SURVEILLANCE OF LISTERIOSIS IN FINLAND DURING 1995-2004

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We analysed the surveillance data from listeriosis cases notified to the Finnish National Infectious Diseases Register between 1995 and 2004 and describe our recent experience in investigating clusters of listeriosis cases. The number of annual cases varied between 18 and 53 but no trends in incidence were identified (average annual incidence was 7 cases per million inhabitants). Only a few cases affected pregnant women or newborns. Most of the patients were elderly people with non-malignant underlying illnesses; 25% of them died from their infections. By routine sero- and genotyping of the listeria isolates, we detected several clusters; the vehicle for infection was only identified for two outbreaks. At least one quarter of listeriosis cases (78/315) was caused by a certain sero-genotype or closely related genotypes, which have also been found from vacuum-packed cold-smoked or cold-salted fish products. During 2000-2003, Finnish consumers were repeatedly informed about food precautions for risk groups. The information was also given to attending physicians and prenatal clinics.

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Introduction

Listeriosis most commonly affects pregnant women, newborns, and adults with weakened immune systems, including those with cancer, AIDS or kidney diseases, and those who take glucocorticosteroid medications, and the elderly [1,2]. Unlike most other foodborne infections, listeriosis is associated with high case fatality. The food precautions targeted at people at high risk of contracting listeriosis are crucial for prevention.

In Finland, the annual incidence of listeriosis has been comparable to the rates reported by other industrialised countries [3]. The vehicle for infection has only been identified for two outbreaks [4,5]. In 1997, febrile gastroenteritis in five people without underlying disease was associated with the consumption of vacuum-packed cold-smoked rainbow trout, containing high concentration (1.9x105 colony forming units (cfu) per gram) of *Listeria monocytogenes* [4]. During 1998-1999, butter contaminated with low levels (5-60 cfu/g) of *L. monocytogenes* after pasteurisation in a dairy caused an outbreak in acutely immunosuppressed people [5,6]. Most cases of listeriosis have been sporadic and could not be linked to any specific food. The incubation period, which may be as long as one month, and high mortality make outbreaks difficult to recognise and investigate, especially for smaller clusters.

To assess the trends in incidence and persons at risk, we analysed surveillance data from listeriosis cases notified to the National Infectious Diseases Register (NIDR) during 1995-2004. We also describe our recent difficulties in investigating clusters of listeriosis cases.

Methods

Since 1995, physicians in Finland have been obliged to notify culture confirmed cases of listeriosis to the NIDR, which is maintained at the National Public Health Institute (KTL)'s Department of Infectious Disease Epidemiology, and the microbiology laboratories that isolate *L. monocytogenes* from blood, cerebrospinal fluid, genital tract, newborn, deep puncture, and surgical specimens. Strains of *L. monocytogenes* must also be sent to KTL's Enteric Bacteria Laboratory for serotyping and pulsed field gel electrophoresis (PFGE).

L. monocytogenes isolates were serotyped for their O and H antigens by slide and tube agglutination methods, respectively, using commercially available antisera (Denka Seiken Co., Ltd, Tokyo, Japan) according to the manufacturers' instructions with minor modifications [7]. In situ DNA isolation and macrorestriction analyses by PFGE using the restriction enzyme AscI were performed as described [7].

When a cluster of listeriosis cases was detected, clinical information (underlying conditions/illnesses and outcome) was collected from the attending physician using a standardised form. In addition, patients or their family members were interviewed by phone about food and drink consumed during the four weeks before the onset of illness. One matched case-control study was performed to identify the potential association between illness and the consumption of a certain food.

Results

Between 1995 and 2004, 18 to 53 cases of listeriosis were identified annually in Finland; 3-10 cases per 1 000 000 inhabitants per year [FIGURE 1, data are based on NIDR notifications]. The average annual incidence rate varied from 2 to 13/1 000 000 inhabitants by region. Of all patients with listeriosis, 57% were 65 years of age or older and 55% were male. Between zero and three cases each year were occurred in pregnant women or newborns.

The most common serotypes were 1/2a (60%) and 4b (23%); only during 1998-1999 serotype 3a was more common than serotype 4b [Table 1, data are based on the 315 strains submitted to the Enteric Bacteria Laboratory].

PFGE types among the strains of serotypes 1/2a and 4b were diverse and no single dominating type was found, whereas PFGE type 71 ('butter type', the strain type that was responsible for the

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TABLE 1

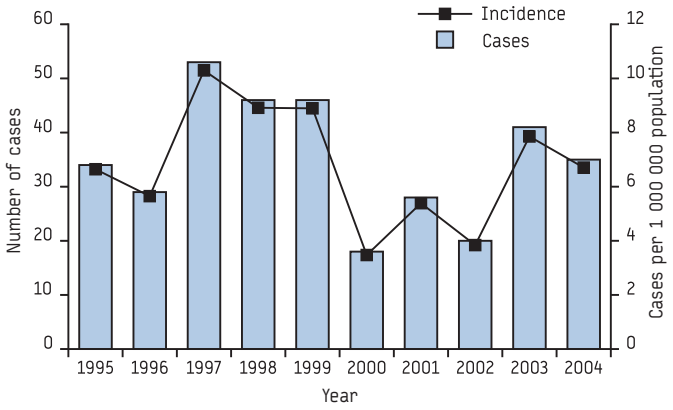
Distribution of serotypes of *Listeria monocytogenes* strains, Finland, 1995-2004

Serotype	1995 n=21	1996 n=21	1997 n=47	1998 n=43	1999 n=45	2000 n=19	2001 n=27	2002 n=20	2003 n=40	2004 n=32*	Overall n=315
1/2a	12	12	26	19	25	12	18	12	32	21	189
1/2b	2	2	1	0	0	3	0	0	3	0	11
1/2c	1	1	0	0	0	1	2	1	1	1	8
3a	1	0	4	19	10	0	0	0	0	0	34
4b	5	6	16	5	10	3	7	7	4	9	72

* The serotype of one strain could not be defined

FIGURE 1

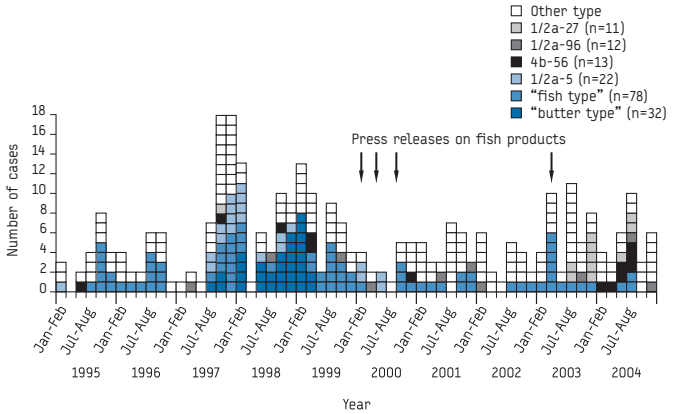
Annual number of listeriosis cases and annual incidence per 1 000 000 population, Finland, 1995-2004



outbreak link to butter) dominated among strains of serotype 3a with 94% (32/34) [FIGURE 2]. Strains of serotype 1/2a divided into 55 PFGE types; the most common types were 1 (21%), 5 (11%) and 23 (11%). Five PFGE types ('fish types', including type 1, the strain type that was responsible for the outbreak link to vacuum-packed cold-smoked rainbow trout, and four types -23, 58, 240 and 251- that were closely related to type 1) accounted for 41% of the serotypes 1/2a strains (78/189). Most of the cases caused by sero-genotype 1/2a-5 strains were detected in 1997-1998 (77%, 17/22). In contrast, all but one case caused by the genotype 1/2a-27 strains were from 2003-2004 (91%, 10/11). Strains of serotype 4b could be divided into 19 PFGE types; the most common was type 56 (18%, 13/72).

FIGURE 2

Cases of listeriosis by month based on cultures yielding *Listeria monocytogenes*, Finland, 1995-2004



Note: Only types that caused at least 10 cases are indicated

Most of the cases caused by this genotype occurred in 2004 (7/13); with a maximum of two cases per year during 1995-2003. The cases caused by this strain occurred in several regions around Finland.

During 1999-2004, after the outbreak linked to butter, clinical information was collected from 75 cases of listeriosis during three different time periods when infection clusters were suspected [TABLE 2]. Of the positive cultures, 60 (80%) were from blood, five (7%) from cerebrospinal fluid and 10 (13%) from other sources (three from fluid in the abdomen, two from pleural fluid, two from deep puncture, one from pus, one from an abscess and one from urine). Only four cases (5%) occurred in pregnant women or newborns. Almost all patients (67/70) who were not pregnant had at least one underlying illness, but illness was malignant in less than one third of these cases (20/67). A total of 20 patients died; 12 (16%) died within one week after positive listeria culture and 19 (25%) within one month.

Between 7 June 1999 and 15 March 2000, 27 cases of listeriosis were reported, of which 13 were caused by strains of 'fish types'. Of the 27 cases, 25 were included in the case-control study (one newborn and a patient with skin infection were excluded). Three control subjects matched by age, underlying medical conditions and hospital were identified for each case with the help of the attending physicians. Analysis of the 25 cases and 62 matched controls showed no association between illness and consumption of fish products (Odds ratio (OR) 1.7; confidence intervals (CI) 95% 0.6-5.8), and nor did the subanalysis, which included only the 13 cases caused by strains of 'fish types' and their matched controls (OR 1.8; CI 95% 0.4-9.6). However, 17 (68%) of the 25 case-patients and 9 (69%) of the 13 cases caused by strains of 'fish types' had eaten uncooked fish products within the incubation period; most often cold-salted fish. The fish products consumed by the case-patients could not be traced back to any single fish processing facility.

During a short period at the beginning of 2002 (5.1.2002-4.2. 2002) listeriosis was detected in six people, five of whom were from southwest Finland. However, this local cluster of listeriosis cases was caused by strains of two different serotypes and three genotypes (4b-65, 1/2a-96 and 1/2a-253). Five of the six patients were interviewed about food histories but the interviews did not identify any common food.

From 12 November 2003 to 31 December 2004, we attempted to interview all people who had been ill with listeriosis, or if the patient had died, family members of the deceased. We succeeded in interviewing approximately half of the patients (22/42). Genotyping simultaneously revealed two clusters with seven cases each [FIGURE 2: sero-genotypes 1/2a-27 and 4b-56]. The food histories of the people infected by sero-genotype 1/2a-27 were strongly suggestive of cold-salted fish products (four out of five patients cases had consumed these products). During the same period of time, four additional people became ill with listeriosis caused by strains of 'fish types', but they were not interviewed. Only three of the people infected by sero-genotype 4b-56 were interviewed, and no common food history of well known risk foods (raw, unpasteurised) milk and foods made from raw milk, soft cheeses, paté, meat and fish products) was identified.

Table 2

Clinical and demographic characteristics of 75 listeriosis cases in Finland during three different time periods, 1999-2004

Date	7 June 1999 – 15 March 2000	5 January 2002 – 4 February 2002	12 November 2003 – 31 November 2004
Characteristic	Total number (n=27) n (%)	Total number (n=6) n (%)	Total number (n=42) n (%)
Source of positive culture			
Blood	22 (81)	6 (100)	32 (76)
Cerebrospinal fluid	2 (7)	0 (0)	3 (7)
Other	3 (11)	0 (0)	7 (17)
Median age, years (range)	69 (0-86)	59 (41-80)	72 (22-91)
Male sex	14 (52)	4 (67)	22 (53)
Underlying condition			
Haematologic malignancy	4(15)	2 (33)	8 (19)
Solid malignancy	4 (15)	1 (16)	1 (2)
Solid organ transplantation	0 (0)	0 (0)	0 (0)
Pregnancy	3 (11)	0 (0)	1 (2)
Newborn	1(4)	0 (0)	0 (0)
No underlying condition (not pregnant)	1 (4)	0 (0)	2 (5)
Death			
Within 1 week after positive culture	6 (22)	3 (50)	3 (7)
Within 1 month after positive culture	9 (33)	3 (50)	7 (17)

Discussion

The annual incidence of listeriosis in Finland has not decreased during the last ten years. Pregnancy related cases are still rare. Most of the persons who became ill with listeriosis were elderly people with underlying illnesses, less than third of which were malignant. A quarter of the case-patients died.

The routine subtyping of listeria isolates by both pheno- and genotypic methods allowed us to identify clusters that might have had a common vehicle and source. Several small clusters were detected. The comparison of typing results of human listeria strains with those obtained from foods may give clues about the implicated food and the interviews may then focus on this type of food. In 2004, three people became ill with listeriosis caused by a sero-genotype that had previously been found in vacuum-packed cold-smoked or cold-salted fish products, or caused by its closely related sero-genotypes [4,7]. In 2002, there were also three such cases, and there were 11 such cases in 2003 and 14 such cases in 1999. Similar linkages between human clusters and fish products without epidemiological association have also been reported from Sweden, Norway and Iceland [8-10]. Based on these human findings, the National Food Agency, the National Veterinary and Food Research Institute, and KTL made several announcements (press release) (three times in 2000 and once in spring 2003) that vacuum-packed cold-salted and cold-smoked fish products may contain *L. monocytogenes*, which may cause listeriosis, especially in people at high risk [11]. In 2000, attending physicians and Finnish prenatal clinics were also given information about food precautions for risk groups [see Box] [12].

In practice, listeriosis cases caused by the same listeria sero- and genotype often occur over a relatively long period of time and are geographically dispersed. To minimise recall bias, food history interviews should be performed as soon as possible after the onset of illness. However, culture findings from human specimens for detailed typing are usually not yet available at that point in time, and without typing results, the cluster cannot easily be recognised. Therefore, if interviews are carried out before typing results are available, it is not possible to include more detailed questions concerning certain foods.

Box

Current food precautions to reduce the risk of listeriosis in Finland

General recommendations:

- Cook all meat thoroughly
- Wash raw vegetables thoroughly before eating
- Keep uncooked meat separate from vegetables and from cooked foods and ready-to-eat foods
- Avoid raw (unpasteurised) milk or foods made from raw milk
- Wash hands, knives, and cutting boards after handling uncooked foods
- Recommendations for persons at high risk:
- Avoid soft aged cheeses, such as blue cheese, and fresh cheeses
- Cook left-over food or ready-to-eat food until steaming hot
- Avoid vacuum-packed cold-salted or cold-smoked fish products

From: (www.ktl.fi and www.elintarvikevirasto.fi)

By performing an analytical epidemiological study, we potentially could show an association between illness and consumption of a certain food item: whether the case-patients are more likely to have consumed certain food in comparison with the controls. In listeriosis outbreaks, the number of cases is usually small, many case-patients die and some are too ill to be interviewed. Matching according to underlying condition may lead to matching by level of exposure, and bias the results to zero (that is, less likely to identify a risk factor) [5,13]. Finding controls with the help of an attending physician can be laborious. Sometimes, the suspected foods are very commonly consumed and it is not possible confirm the association with a relatively small number of study subjects. For the above mentioned reasons, it is often advisable to inform the public, particularly those people at high risk, to avoid certain foods even if there is no evidence of the vehicle or source of infection. Communication between health and food authorities about the typing results of human and food

isolates might improve control measures. It is hoped that the recently established network, PulseNet Europe (http://www.pulsenet-europe.org), will improve listeria surveillance in Europe. Public health, food and veterinary laboratories in Europe participate in the network, which will have a database of real-time typed sero-genotypes, and this communication platform should simplify the exchange of information between these different sectors.

Foods that are not heated before consumption, and that have a long shelf life, and in which listeria can grow, are considered risk foods for listeriosis. The presence of *L. monocytogenes* in meat and fish products is not regulated by Finnish food legislation. In recent years, the Finnish food authorities have published several guidelines on the control of listeria in food chain targeted at meat and fish processing facilities and establishments that sell food. The National Food Agency has reminded (through press releases) consumers also have to pay special attention to the time and temperature in which the vacuum-packed fish products are stored. The safe temperature in a home refrigerator is £ 3º C. Products should not be consumed after the sell-by date, and once open, the products should be consumed rapidly.

Based on our experience described above, we are continuing to inform people at high risk of listeriosis to avoid vacuum-packed cold-salted and cold-smoked fish products [see Box]. We do not know whether other risk foods, such as certain meat products or fresh produce, exist.

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ORIGINAL ARTICLES

Surveillance report

SIGNIFICANT INCREASE OF LISTERIOSIS IN GERMANY - EPIDEMIOLOGICAL PATTERNS 2001-2005

J Koch, K Stark

Listeriosis has been a mandatorily notifiable disease in Germany since January 2001. Clinical cases with isolation of *Listeria monocytogenes* from sterile specimens or neonates are reported to the Robert Koch-Institut. Listeriosis incidence significantly increased from 0.26 per 100 000 inhabitants (217 cases) in 2001 to 0.62 per 100 000 (519 cases) in 2005. The increase only occurred among non pregnancy-associated cases and was mainly due to a rise in cases in the age group ≥60 years. The highest incidences were observed in neonates and adults ≥70 years. Male cases predominated, except for cases occurring in adults of child-bearing age. The overall case fatality rate was 9%. No temporal or spatial clusters of cases were observed and no outbreaks with a common source vehicle were identified. In 46% of the cases malignancies were reported as predisposing factor. Reasons for the increase of listeriosis in Germany remain unclear. The newly implemented surveillance system, and raised diagnostic awareness, cannot explain the particularly high increase in incidence from 2004 to 2005. Increased contamination of common foodstuffs or changes in underlying medical conditions or treatment options may have contributed to the increase. A project for enhanced listeriosis surveillance was begun in 2005 to obtain more detailed information about the clinical course, underlying conditions, medical treatment, knowledge about listeriosis and possible food risk factors from all newly diagnosed cases. For better outbreak detection, a nationwide system for molecular subtyping of listeria strains from humans and food is necessary. Recommendations for prevention should be extended to all risk groups with predisposing conditions.

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