lot was implicated in the illnesses and was recalled. FSIS performed

a food safety assessment, a specialized and comprehensive investigation of the establishment's food safety system decisions, design, and controls, from April to May 2011; FSIS issued a Notice of Intended Enforcement (NOIE) in early May 2011 to Company A. An NOIE is issued for noncompliance that does not pose an imminent threat to public health but may warrant a withholding or suspension action if not corrected. Among other findings, the issuance cited lack of validated cooking instructions.

FSIS worked with the Centers for Disease Control and Prevention (CDC) to monitor PulseNet for new case-patients with indistinguishable PFGE patterns for the next 60 days to determine whether the scope of the recall was adequate. The FSIS Consumer Complaint Monitoring System (CCMS) logged several illness-related complaints related to Company A turkey burgers during this time. Leftover product from two complainants' homes was tested for *Salmonella*. Neither of the samples was positive for the outbreak strain.

DISCUSSION

Although a small number of cases were identified during this specific outbreak investigation, previous studies have demonstrated an estimated 38.6 cases of salmonellosis for each culture-confirmed case *(20)*. Among those in the cluster exposed to Company A turkey burgers within a week of illness onset, FSIS was concerned by the unusually high proportion of hospitalized case-patients and the multidrug resistance of the *Salmonella* involved. It is not known whether the multidrug resistance of this strain resulted in treatment failure for any of the hospitalized case-patients; such information would be useful for further understanding of the public health impacts of MDR *Salmonella* infections.

A number of factors affect the susceptibility of poultry to *Salmonella* colonization, including age, serotype, dose level, stress, feed additives, and genetic background *(1, 12)*. Additionally, in high-density production environments such as in poultry settings, the potential for disease spread increases. In a 2010 NARMS survey of *Salmonella* Hadar from 1996 to 2008, 41.8% of isolates from retail meat were resistant to three or more antimicrobial classes. Among *Salmonella* Hadar isolates from the food animals at slaughter, 19.4% were MDR *(17)*. It is important to note that these resistance results are less striking than the 73.9% of *Salmonella* Hadar MDR PR/HACCP samples found at Company A.

Based on recent FSIS nationwide microbiological baseline data collection, new, stricter *Salmonella* standards were implemented by FSIS in July 2011. Following these standards, an establishment passes *Salmonella* verification testing if no more that five samples are positive in a 51-sample set for young chickens and if no more than four samples are positive in a 51-sample set for turkeys. FSIS estimates that 20,000 illnesses will be avoided under the revised standards, which are set at 7.5 and 1.7 percent *Salmonella* positive in young chicken (broilers) and young turkey, respectively, compared to the former standards of 20 and 19 percent positive *(5, 16, 19)*. This investigation, which resulted in the first-ever FSIS raw poultry recall due to contamination with MDR *Salmonella* in the United States, would not have been possible without extensive coordination among public health partners, including regulatory agencies.

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