

Multistate Outbreak of Listeriosis Linked to Turkey Deli Meat and Subsequent Changes in US Regulatory Policy

Sami L. Gottlieb,¹ E. Claire Newbern,^{1,4} Patricia M. Griffin,¹ Lewis M. Graves,¹ R. Michael Hoekstra,¹ Nicole L. Baker,¹ Susan B. Hunter,¹ Kristin G. Holt,² Fred Ramsey,² Marcus Head,³ Priscilla Levine,⁵ Geraldine Johnson,⁶ Dianna Schoonmaker-Bopp,⁶ Vasudha Reddy,⁷ Laura Kornstein,⁷ Michal Gerwel,⁸ Johnson Nsubuga,⁹ Leslie Edwards,¹⁰ Shelley Stonecipher,¹¹ Sharon Hurd,¹² Deri Austin,¹³ Michelle A. Jefferson,¹ Suzanne D. Young,¹ Kelley Hise,¹ Esther D. Chernak,⁴ Jeremy Sobel,¹ and the Listeriosis Outbreak Working Group^a

¹Centers for Disease Control and Prevention and ²United States Department of Agriculture–Food Safety and Inspection Service, Atlanta, and ³United States Department of Agriculture–Food Safety and Inspection Service, Athens, Georgia; ⁴Philadelphia Department of Public Health, Pennsylvania; ⁵United States Department of Agriculture–Food Safety and Inspection Service, Washington, DC; ⁶New York State Department of Health, Albany, and ⁷New York City Department of Health and Mental Hygiene, New York; ⁸New Jersey Department of Health and Senior Services, Trenton; ⁹Massachusetts Department of Public Health, Boston; ¹⁰Maryland Department of Health and Mental Hygiene, Baltimore; ¹¹Michigan Department of Community Health, Lansing; ¹²Connecticut Emerging Infections Program, New Haven; and ¹³Delaware Health and Social Services, Dover

Background. Listeriosis, a life-threatening foodborne illness caused by *Listeria monocytogenes*, affects ~2500 Americans annually. Between July and October 2002, an uncommon strain of *L. monocytogenes* caused an outbreak of listeriosis in 9 states.

Methods. We conducted case finding, a case-control study, and traceback and microbiological investigations to determine the extent and source of the outbreak and to propose control measures. Case patients were infected with the outbreak strain of *L. monocytogenes* between July and November 2002 in 9 states, and control patients were infected with different *L. monocytogenes* strains. Outcome measures included food exposure associated with outbreak strain infection and source of the implicated food.

Results. Fifty-four case patients were identified; 8 died, and 3 pregnant women had fetal deaths. The case-control study included 38 case patients and 53 control patients. Case patients consumed turkey deli meat much more frequently than did control patients ($P = .008$, by Wilcoxon rank-sum test). In the 4 weeks before illness, 55% of case patients had eaten deli turkey breast more than 1–2 times, compared with 28% of control patients (odds ratio, 4.5; 95% confidence interval, 1.3–17.1). Investigation of turkey deli meat eaten by case patients led to several turkey processing plants. The outbreak strain was found in the environment of 1 processing plant and in turkey products from a second. Together, the processing plants recalled >30 million pounds of products. Following the outbreak, the US Department of Agriculture's Food Safety and Inspection Service issued new regulations outlining a *L. monocytogenes* control and testing program for ready-to-eat meat and poultry processing plants.

Conclusions. Turkey deli meat was the source of a large multistate outbreak of listeriosis. Investigation of this outbreak helped guide policy changes designed to prevent future *L. monocytogenes* contamination of ready-to-eat meat and poultry products.

Listeriosis, a life-threatening, primarily foodborne illness caused by *Listeria monocytogenes*, affects an estimated 2500 people in the United States annually [1].

Immunocompromised persons, elderly persons, and pregnant women and their fetuses or newborns are at highest risk for infection [2]. Listeriosis most commonly presents as an invasive illness with bacteremia or meningitis and has a case-fatality rate of 20% [3]. In pregnancy, listeriosis may lead to fetal death, preterm labor, or invasive listeriosis in the newborn child [2]. We describe the investigation of a large, multistate listeriosis outbreak in 2002 that was linked to turkey deli meat and prompted new changes in US food regulatory policy.

Received 26 April 2005; accepted 7 August 2005; electronically published 23 November 2005.

^a Listeriosis Outbreak Working Group members are listed at the end of the text. Reprints or correspondence: Dr. Sami Gottlieb, Div. of STD Prevention, Centers for Disease Control and Prevention, 1600 Clifton Rd., MS E-02, Atlanta, GA 30333 (stg8@cdc.gov).

Clinical Infectious Diseases 2006;42:29–36

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METHODS

Case finding. During July and August 2002, there were 22 cases of listeriosis reported in Pennsylvania, a nearly 3-fold increase over baseline. Clinical isolates were sent to the Centers for Disease Control and Prevention (CDC; Atlanta, GA) for molecular subtyping by PFGE, which identified a cluster of cases caused by a single *L. monocytogenes* strain. The CDC asked health departments in the northeast United States to conduct active case finding, prompt reporting of listeriosis cases, and retrieval of clinical isolates for rapid PFGE testing via PulseNet. PulseNet, the National Molecular Subtyping Network for Foodborne Disease Surveillance, is the CDC-coordinated network of public health laboratories that perform PFGE on foodborne bacteria [4]. The network permits rapid electronic comparison of PFGE patterns through a database at the CDC. PulseNet staff compared the electronically posted PFGE patterns from all public health laboratories to the PFGE pattern from the Pennsylvania cluster.

Definitions. Listeriosis was defined as illness in a person from whom *L. monocytogenes* was isolated (from any clinical specimen). The 2-enzyme PFGE pattern from the Pennsylvania listeriosis cluster was designated as the outbreak pattern. Infection with the outbreak strain was defined as having listeriosis with an *L. monocytogenes* isolate yielding a PFGE pattern indistinguishable from the outbreak pattern. For the purposes of case counting, a mother-neonate pair was considered to be 2 cases if both mother and newborn were ill and had culture-confirmed *L. monocytogenes* infection; if only one of the pair was ill with culture-confirmed *L. monocytogenes* infection, only 1 case was counted. However, for the purposes of the case-control study, a mother-neonate pair was always considered to be a single case. For an ill pregnant woman with an associated fetal death (stillbirth or miscarriage), only the mother's illness was counted as a case.

Case-control study. We conducted a case-control study to identify the contaminated food source. A case patient was defined as a person with culture-confirmed listeriosis between 1 July and 30 November 2002, whose infection was caused by the outbreak strain. A control patient was defined as a person with culture-confirmed listeriosis between 1 July and 30 November 2002, whose infection was caused by any other non-outbreak strain of *L. monocytogenes*, and who was from a state with at least 1 case patient. Case patients and control patients were interviewed with a standard questionnaire that addressed medical and food histories during the 4 weeks preceding culture for *L. monocytogenes* (all patients except mother-neonate pairs) or delivery date (mother-neonate pairs). The questionnaire included >70 specific food items.

Statistical methods. Statistical analyses were performed with SAS software, version 8.2 (SAS). Food exposures of case patients and control patients were compared using the Wil-

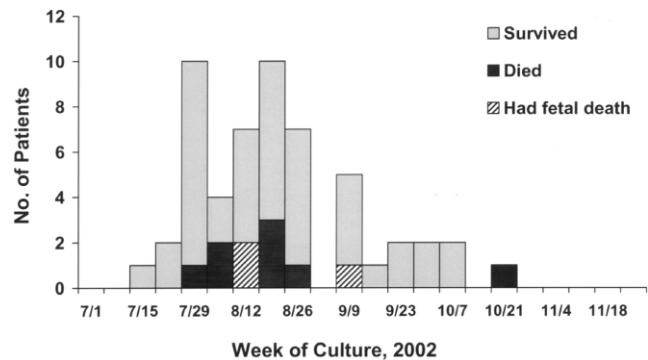


Figure 1. Number of patients infected with the outbreak strain of *Listeria monocytogenes*, by week of culture, July to November 2002 ($n = 54$).

coxon rank-sum test. ORs and exact 95% CIs were calculated, controlling for state or city by conditional logistic regression.

Traceback investigation. Health and regulatory officials traced back the food implicated in the case-control study. A purchase site was defined as any delicatessen, grocery store, or restaurant where the implicated food consumed by a case patient was purchased. Inventories and invoice information were obtained from purchase sites to determine which processing plants had supplied the food.

Plant investigations. Plants A, B, C, and D were investigated by teams led by the US Department of Agriculture's Food Safety and Inspection Service (FSIS). Noncompliance reports, production and construction records, and records of product and environmental sampling for *Listeria* species maintained by plant staff were reviewed. Environmental samples were collected aseptically by cellulose sponge. Unopened food products were collected from each plant's "shelf-life" stock and from current production. Recalled products from plant A were also collected.

Laboratory investigation. PFGE testing was performed in accordance with the standard PulseNet protocol using restriction endonucleases *AscI* and *Apal* [5]. Study isolates were confirmed at the CDC to be *L. monocytogenes* by AccuProbe (GenProbe), ribotyped using the RiboPrinter microbial characterization system (Qualicon), and serotyped using standard methods [6].

Food samples were transported at 4°C and cultured for *L. monocytogenes* using standard methods [7]. Environmental sponges were transported at 4°C in Dey-Engley neutralizing media and tested using the standard methods mentioned above. *L. monocytogenes* isolates were subtyped by PFGE in the same manner as were human isolates. PFGE patterns were electronically compared with human isolate patterns through PulseNet.

RESULTS

Case finding and description. Between 1 July and 30 November 2002, there were 188 patients with *L. monocytogenes*

infection identified in 9 states: Pennsylvania, New York, New Jersey, Delaware, Maryland, Connecticut, Massachusetts, Michigan, and Illinois. Of these patients, 54 were infected with the outbreak strain, 1 was infected with a strain that resembled the outbreak strain but differed by 1 band on the *ApaI* PFGE analysis, and 122 were infected with unrelated *L. monocytogenes* strains; no isolates were available for 11 patients. The dates of specimen collection for the 54 case patients ranged from 18 July to 26 October (figure 1). Of the ~2000 human *L. monocytogenes* isolates in the PulseNet database from the 6 years before the outbreak, only 20 were indistinguishable from the outbreak PFGE pattern (PulseNet pattern designation GX6A16.0235-GX6A12.0003). All outbreak strain isolates tested were serotype 4b and ribotype DUP-1044.

Characteristics of the 54 case patients and 122 control patients are shown in table 1. Eight case patients (15%) were pregnant women, and 4 (7%) were neonates. Prior medical information was available for 41 of the 42 non-maternal-neonatal case patients. Thirty patients (71%) had the following medical conditions or factors, which are considered to be im-

munocompromising or predisposing for listeriosis: hematologic malignancy (5 patients), corticosteroid use (4 patients), HIV infection and/or AIDS (4 patients), solid malignancy (3 patients), diabetes (3 patients), liver disease (3 patients), inflammatory bowel disease (3 patients), organ transplantation (2 patients), end-stage renal disease (1 patient), rickets and malnutrition (1 patient), and sickle-cell anemia (1 patient). Most elderly case patients also had an underlying immunocompromising condition; only 4 (7%) of the 54 case patients were aged ≥ 65 years and were not immunocompromised. Seven patients (13%) were aged 1–64 years and were not pregnant or immunocompromised. Case patients were more likely than control patients to be pregnant or young and healthy (i.e., aged 1–64 years without predisposing medical conditions [$P < .001$]).

Eight (15%) of 54 case patients died. Of these, 4 patients were aged 1–64 years and were immunocompromised, 3 were aged ≥ 65 years and were also immunocompromised, and 1 was a neonate. The case-fatality rate among case patients was lower than that among control patients (15% vs. 26%), although not significantly ($P = .14$). However, among immu-

Table 1. Characteristics of case patients and control patients, 1 July–30 November 2002.

Characteristic	Case patients (n = 54)	Control patients (n = 122)
State and/or city		
Pennsylvania	15 (28)	27 (22)
New York (excluding New York City)	9 (17)	20 (16)
New York City	12 (22)	12 (10)
New Jersey	5 (9)	19 (16)
Delaware	4 (7)	1 (1)
Maryland	2 (4)	10 (8)
Connecticut	1 (2)	8 (7)
Michigan	1 (2)	10 (8)
Massachusetts	3 (5)	12 (10)
Illinois	2 (4)	3 (2)
Sex ^a		
Male	32 (59)	54 (45)
Female	22 (41)	67 (55)
Pregnant	8 (15)	4 (3)
Neonate	4 (7)	9 (7)
Immunocompromised, by age ^b		
≥ 65 years	13 (25)	45 (45)
1–64 years	17 (32)	30 (30)
Not immunocompromised, by age ^b		
≥ 65 years	4 (7)	7 (7)
1–64 years	7 (13)	4 (4)
Death	8 (15)	32 (26)
Pregnancy complication(s)	6	3
Fetal death	3	2

NOTE. Data are no. (%) of patients.

^a Sex was unknown for 1 control patient.

^b Prior medical information was unavailable for 1 case patient and 23 control patients.

Table 2. Selected food exposures among case patients and control patients.

Food item, by frequency of consumption during 4 weeks before illness	No. (%) of case patients ^a	No. (%) of control patients ^a	<i>P</i> ^b	OR ^c	95% CI	<i>P</i>
Turkey breast deli meat from restaurant or deli counter			.008			
More than 1–2 times	21 (55)	14 (29)		4.5	1.3–17.1	.012
1–2 times	8 (21)	14 (29)		1.1	0.3–4.7	1.000
Never	9 (24)	21 (43)		1.0	Referent	...
Other turkey deli meat ^d from restaurant or deli counter			.030			
More than 1–2 times	6 (17)	3 (6)		3.0	0.6–20.3	.240
1–2 times	3 (8)	1 (2)		5.7	0.4–305.3	.260
Never	27 (75)	45 (92)		1.0	Referent	...
Loose lettuce			.030			
More than 1–2 times	8 (22)	22 (44)		0.3	0.1–0.9	.039
1–2 times	10 (27)	10 (20)		0.7	0.2–2.4	.706
Never	19 (51)	18 (36)		1.0	Referent	...

^a In some cases, data were not available for all patients.

^b By Wilcoxon rank-sum test. The Wilcoxon *P* value reflects comparisons of all levels of food consumption.

^c Adjusted odds ratio, controlling for state or city (for New York City), for categorized levels of food consumption.

^d For example, turkey ham or turkey pastrami.

nocompromised and neonatal patients, the case-fatality rates were similar: 24% for case patients versus 29% for control patients. Of the 8 pregnant case patients, 6 (75%) had complications: 3 had fetal deaths, 2 gave birth to infants with listeriosis (1 birth was premature), and 1 woman gave birth prematurely to an infant without listeriosis. Complications among the 4 pregnant control patients were similar, with 2 fetal deaths and 1 birth of an infant with listeriosis.

Institution-associated infections. Some listeriosis infections appeared to have been acquired nosocomially, presumably from food served at medical institutions. Although we did not explicitly ask about prior hospitalization, review of written comments on 122 interview forms revealed that 22 patients (18%) reported staying in a hospital, nursing home, or rehabilitation center in the 4 weeks before submitting specimens for *L. monocytogenes* culture. Dates of institutionalization were recorded for 15 patients, most of whom had been in the institution for almost the entire 4-week period (median, 28 days [range, 5–28 days]). We obtained institution menus or interviewed dietary staff for 10 patients. Turkey deli meat (not specified as being “heated” or “hot”) was offered to 8 of these patients during their stays in the institutions. An additional 3 patients, for whom hospital menus were not available, reported being served turkey deli meat while hospitalized.

Case-control study. Questionnaire responses were obtained from 91 (91%) of 100 eligible case patients and control patients. We excluded patients identified after the announcement of case-control study findings on 4 October 2002 (*n* = 73). Three mother-neonate pairs were counted as single patients. The final epidemiologic analysis included data obtained from 38 case patients and 53 control patients (table 2). Infection with the outbreak strain was strongly associated with consumption of

precooked turkey breast products sliced at the deli counter of groceries and restaurants (*P* = .008, by Wilcoxon rank-sum test). The Wilcoxon rank-sum test captures differences in the frequency of consumption. Overall, 55% of case patients ate turkey deli meat more than 1–2 times in the 4-week period, compared with 29% of control patients (OR, 4.5; 95% CI, 1.3–17.1). Other turkey deli meats, such as turkey ham and turkey pastrami, were eaten by fewer patients and primarily by persons who also ate turkey breast products. Therefore, it was difficult to exclude risk from these deli meats as well. No other single food item was significantly associated with outbreak strain infection, except for lettuce, which was protective.

Traceback. Interviews of the first 29 case patients who had eaten turkey deli meat identified 80 purchase sites (mean, 3 sites per person [range, 1–8 sites]). None of the patients recalled the brand names of all turkey deli meat purchased. Sixty-eight of the 80 purchase sites could be located; 57 (84%) of these

Table 3. Results of testing of the environment and previously unopened turkey products at 4 turkey processing plants.

Plant	No. of environmental samples			No. of unopened product samples		
	Total tested	LMP	With outbreak strain	Total tested	LMP	With outbreak strain
A	57	25	2	108	2 ^a	0
B	48	1	0	18	2	2
C	50	0	...	6	0	...
D	51	0	...	6	0	...

NOTE. LMP, *Listeria monocytogenes*-positive.

^a Two different strains were identified; both were also found in the plant’s environment and isolated from 2 control patients during the outbreak.

Table 4. Previously opened turkey product testing yielding the outbreak strain of *Listeria monocytogenes*.

Product	How and where product was obtained	Brand on product label	Plant(s) supplying turkey to purchase site
1	Routine inspection of New York City delicatessen	Unknown	Plants A and B
2	Traceback evaluation of New York City delicatessen	Plant C	Plants A, B, C, and D
3	Traceback evaluation of New York City delicatessen	Plant B	Plant B
4	Case patient's sandwich, Massachusetts	Plant A ^a	Plants A and B

^a A relative of the patient called the market where the turkey was purchased and, after describing its label information, was told the turkey was a plant A product.

were investigated, with identification of products from >50 turkey processing plants. FSIS evaluated the 15 most frequently identified plants, using a standardized survey to address such factors as previous food safety infractions, history of recent construction, and records of in-plant *Listeria* species sampling. On the basis of these survey results, plants A, B, C, and D were found to warrant in-plant investigation.

Processing plant and marketplace investigations. Multiple *L. monocytogenes* strains were identified in the environment of plant A (table 3). Two samples, both collected from floor drains, yielded the outbreak strain. Another isolate yielded a PFGE pattern differing from the outbreak pattern by 1 band, which was indistinguishable from that of 1 patient's isolate during the outbreak. Records of the plant's in-house environmental sampling in the room where cooked turkey was handled revealed an increase in the number of samples that yielded *Listeria* species during July and August 2002, compared with previous months and with the same months in 2001. This increase in positive test results coincided with a large construction project performed in the same room. Testing of previously unopened turkey products from plant A did not yield the outbreak strain (table 3). However, it did yield 2 *L. monocytogenes* strains that were also found in the plant's environment and that were isolated from 2 control patients. The outbreak strain of *L. monocytogenes* was not recovered from any environmental samples from plant B. However, the outbreak strain was isolated from 2 of 18 previously unopened turkey samples produced by plant B. Plant B is located ~30 miles from plant A.

Sampling of previously opened packages of turkey yielded the outbreak strain on 4 occasions (table 4). At the time of interview, only 1 case patient still had a sample of the turkey eaten before illness. A sandwich made with the same turkey deli meat consumed on 2 previous days was left in a cooler when an otherwise healthy young man was admitted to a hospital with *L. monocytogenes* bacteremia. The sandwich was retrieved from the cooler 2 weeks later, and *L. monocytogenes* with the outbreak PFGE pattern was isolated from the turkey. Invoice records revealed that only turkey products from plant

A and plant B were sold at the market where the patient purchased the turkey.

Regulatory outcomes. In response to these findings, plants A and B voluntarily suspended operations and began intensive cleanup, and together they recalled >13.5 million kg (>30 million lbs) of ready-to-eat poultry products. The first recall occurred on 9 October 2002. In December 2002, immediately following the outbreak, FSIS issued a policy directive outlining an intensified microbiological testing program for ready-to-eat meat and poultry plants [8]. Over the following year, FSIS completed a risk assessment for *L. monocytogenes* in deli meats [9] and finalized and issued a new regulation aimed at further reducing *L. monocytogenes* contamination of ready-to-eat meat and poultry products [10].

DISCUSSION

We investigated a multistate outbreak of listeriosis that affected 54 persons and caused 8 deaths and an additional 3 fetal deaths. An epidemiologic investigation linked outbreak strain infection with consumption of precooked, ready-to-eat turkey deli meat, making this the third multistate listeriosis outbreak related to ready-to-eat meat and poultry products in recent years [11, 12]. The outbreak strain of *L. monocytogenes* was found in the environment of plant A and in turkey breast products from plant B. Both plants suspended production and together recalled >13.5 million kg (>30 million lbs) of products, resulting in one of the largest meat recalls in US history. In the year following the outbreak, federal regulators issued new, more-stringent rules designed to prevent further *L. monocytogenes* contamination of ready-to-eat meat and poultry products [8, 10].

L. monocytogenes has 2 unique characteristics that influence its transmission to humans through ready-to-eat foods. First, it is a tenacious colonizer that favors moist, cool environments, such as food processing plants; eradication is difficult [13]. Second, although it is easily killed by cooking, *L. monocytogenes* multiplies readily at refrigeration temperatures, whereas most other competing microflora do not [14]. A small amount of

L. monocytogenes contamination at a processing plant that occurs after cooking but before packaging may lead to a large infectious dose being delivered to a susceptible consumer, because of multiplication of bacteria during storage [15]. Ready-to-eat poultry products, such as turkey deli meat, provide a particularly favorable environment for growth of *L. monocytogenes* during refrigeration [15]. Recent risk assessment models have estimated that, among ready-to-eat foods, deli meats and nonreheated hot dogs have the highest risk of listeriosis per serving [16].

Outbreak investigations can highlight high-risk food items and target regulatory, industry, and public health action. Our investigation led us to 2 plants. Plant B was likely linked to illnesses, because the outbreak strain was found in its turkey products. It is also possible that plant A was linked to illnesses, because the outbreak strain and several other *L. monocytogenes* strains were found throughout the main room where unpackaged turkey products were handled. In addition, 2 nonoutbreak strains were found in both the plant environment and in packaged turkey products, demonstrating the likelihood of ongoing contamination of products within the plant. The geographic proximity of plants A and B could allow introduction of a shared strain by receiving raw turkey products from the same slaughterhouse, purchasing equipment from the same source, or having employees in common [17]. A better understanding of the ecology of *L. monocytogenes* strains in ready-to-eat food plants would help guide efforts to prevent *L. monocytogenes* contamination of high-risk products.

Findings from this investigation helped guide FSIS in developing its new regulatory policy [8, 10]. Under these regulations, plants producing high-risk, ready-to-eat meat and poultry products must develop scientifically validated *L. monocytogenes*-control programs, which are stratified according to the number of control measures taken. One such measure is the institution of pathogen-elimination treatments after the product has been packaged, such as postpackaging heat treatments or "pasteurization" [18, 19]. Irradiation has been shown to be effective as a postpackaging treatment in studies, yet it has not been approved by the US Food and Drug Administration for use with ready-to-eat meat and poultry [20]. Additives that suppress the growth of *L. monocytogenes* in products are another strategy [21]. Plants with less rigorous control programs, particularly those relying solely on sanitation, are placed under an intensified microbiological testing program by FSIS. The new regulations also clarify, for the first time, that recalls can be based on identification of *L. monocytogenes* on equipment, not just in products, and that plant-generated microbiological testing data must be shared with FSIS officials.

A 2003–2004 FSIS survey revealed that the percentage of plants using new technologies to kill or suppress the growth of *L. monocytogenes* inside packaging has increased dramatically

since release of the first FSIS policy changes, which were made in December 2002, as has the number of plants testing the processing environment for *L. monocytogenes* [22]. More than 87% of the >2900 establishments surveyed had made at least 1 change in their food safety process [22]. One year after the outbreak, FSIS reported a 25% decrease in the number of *L. monocytogenes*-positive samples detected by means of its regulatory testing program between January and September 2003, compared with 2002 [23]. Most importantly, preliminary 2004 national surveillance data revealed a 40% decrease in the incidence of human listeriosis, compared with 1996–1998, with 2.7 listeriosis cases per million persons [24]. This rate approaches the 2005 national objective of cutting listeriosis incidence to 2.5 cases per million persons [25].

In addition to regulatory and industry changes, another important aspect of listeriosis control is educating high-risk populations and their food preparers about high-risk foods, such as deli meats and hot dogs, soft cheeses made from unpasteurized milk, and smoked seafood [26]. Current recommendations to prevent foodborne listeriosis can be found at the CDC's Web site [27]. Prevention messages are straightforward for pregnant women and immunocompromised patients, who have a markedly increased risk of listeriosis [28]. Older age has long been considered a risk factor for listeriosis [2]; however, most patients with listeriosis aged ≥ 65 years that we identified (93%) had other immunocompromising conditions, a finding in other outbreak investigations [29, 30]. Interestingly, patients infected with the outbreak strain were significantly more likely to be either young and healthy or pregnant than were patients with sporadic listeriosis. High doses of *L. monocytogenes* have been linked to illness in healthier people, yet primarily in the context of febrile gastroenteritis [31]. The role of organism pathogenicity in determining populations affected by invasive listeriosis is poorly understood [32, 33].

Although the precise risk to older persons may be difficult to define, institutions providing food to any at-risk population, including elderly persons, should implement appropriate policies regarding deli meats and other high-risk foods to reduce the risk of listeriosis. Several hospitalized or institutionalized patients identified during this outbreak probably acquired foodborne *L. monocytogenes* infection nosocomially, which is a scenario that has been documented previously [34, 35]. These findings indicate an urgent need for changes in these health care settings.

Finally, this investigation demonstrates the importance of PFGE subtyping through PulseNet in the detection and investigation of listeriosis outbreaks, as was recently discussed by Olsen et al. [12]. In 2003, the Council of State and Territorial Epidemiologists issued a position statement calling for prompt interviewing of all patients with listeriosis with a nationally standardized form and expedited referral of *L. monocytogenes*

isolates from clinical laboratories to state public health laboratories for real-time PFGE subtyping [36]. We encourage clinicians and laboratories to promptly report all cases of listeriosis to health departments, and we encourage states to adopt the Council of State and Territorial Epidemiologists' proposal.

In conclusion, our investigation linked a large outbreak of listeriosis to turkey deli meat and reinforced findings of previous outbreaks [11, 12] and risk models [9, 16] that ready-to-eat meat and poultry products continue to be a concern for at-risk populations. This investigation helped stimulate and guide new regulatory policies designed to prevent contamination at processing plants that produce these products. Industry surveys and national surveillance data already suggest a positive impact. Additional prevention measures implemented by institutions that serve high-risk populations could complement regulatory and industry efforts to reduce *L. monocytogenes* infections nationwide.

LISTERIOSIS OUTBREAK WORKING GROUP

Balasubramanian Swaminathan, CDC (Atlanta); Caroline Johnson, Philadelphia Department of Public Health (Philadelphia); André Weltman, Pennsylvania Department of Health (Harrisburg); Bridget Anderson, Al Bugenhagen, Curtis Vincent, Ray Woron, and Shelley Zansky, New York State Department of Health (Albany); Sharon Balter and Faina Stavinsky, New York City Department of Health and Mental Hygiene (New York); Michelle Malavet and Corey Robertson, New Jersey Department of health and Senior Services (Trenton); Jessica Totaro, Maryland Department of Health and Mental Hygiene (Baltimore); Sally Bidol and John Tilden, Michigan Department of Community Health (Lansing); Ruthanne Marcus, Connecticut Emerging Infections Program (New Haven); Quyen Phan, Connecticut Department of Public Health and Social Services (Hartford); Marci Drees and Marjorie Postell, Delaware Health and Social Services (Dover); Patrick Piercy, Illinois Department of Public Health (Springfield); James Borda and Raza Haq, US Department of Agriculture–Food Safety and Inspected Service (Philadelphia); and David Goldman, Gerri M. Ransom, and Richard Roloff, US Department of Agriculture–Food Safety and Inspected Service (Washington, DC).

Acknowledgments

We thank Lauren Doctoroff, Taha Kass-Hout, Michael F. Lynch, Paul Mead, John Painter, and Andi L. Shane (CDC); Arthur Bagelman, Wendy Bamberg, Michael Eberhart, Robert Levenson, and George Zameska (Philadelphia, PA); Wayne Chmielecki and Maria Moll (Pennsylvania); Barbara Gerzonich, Christina Hidalgo, Dina Hoeffler, Stephanie Novello, Glenda Smith, Nancy Spina, and Christine Waters (New York); Carrie Bogert, Eddy Bresnitz, Vaidehi Dave, Layla Fakhzadeh, Barbara Gibson, Lisa McHugh, Maria Orsini-Lidicker, Marc Paladini, Nancy Sullivan, and Bijal Tamakwala (New Jersey); John Fontana and Ellen Gould (Massachusetts); Naomi Barker and Jason Spangler (Maryland); James Averill (Michigan); Frank Green, Stacey Kinney, and Tracey Weeks (Connecticut); Gregory Huhn

(Illinois); and Jan Behney, Walter Hill, Diane Loulis, Michael Ronczka, Zygmunt Sala, Susan Scarcia, and Armia Tawadrous and field, headquarters, and laboratory personnel (FSIS).

Potential conflicts of interest. All authors: no conflicts.

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