

Foodborne Listeriosis Acquired in Hospitals

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Listeriosis is characterized by bacteremia or meningitis. We searched for listeriosis case series and outbreak investigations published in English by 2013, and assessed the strength of evidence for foodborne acquisition among patients who ate hospital food. We identified 30 reports from 13 countries. Among the case series, the median proportion of cases considered to be hospital-acquired was 25% (range, 9%–67%). The median number of outbreak-related illnesses considered to be hospital-acquired was 4.0 (range, 2–16). All patients were immunosuppressed in 18 of 24 (75%) reports with available data. Eight outbreak reports with strong evidence for foodborne acquisition in a hospital implicated sandwiches (3 reports), butter, precut celery, Camembert cheese, sausage, and tuna salad (1 report each). Foodborne acquisition of listeriosis among hospitalized patients is well documented internationally. The number of listeriosis cases could be reduced substantially by establishing hospital policies for safe food preparation for immunocompromised patients and by not serving them higher-risk foods.

Keywords. foodborne; hospital; immunosuppression; listeriosis; outbreak.

Invasive *Listeria* infection (listeriosis) is defined by isolation of *Listeria monocytogenes* from a normally sterile site. Most infections ($\geq 95\%$) are characterized by bacteremia or meningitis and caused by 1 of 3 serotypes (1/2a, 1/2b, and 4b) [1]. Although rare (0.27 and 0.39 annual reported cases per 100 000 population in the United States and France, respectively) [1, 2], listeriosis has much higher probabilities of hospitalization (approximately 95%) and mortality (approximately 20%) than most other foodborne pathogens [3]. The risk of listeriosis is higher during pregnancy and among persons with leukemia and other cancers, impaired cell-mediated immunity (eg, solid organ and bone marrow transplant recipients), AIDS, autoimmune disease

(eg, systemic lupus erythematosus), and certain chronic conditions, including liver and end-stage renal diseases, alcoholism, and diabetes mellitus [2, 4]. Receipt of immunosuppressive therapies, particularly cytotoxic medications and corticosteroids, have been identified as risk factors [5]. Older adults are at higher risk [1], due to immunosenescence and an increased prevalence of the aforementioned conditions.

Listeriosis is a foodborne infection, and investigations of large outbreaks in hospitals have demonstrated the consequences of serving unsafe food to highly vulnerable populations [6–8]. Some studies of sporadic listeriosis have also identified recent hospitalization as a risk factor [9]. However, determining whether exposure to food contaminated with *L. monocytogenes* occurred before, during, or after hospitalization can be difficult because the incubation period of listeriosis can vary from a few days to weeks [10]. Also, immunosuppressing conditions and advanced age can confound the association of prior hospitalization with listeriosis because these conditions are associated with both listeriosis and hospitalization, during which contaminated hospital food (the exposure of interest) may be consumed. Therefore, foodborne listeriosis acquired in a hospital may not be recognized.

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To better understand the epidemiology and scope of the problem of hospital-acquired listeriosis, we reviewed published reports of cases and of outbreak investigations. Opportunities for prevention also are discussed.

METHODS

We searched PubMed for articles using the following Medical Subject Headings (MeSH) terms: *Listeria*, *Listeria* infections, and *Listeria* cross-infection. We examined primary reports of human illnesses (either sporadic or associated with a foodborne disease outbreak) that were written in English and published in a peer-reviewed journal by September 2013. We also examined lists of references in all articles we located that met these criteria to ensure that all reports were identified. We selected listeriosis case reports, case series, and outbreaks among persons who were or had recently been hospitalized for another reason or who consumed food in a hospital. Most reports we excluded provided insufficient information to determine whether hospital acquisition had been investigated (eg, a 19-year series of 74 cases from Finland [11]) or how it was defined (eg, a 5-year series of 161 cases from Israel [12]). We excluded a report of 31 patients with listeriosis during a 16-year period because hospital acquisition was determined not to have occurred [13]. We also excluded reports of outbreaks, including 2 large, multistate outbreaks [14, 15], in which most cases occurred among persons who consumed the implicated food in a community setting, even though some patients may have consumed the contaminated food in a hospital.

To quantify the strength of evidence for foodborne listeriosis acquired in hospitals, we developed a novel quality score (Figure 1). Scoring was based on 5 steps. Step 1 assessed eligibility for inclusion in this review, which was the identification of a culture-confirmed case of listeriosis in a patient either (a) hospitalized at least 48 hours before symptom onset (if the report's definition for hospital acquisition was more stringent, the report's definition was used), or (b) with evidence of having recently been in a hospital that had another patient with listeriosis. The next scoring steps determined progression through the flowchart, depending on characterization and matching of a *L. monocytogenes* patient isolate to an isolate from 1 or more patients from the same hospital (step 2) and implication of a food vehicle (step 3). Final steps assessed quality of evidence for hospital acquisition, increasing with microbiological similarity (eg, serotyping or pulsed-field gel electrophoresis [PFGE] subtyping) of patient isolates (step 4) or epidemiological and microbiological linkages of food isolates to patient isolates (step 5). The quality score was assigned from 1 to 9 to suggest relatively weak (1–2), moderate (3–5), stronger (6–7), and strongest (8–9) evidence for attributing listeriosis to food consumed in a hospital.

For the hospital-acquired cases in each report with specific information, we determined the median age, age range, male-to-female ratio, and percentage of patients with a blood isolate, a cerebrospinal fluid (CSF) isolate, an underlying immunocompromising condition, and a fatal infection. Case-fatality ratios were calculated only for nonpregnancy-associated cases.

RESULTS

We identified 30 reports of foodborne listeriosis that included patients who were or had recently been hospitalized or who had consumed food in a hospital (Tables 1 and 2). One report described a single case [16], 12 described case series [17–28], and 17 described outbreak investigations [6–8, 29–42]. Reports originated from hospitals in 13 countries, and most were from major US cities or European countries. In the case series, a median of 25% of cases were considered to be hospital acquired (range, 3%–67%). Among the 5 case series covering >2 years and with >50 cases [17, 19, 24–26], the median was 27% (range, 16%–51%). A median of 4 hospital-acquired cases occurred in the outbreaks (range, 2–16).

The number of reports with specific information on the hospital-acquired listeriosis cases varied (range, 17–23) (Tables 1 and 2). Among the 17 reports that included patient age, the median age ranged from 28 to 80 years. In 15 of the 18 (83%) reports that specified isolate source, all isolates were from blood, CSF, or both. Among the 32 patients in 4 reports with the highest quality score (score 9) and information on source [8, 38, 39, 42], 28 (88%) had isolates from blood; the others had isolates from CSF, placental tissue, pleural fluid, or stool (1 patient each). The median case-fatality ratio was 25% (range, 0%–100%) in the 19 reports that included this information.

Twenty-four reports included the specific immune status of patients with hospital-acquired listeriosis. In 18 of the 24 (75%), all patients were immunosuppressed; the proportions of patients with immunosuppression ranged from 73% to 95% in the 6 remaining reports. Among the 50 patients with listeriosis in the 6 outbreak reports with the strongest evidence (quality score 9) supporting acquisition in a hospital [8, 38–42], 48 had either cancer or an underlying condition. Among the 29 patients with cancer, 16 had a solid tumor, 7 had a hematologic malignancy, and 6 had an unspecified cancer. Twenty-four patients, including some of those with cancer, had 1 or more of the following underlying conditions: cardiovascular disease (12 patients), renal disease (7 patients), pulmonary disease (7 patients), autoimmune disease (6 patients), diabetes mellitus (6 patients), pregnancy (6 patients), liver disease (5 patients), and blood disorder (3 patients). Two of these reports, involving 27 patients, had patient-specific information on immunotherapy [8, 42]; 17 patients were taking a steroid and 4 were taking another immunosuppressive agent.

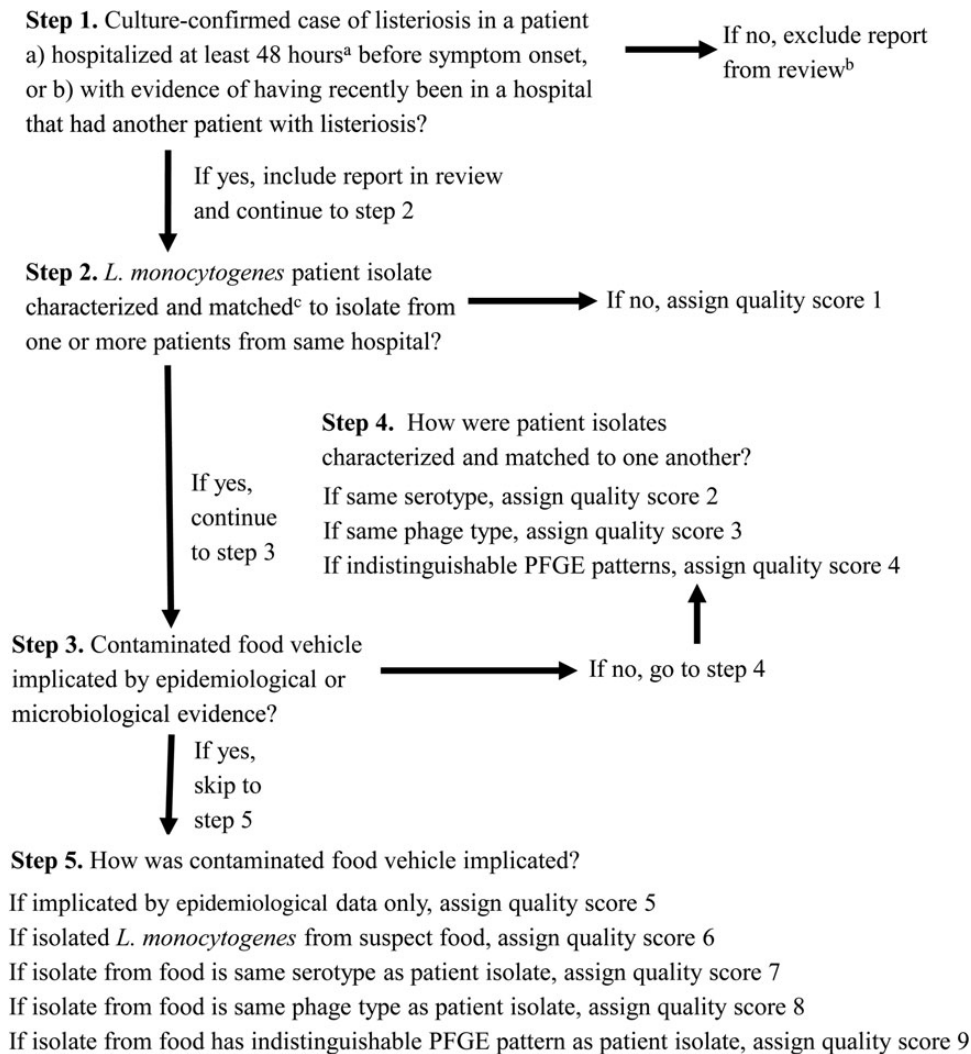


Figure 1. Flowchart for scoring quality of evidence for attributing listeriosis to food consumed in a hospital. Scoring indicates relatively weak (quality score: 1–2), moderate (3–5), stronger (6–7), and strongest (8–9) evidence for attributing listeriosis to food consumed in a hospital. ^aIf more stringent (>48 hours), the report’s definition was used. ^bMany reports were excluded because information was insufficient to determine whether any patients were hospitalized at least 48 hours before symptom onset. ^cCriterion includes isolates matched by serotyping, phage typing, or pulsed-field gel electrophoresis. Abbreviation: PFGE, pulsed-field gel electrophoresis.

The 1 report with information on acid-reducing treatment indicated that 5 of the 10 patients were taking such treatment [42]. Use of cancer chemotherapeutic agents was not recorded consistently.

Four case series included some cases that were maternal or neonatal [19–21, 27]. Two reports indicated that all maternal or neonatal cases were community-acquired, including a miscarriage in one report and a neonatal death in the other [21, 27]. The remaining case series with pregnancy-associated cases included an infant who recovered from *Listeria* meningitis that may have been nosocomial [19] and a report with insufficient detail on fetal loss or neonatal death [20]. One outbreak investigation of 4 cases among pregnant women, which did

not include any fetal loss or neonatal death, determined that they had consumed hospital food during prenatal visits [38]. Four outbreaks occurred in a hospital setting designated for immunosuppressed patients; 2 occurred in renal transplant units [31, 33], 1 in a tertiary care hospital that was the country’s only facility for organ transplant [7], and another in an oncology unit [39]. Other outbreaks occurred among patients in different departments of the same hospital [34] or at 2 or more hospitals in the same city or region that received food from a common source [6, 37, 42].

The case report and the 12 case series all had relatively weak evidence supporting acquisition of listeriosis in a hospital (quality score 1) (Table 1). Eight outbreak reports implicated a food

Table 1. Foodborne Listeriosis Case Series in Hospitals, Sorted by Years

Quality Score ^a	Years ^b	Cases		Among Persons With Hospital-Acquired Listeriosis									
		Hospital-Acquired, No.	All, (No.)	Age, y ^c , Median (Range)	M:F ^c , No.	<i>Listeria monocytogenes</i> Isolated, %		Immunocompromised ^{c,d} , %	Died ^{c,d} , %	Serotype Isolated	PFGE or Other Subtyping Results	Country	Reference
						From Blood ^c	From CSF ^c						
1 ^e	1989	1	(1)	74 . . .	1:0	uk	uk	100	uk	1/2a, 1/2c ^e	na	England	[16]
1	1983–1991	26	(51)	uk uk	uk	uk	uk	81	uk	uk	na	Spain	[17]
1	1983–1992	1	(29)	28 . . .	0:1	100	0	100	0	1/2a, 1/2b, 4b	na	England	[18]
1	1983–1992	19 ^f	(84)	51 (<1–86)	8:11	uk	uk	95	56	uk	na	Australia	[19]
1	1989–1990	12	(59)	uk uk	uk	uk	uk	92	uk	uk	na	Denmark	[20]
1	1990	13	(31)	uk uk	uk	uk	uk	uk	uk	uk	na	Spain	[21]
1	1992	20	(225)	uk uk	uk	uk	uk	100	uk	uk	na	France	[22]
1	1964–1997	5	(42)	68 (39–75)	3:2	40	100	80	80	uk	na	USA	[23]
1	1983–2006	31	(102)	uk uk	uk	uk	uk	uk	uk	uk	na	Spain	[24]
1	1986–2007	18	(111)	uk uk	uk	uk	uk	uk	uk	uk	na	Spain	[25]
1	1995–2008	17	(64)	uk uk	uk	uk	uk	uk	uk	uk	na	Spain	[26]
1	1999–2011	11	(38)	42 (22–60)	2:9	82	18	100	27	uk	na	China	[27]
1	1997	2	(3)	69 (66–72)	0:2	100	0	100	0	4b ^g	Divergent ^g	France	[28]

Abbreviations: CSF, cerebrospinal fluid; M:F, ratio of males to females; na, not available; PFGE, pulsed-field gel electrophoresis; uk, unknown.

^a Quality score based on quality of published evidence to support acquisition in healthcare setting (see text and Figure 1).

^b Year of case diagnoses; when unavailable, year of publication [16, 28].

^c Calculated for hospital-acquired cases.

^d Immunocompromised status as determined by the authors of the report; 4 reports included maternal or neonatal listeriosis cases with evidence for foodborne transmission in a hospital [19–21, 27]. Death not necessarily attributed to listeriosis as primary cause. Case-fatality rates were calculated only for nonpregnancy-associated cases.

^e *Listeria monocytogenes* serotype 1/2a contamination of lettuce detected during investigation of a listeriosis case with serotype 1/2c infection.

^f Case series includes 1 full-term baby who recovered after developing *Listeria* meningitis at day 5 of life. The infant nursed in the same room as another baby with listeriosis [19].

^g Clustering of sporadic cases of *L. monocytogenes* serotype 4b infections with divergent PFGE subtypes (ie, a pseudo-outbreak).

Table 2. Foodborne Listeriosis Outbreak Investigations in Hospitals, Sorted by Quality Score for Evidence of Acquisition From Food Consumed in a Hospital, and by Years

Quality Score ^a	Years	Among Persons With Hospital-Acquired Listeriosis											Country	Reference	
		Cases		Age, y ^b , Median (Range)	<i>Listeria monocytogenes</i> Isolated, %			Immunocompromised ^{b,c} , %	Died ^{b,c} , %	Serotype Isolated	PFGE or Other Subtyping Results	Food Vehicle Implicated?			
		Hospital-Acquired, No.	All, (No.)		M:F ^b	From Blood ^b	From CSF ^b								
1	1972–1973	2	(8)	44	(39–49)	0:2	100	0	100	0	1a, 1b	na	No	USA	[29]
1	1981–1982	2	(3)	uk	uk	0:2	100	uk	100	uk	uk	na	No	New Zealand	[30]
2	1979	15	(20)	uk	uk	uk	93	33	73	25	4b	na	No	USA	[6]
2	1979	4	(6)	36	(24–51)	4:0	75	75	100	75	1b	na	No	USA	[31]
3	1978	3	(4)	69	(66–74)	1:2	100	0	100	100	4	na	No	England	[32] ^d
4	1994–1995	4	(6)	49	(31–57)	2:2	100	uk	100	0	1/2b	Match	No	Germany	[33]
4	1994–1995	5	(11)	55.5	(31–67)	3:2	100	20	100	20	1/2b	Match	No	Germany	[34]
4	2006–2007	4	(6)	78.5	(62–92)	2:2	75	0	100	75	1/2b	95% similar	No	Brazil	[35]
4	2011	3	(3)	uk	uk	2:1	100	0	uk	0	4	Match	No	England	[36]
7	1999	2	(4)	75	(71–79)	1:1	100	0	100	0	4b	na	Sandwiches ^e	England	[37]
9	1998–1999	10	(25)	uk	uk	uk	uk	uk	uk	uk	3a	Match	Butter	Finland	[7]
9	2003	4	(5)	uk	uk	0:4	100	0	100	0	1/2	Match	Sandwiches ^e	England	[38]
9	2003	2	(2)	54.5	(46–63)	0:2	100	uk	100	50	1/2a	Match	Sandwiches ^e	Wales	[39]
9	2006–2007	4	(11)	72.5	(62–76)	3:1	uk	uk	100	uk	4b	Match	Scalded sausage	Germany	[40]
9	2007	16	(17)	64.5	(27–84)	5:11	81	13	88	19	1	Match	Camembert cheese	Norway	[8]
9	2008	5	(5)	uk	uk	uk	uk	uk	100	60	1/2a	Match	Tuna salad	USA	[41]
9	2010	10	(10)	80	(56–93)	5:5	90	0	100	50	1/2a	Match	Precut celery	USA	[42]

Abbreviations: CSF, cerebrospinal fluid; M:F, ratio of males to females; na, not available; PFGE, pulsed-field gel electrophoresis; uk, unknown.

^a Quality score based on quality of published evidence to support acquisition in healthcare setting (see text and Figure 1).

^b Calculated for hospital-acquired cases.

^c Immunocompromised status as determined by the authors of the report; 1 report included pregnant women [38]. Death not necessarily attributed to listeriosis as primary cause. Case-fatality rates were calculated only for nonpregnancy-associated cases.

^d For phage typing results, see Taylor AG, et al. Hospital cross-infection with *Listeria monocytogenes* confirmed by phage-typing. Lancet 1981; 2:1106.

^e Unspecified sandwiches ingredients from hospitals' shops [37]; meat and cheese sandwiches from hospitals' shops, and outbreak strain isolated from sample of brie and cranberry sandwich [38]; ham salad and tuna salad sandwiches consumed by patients, and outbreak strain of *L. monocytogenes* isolated from numerous sandwich samples with a variety of unspecified ingredients [39].

vehicle and provided relatively strong evidence (quality score ≥ 6) for foodborne acquisition in a hospital; all were published after 1999. Seven reports linked patients' isolates and *L. monocytogenes* isolated from a food vehicle via a common PFGE subtype (quality score 9). The 8 food products implicated were sandwiches (3 outbreaks), butter, pre-cut celery, Camembert cheese, sausage, and tuna salad (1 outbreak each) (Table 2). The sandwiches had a variety of ingredients, including meat, cheese, and cranberries in 1 outbreak [38], and ham salad and tuna salad in another [39]; ingredients were not specified in one report [37]. Some sandwiches were supplied ready-to-eat by caterers to hospital shops [37, 38]. In 2 reports, outbreak strains of *L. monocytogenes* were likely introduced into hospital kitchens via contaminated butter and celery [7, 42]. Bulk preparation of tuna and chicken salads, which were stored and served in sandwiches made over several days, was noted in 2 investigations [41, 42].

DISCUSSION

Our review of 30 published reports of foodborne listeriosis acquired in hospitals indicates that a substantial number of nonpregnancy-associated listeriosis cases result from immunocompromised patients consuming food contaminated with *L. monocytogenes* during hospital visits and stays. The problem extends beyond hospitals; at least 3 reports demonstrate that patients in other healthcare settings (eg, long-term care facilities) are also at risk [43–45]. This implies that many cases could be prevented by improving the safety of food served in hospitals and other healthcare settings. Nearly all of the implicated food vehicles in the outbreaks we reviewed were intended for consumption without further preparation or heating (ie, ready-to-eat).

Evidence for the problem of unsafe food preparation and service for immunocompromised and elderly patients is not only widespread, but also can be expected to grow. Improvements over the study period in the strength of evidence of outbreak investigations, as reflected in the quality score we developed, resulted from increased use of molecular subtyping methods. Ongoing advances in epidemiological investigation and characterization of *L. monocytogenes* isolates (eg, whole-genome sequencing), including hospital-based case series of seemingly sporadic cases, are likely to improve further the ability of health officials and hospital epidemiologists to link infections to food served in hospitals. In addition, hospital preventionists could evaluate nonpregnant persons with a culture that yielded *L. monocytogenes* ≥ 48 hours after admission as possible hospital-acquired cases, assess the possibility of a cluster of linked cases, and routinely report this information to public health authorities. Such investigations can identify vehicles and sources of contamination, which may reveal additional opportunities for prevention. Improvements in investigations are occurring

during a period when the population at risk—patients receiving immunosuppressive treatments (eg, chemotherapy, glucocorticoids, or other immunosuppressive agents) who are also more likely to be hospitalized—continues to grow. Overall, the population is also aging [46, 47].

Other reports and investigations not included in our review suggest that many more cases of foodborne listeriosis acquired in hospitals have occurred. For example, a series of 161 cases identified over 5 years in Israel estimated that 16% of cases were hospital acquired, but did not include sufficient detail for us to determine how long patients had been hospitalized before symptom onset [12]. A summary report [48] from the United Kingdom of 8 outbreak investigations that implicated or suspected sandwiches purchased from or provided in hospitals included 4 outbreaks in our review [36–39] and 4 other outbreaks published only in agency-specific bulletins or reports. One outbreak in our review resulted from consumption of hospital food during outpatient visits for prenatal care [38]. In 2013, 3 patients hospitalized at 3 hospitals in Australia acquired listeriosis from contaminated profiteroles (cream puff pastries) [49]. Furthermore, we only reviewed reports published in English. There also may be a publication bias favoring investigations that conclusively identify a confirmed food vehicle [36].

Several other issues complicate our review. We calculated a case-fatality rate for hospital-acquired listeriosis limited to nonpregnancy-associated cases because fetal demise and neonatal mortality generally result from maternal food consumption in community settings. Distinguishing community-acquired versus hospital-acquired listeriosis can be challenging, given confounding by health status and the fact that the incubation period for listeriosis can range from a few days to several weeks. Definitions of hospital-acquired listeriosis used in other studies have varied in stringency from onset of symptoms >48 hours [7, 19, 22] to >3 weeks after admission [15]. Our review did not include reports of community-based outbreaks, which may not indicate whether the implicated food could have also been consumed in hospitals, but it is clear that community-based and hospital-acquired outbreaks can overlap [14, 15].

Many case series not included in our review have reported higher proportions of nonpregnancy-associated cases with meningitis (eg, 38% of 553 cases [50] and 31% of 179 cases [51]) than in our review. We found that more isolates were generally obtained from blood than CSF among patients with hospital-acquired listeriosis, suggesting that the pathophysiology, age distribution, or clinical presentation of patients who are already hospitalized may differ from that of patients with community-acquired listeriosis. Alternatively, patients who are already hospitalized may be diagnosed earlier due to close monitoring compared with patients with community-acquired listeriosis; delayed diagnosis could afford additional time for central nervous system invasion [10].

Several listeriosis outbreak investigations in the United Kingdom have implicated sandwiches manufactured off-site and delivered to affected hospitals [48]. A large study investigating sandwich contamination in the UK healthcare system found that 2.7% of sandwiches were contaminated with *L. monocytogenes* [52]. It has been suggested that the European guideline of 100 colony-forming units (CFU) per gram should be reduced when products are being served to patients with immunosuppression [53]; accordingly, the British Sandwich Association recommended a contamination level of <10 CFU/g for *L. monocytogenes* in sandwiches [54]. The US Food and Drug Administration (FDA) standard is no detectable *L. monocytogenes* in a 25-g sample of ready-to-eat food, as even low contamination levels are sufficient to cause infection [7].

Serving ready-to-eat foods to higher-risk patients without proper storage (eg, limiting time at room temperature) and preparation (eg, assuring adequate reheating) carries a risk of listeriosis. Although specialized diets are often provided for neutropenic and immunocompromised patients, there is considerable variability in ordering and implementation of these restricted diets. To reduce the risk of listeriosis and other foodborne illnesses, a tertiary care medical center in New York City implemented a policy that does not allow certain foods to be served to any patient [55]. Model guidelines could be established nationally through the leadership of medical associations with input from public health agencies. Furthermore, the quality of records on foods ordered and served to patients varies substantially; improved data quality would aid epidemiological investigations and could help ensure that safer, nutritious food is served in hospitals. Environmental monitoring of the food service areas of healthcare facilities is recommended in Australian guidelines for *L. monocytogenes* management [56].

Hospital policy committees, administrators, food service managers, infection preventionists, oncologists, and other healthcare providers can evaluate their hospitals' food preparation practices and the foods that are offered to patients, especially older adults and patients with underlying conditions and immunosuppression. Resources exist through professional organizations (eg, Academy of Nutrition and Dietetics, American Cancer Society), scientific journals, and textbooks [57] to support these evaluations. If professional organizations promote and large healthcare systems establish policies to prepare safe food for immunocompromised patients and not serve them higher-risk foods, such practices could be implemented as the standard of hospital care. Other groups that provide food services to higher-risk patients (eg, home-delivered meals) may consider adopting some best practices used by hospital food services [58]. The FDA provides a Model Food Code with special requirements and safeguards (eg, not serving raw sprouts) for highly susceptible populations [59]. The US Centers for Disease Control and Prevention and federal regulatory partners

also offer advice on safe preparation and storage of foods prone to contamination with *L. monocytogenes* (www.cdc.gov/listeria/resources.html). Public health officials, including environmental health specialists, can help guide implementation of these and other food safety measures. As an additional benefit, prevention measures for reducing hospital-acquired listeriosis are also likely to decrease the incidence of other foodborne illnesses.

A systematic approach to reducing the risks of foodborne illnesses caused by pathogens such as *L. monocytogenes* is needed for hospitals and healthcare systems. The immediate need to establish policies for safe food preparation and service for immunocompromised patients is compelling because foodborne acquisition of listeriosis in hospitals is now well documented internationally; listeriosis causes life-threatening, invasive disease in well-defined populations, and such policies could substantially reduce the billions of annual healthcare expenditures and the unrecoverable costs to health [60, 61].

Notes

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