

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 $\leq 3^{\circ}\text{C}$. 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

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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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Introduction

Listeriosis, caused by *Listeria monocytogenes*, is a foodborne infection of great public health concern due to its clinical severity (resulting in, for example, abortion, septicaemia or meningitis) and high case fatality. Most affected by severe disease are people who are elderly or immunocompromised, pregnant women and neonates (younger than four weeks). In recent years, an increase of listeriosis cases including larger outbreaks has been observed in several European countries. In this paper, we report the time trends and epidemiological data of listeriosis cases reported in national surveillance in Germany from 2001 to 2005.

Methods

In Germany, listeriosis has been a notifiable disease since 2001 [1, 7]. All cases from whom *L. monocytogenes* is cultured from blood, cerebrospinal fluid, or other usually sterile specimens must be reported to the local public health department by the identifying laboratories. The health departments complete and verify the case information based on the national case definition for listeriosis. Information about clinical signs and outcome is obtained either from the patients or their physicians. The data of case reports is electronically transmitted to the state health department and from there to the Robert Koch-Institut (RKI), the national public health institute. For quality assurance each individual case report is checked at RKI for plausibility of the laboratory and clinical data according to the case definition. In neonates, the isolation of *L. monocytogenes* from any specimen is notifiable and fulfils the case definition independent of clinical signs and symptoms. According to the case definition data of listeriosis, cases not in neonates are included in the national surveillance database if the infection is laboratory confirmed and clinical disease is present [2]. Until 2001 only cases of congenital listeriosis had to be reported.

Since the beginning of 2004 when the listeriosis case definition was revised, mothers of neonates with listeriosis are also reported (as epidemiologically linked cases), irrespective of their clinical picture or laboratory results. Therefore, the number of pregnancy related listeriosis cases for the years 2004 and 2005 cannot be directly compared with these cases from 2001 to 2003. In addition, the clinical signs and symptoms of premature delivery, flu-like symptoms and fever were added to the list of possible manifestations for pregnancy-associated cases.

Results

Between 1 January 2001 and 31 December 2005, 1519 cases of *L. monocytogenes* were reported to the RKI.

The case numbers significantly increased from 217 cases in 2001 (incidence: 0.26 per 100 000 inhabitants) to 510 cases in 2005 (incidence: 0.62 per 100 000) ($p < 0.001$; z-test). The overall incidence has more than doubled since the introduction of a mandatory notification system of culture confirmed listeriosis cases at the beginning of 2001. From 2001 to 2004 the annual increase of listeriosis cases ranged from 7% to 16%. In 2005, cases increased 72% compared to 2004. No seasonal trends were observed in listeriosis incidence, and no outbreaks were reported. The temporal and spatial distribution of cases, especially during the increase of 2005, did not reveal any clusters suggestive of local outbreaks. Cases could not be linked to any common source or vehicle of infection.

Annual totals for the years 2001 to 2005 demonstrate that the number of pregnancy-associated listeriosis cases (including neonates) showed some fluctuation but no clear trend, while non-pregnancy associated listeriosis (excluding neonates) dramatically increased during this time period [FIGURE 1]. A total of 1294 cases (85%) of all reported 1519 cases were not pregnancy related. Of the non-pregnancy related cases, 76% were in patients aged ≥ 60 years. Between 2001 and 2005 the number of cases in the age group ≥ 60

years increased by a factor of 2.6, from 132 to 346 cases, while the case number in the younger group increased by a factor of only 1.7, from 56 to 97 cases. The increase was sharpest in the age group ≥ 80 years where almost four times as many cases were reported in 2005 ($n=86$) as in 2001 ($n=22$). Since 2001, a total of 225 pregnancy-associated cases (including neonates) have been notified, representing 15% of all cases. If we assume that the number of pregnant cases for the years 2001 to 2003 would have been higher if the modified case definition of 2004 had already in place since the beginning of 2001, then we can say that the annual number of pregnancy-associated cases during 2001 to 2005 remained relatively stable.

FIGURE 1

Annual number of reported listeriosis cases by patient category and age group, Germany, 2001-2005

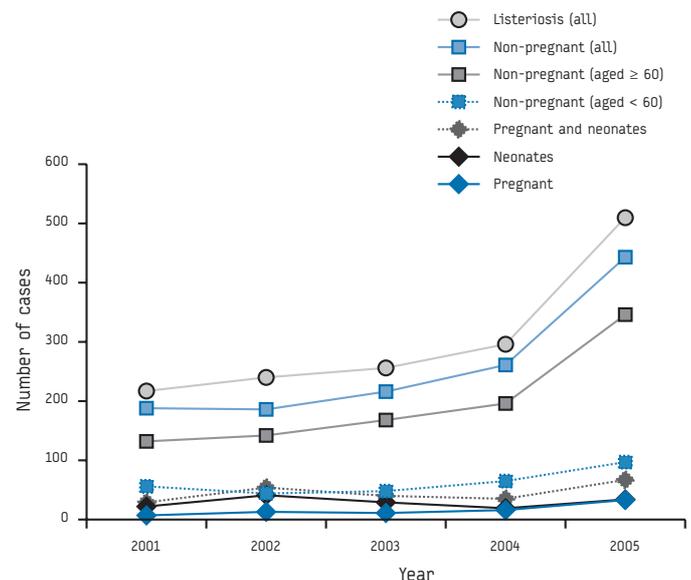
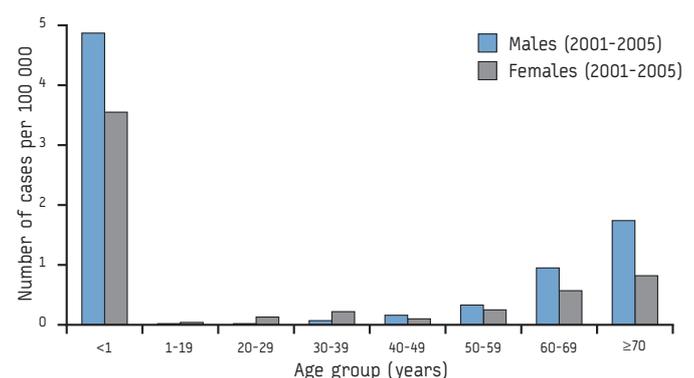


Figure 2 shows annual listeriosis incidence by age group and sex for the years 2001 to 2005. The highest incidences are seen in neonates and adults ≥ 70 years. Neonates show an incidence of 4.2 per 100 000 inhabitants. In neonates, boys (4.9/100 000) were more frequently affected than girls (3.6/100 000). In the age groups 20-29 years and 30-39 years, incidence was higher in women, due to the pregnancy related cases. Of all 126 cases in the age group 20-39 years, 98 (78%) were in women, and 77 (61%) were pregnancy related. Overall incidence increased continuously in the age groups 50-59 years and older and reached 1.2 per 100 000 among those aged ≥ 70 years (men 1.7/100 000, women 0.82/100 000). In the age groups ≥ 40 years, the majority of cases are men.

FIGURE 2

Age and sex distribution of listeriosis cases, Germany, 2001-2005



According to the case definition, only data from cases with clinical symptoms are presented. To fulfil the definition for a clinically and laboratory confirmed case, it is sufficient if the case shows one of the listed clinical signs, and so data collection about the clinical signs is not comprehensive. In the majority of cases only the leading symptom is reported. In 314 cases multiple responses regarding the clinical signs were given. Among the cases not related to pregnancy (n=1294) the signs and symptoms most frequently reported were meningitis (32%), septicaemia (26%), fever without characteristic organ involvement (31%), abscess (4%), and endocarditis (3%) [TABLE 1].

TABLE 1

Clinical symptoms of non-pregnant listeriosis patients (n=1294), Germany, 2001-2005

Clinical symptoms *	Number of cases (percentage)
Meningitis	414 (32%)
Septicaemia	335 (26%)
Others	235 (18%)
Localised infection of other organs	120 (9%)
Abscesses	47 (4%)
Endocarditis	43 (3%)
Joint infection	11 (1%)
Fever	403 (31%)

* Multiple responses possible

Collection of data about pregnant women with listeriosis has improved since the simultaneous notification of these cases was implemented in 2004. From 2001 to 2005 the clinical manifestations of 80 pregnancy associated cases were reported. The proportion of pregnant listeriosis cases for which clinical information was available increased from 68% in 2001 to 2003 to 84% in 2004 and 2005.

The mean annual case number for the period previous to the change of the case definition was about 10, while in 2004 and 2005 about 25 cases annually were reported [TABLE 2]. The most common symptoms and clinical outcomes among pregnant women (n=80) were premature delivery (33%), fever (31%), flu-like symptoms (16%) and miscarriage/abortion (13%).

TABLE 2

Clinical symptoms of pregnant listeriosis patients (n=80), Germany, 2001-2005

Clinical symptoms *	2001- 2003 n=31	2004- 2005 n=49	Total n=80
	n (%)	n (%)	n (%)
Flu-like symptoms	0 (-)	13 (27)	13 (16)
Fever	4 (13)	21 (43)	25 (31)
Septicaemia	1 (3)	1 (2)	2 (3)
Meningitis	1 (3)	0 (-)	1 (1)
Miscarriage/abortion	11 (35)	1 (2)	12 (13)
Premature delivery	2 (6)	24 (49)	26 (33)
Stillbirth	3 (10)	2 (4)	5 (8)
Asymptomatic	10 (32)	8 (16)	18 (23)

* Multiple responses possible

In 138 (9%) of all listeriosis cases reported from 2001 to 2005, the patient died. The case fatality was highest in neonates (11%) [TABLE 3]. It was relatively low (0 to 4%) in the age groups between one year and 49 years, but increased to 11% in the age group 50-59 years and 12% in the age group ≥70 years.

TABLE 3

Case fatality rate for listeriosis cases by age group, Germany, 2001-2005

Age group (years)	Deaths	Case fatality rate
<1	17	11%
1-19	0	0%
20-29	1	3%
30-39	1	1%
40-49	4	4%
50-59	16	11%
60-69	28	7%
≥70	71	12%
Total	138	9%

The mean annual listeriosis incidence in the years 2001 to 2005 was 0.37 cases per 100 000 for the whole of Germany. However, substantial geographic variations of the incidence were observed. It ranged from 0.16 cases per 100 000 in the state of Mecklenburg Vorpommern to 0.63 cases per 100 000 in the city state of Bremen. Figure 3 displays the incidence differences by federal state.

Information about the country where the listeriosis had been acquired was available for 1297 cases (85%). In 98% of the cases the infection had most likely been obtained in Germany.

L. monocytogenes was detected by culture in 1463 cases (from blood 71%, cerebrospinal fluid 24%, other usually sterile patient

FIGURE 3

Mean incidence (cases per 100 000 population) of listeriosis in federal states of Germany, 2001-2005



specimens 4%, material from neonates 2%). Serotyping was only carried out in 5% of cases (n=80). Serotype 1/2a was found in 39 cases, serotype 4b in 38 cases and serotype 1/2b in 3 cases.

Information about the underlying medical conditions of the listeriosis cases cannot be systematically obtained in routine surveillance. In an ongoing project of enhanced listeriosis surveillance we aim to collect such information from all cases. However, information about the underlying conditions or predisposing factors was available for 257 (20%) of the 1294 cases not related to pregnancy. The conditions reported most frequently were malignancies (46%, of which non-haematological malignancies 28%, haematological malignancies 18%), followed by liver cirrhosis (11%), other underlying conditions such as HIV/AIDS, psoriasis, rheumatoid arthritis, collagen vascular disease (11%), immunosuppressive treatment (9%), or diabetes (7%) [TABLE 4].

TABLE 4

Underlying disease or condition in non-pregnant patients with listeriosis, Germany, 2001-2005

Underlying conditions	Number (percentage)
Non-haematological malignancy	71 (28)
Haematological malignancy	45 (18)
Cirrhosis	28 (11)
Other underlying condition	28 (11)
Immunosuppressive treatment	22 (9)
Diabetes mellitus	19 (7)
Dialysis	12 (5)
Organ transplant	11 (4)
Inflammatory bowel disease	10 (4)
Alcoholism	8 (3)
Chronic liver disease	3 (1)
Total	257 (100)

Discussion and conclusions

Listeriosis surveillance data in Germany reveal a continuous increase of cases since 2001, when the national reporting system was introduced. A particularly steep increase was observed in 2005. This trend is mainly due to an increase of non-pregnancy related cases aged ≥ 60 years, and is most pronounced in the age group ≥ 80 years. Incidence of non pregnancy related listeriosis is higher among males. A possible explanation is that the number of several predisposing conditions such as malignancies and alcoholic disease in males is likewise higher in males than in females.

It is a common phenomenon that case numbers may increase in the first one or two years after the implementation of a new surveillance system. However, the further rise in listeriosis in Germany in the previous two years cannot be explained by factors such as better acceptance of the surveillance system among laboratories and physicians, or raised diagnostic awareness. In other European countries with a longer history of listeriosis reporting such as England and Wales or the Netherlands similar trends of increasing listeriosis case numbers have been observed [3,4,8]. In conjunction with the data from Germany this indicates a true rise in incidence rather than a surveillance artefact.

Although we cannot rule out the possibility that part of the increase may be caused by enhanced diagnostic awareness of physicians, the data suggest that listeriosis incidence among elderly people has truly increased. The reasons for this, however, remain unclear. It is likely that the proportion of highly susceptible patients (immunosuppressive treatment, medical conditions, etc.) is increasing over time in an

aging population [6]. However, this would result in a steady but rather slow increase and cannot explain the significant increase in 2005. It is possible that common foodstuffs were more frequently contaminated with *Listeria* in recent years. This remains rather speculative since no systematic and representative large-scale food investigations have been performed. However, there is evidence from routine food safety investigations that substantial proportions of different foodstuff may be contaminated by *L. monocytogenes* (e.g., about 10% of raw meat products in 2005). Unfortunately, serotyping and molecular typing results for *L. monocytogenes* isolates is only rarely performed in Germany. Therefore, we do not have any laboratory data which would allow to identify (diffuse) listeriosis outbreaks and possibly link isolates from human cases to those from certain foods. Although there is no evidence from the surveillance side that larger outbreaks occurred, the relatively long incubation period makes it difficult to establish epidemiological links between cases and to identify a common food vehicle by epidemiological studies only.

The observation that the number of pregnancy associated cases remained relatively stable while the other cases steadily increased over time might be explained by the fact that risk communication and prevention strategies are already well-established in the risk group of pregnant women. For the other risk groups (high age, immunosuppression, malignancies) intensified education and preventive efforts are required.

The further marked increase of listeriosis in 2005 prompted us to start an enhanced surveillance project for listeriosis. The aim of the project is to obtain detailed and standardised information about the clinical course, underlying conditions, medical treatment, knowledge about listeriosis in risk groups and possible alimentary risk factors from all newly diagnosed listeriosis cases in Germany. In order to gain better insight into the epidemiology of listeriosis, enhanced surveillance and epidemiological studies should be combined with the implementation of molecular typing of isolates from humans and food.

Efforts to educate high risk consumers and thereby reduce their risk of listeriosis should be intensified. The recommendation for the prevention of listeriosis that pregnant women should avoid high risk foods should be continued. Other people with predisposing conditions for listeriosis such as immunocompromised individuals and the elderly should also be informed about possible risk factors and prevention strategies.

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