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Human listeriosis: surveillance, epidemiology, transmission and prevention

Introduction

Human listeriosis is one of the most serious foodborne bacterial infections. Clinical illness in adults may range from a mild flu-like illness to bacterial meningitis. Severe disease affects primarily the elderly, pregnant women, newborns, and adults with impaired immune function. Although *Listeria monocytogenes* infection in pregnancy may manifest as a mild flu-like illness in the woman, it can lead to premature delivery, intrauterine death or bloodstream infection or meningitis in the newborn. The morbidity and mortality of listeriosis is very high, with notified cases invariably reported as being hospitalised. In England and Wales in 2000, Adak *et al* (2002) estimated that although listeriosis accounted for less than 0.1% of all foodborne illness, it accounted for approximately 17% of deaths related to foodborne illness.¹

Surveillance in Ireland

Prior to 2004, national surveillance for listeriosis was based on a voluntary laboratory survey conducted annually to fulfil the requirements of the EU Zoonosis Directive. Between 2000 and 2003, 6-7 cases were reported per annum.² The disease became notifiable on January 1st 2004, and the case definition now used is based on the EU case definition. It includes 'clinically compatible cases that have isolation of *L. monocytogenes* from a normally sterile site' (<http://www.ndsc.ie/hpsc/NotifiableDiseases/CaseDefinitions/>). In addition to the basic demographic data usually collected for notifiable diseases, enhanced information is collected on clinical features and on factors that may have contributed to illness (e.g. pregnancy, underlying illness, history of consumption of high-risk foods, etc.).

Table 1. Listeriosis notifications by quarter and year, Ireland 2004-2007

Quarter	2004	2005	2006	2007	Total
Q1	2	2	5	2	11
Q2	3	3	0	1	7
Q3	4	5	1	11	21
Q4	2	2	1	7	12
Total	11	12	7	21	51
CIR per 100,000 (CI)	0.26 (0.11-0.41)	0.28(0.12-0.44)	0.17(0.04-0.29)	0.50(0.28-0.71)	-

Table 2. Listeriosis notifications by HSE area, Ireland 2004-2007

Type	E	M	MW	NE	NW	SE	S	W	Total
Adult	14	6	4	2	2	0	2	7	37
Pregnancy-related/ neonatal	9	1	0	1	1	2	0	0	14
Total	23	7	4	3	3	2	2	7	51

Table 3. Listeriosis notifications by case type, Ireland 2004-2007

Case type	2004	2005	2006	2007	Total
Adult or juvenile	8	12	5	12	37
Pregnancy-related	3	0	1	6	10
Neonatal	0	0	1	3	4
Total	11	12	7	21	51

Of the 37 non-pregnancy-associated adult cases notified between 2004 and 2007 (table 2), 60% were male and the median age was 72 years (range 30-87 years). Thirty cases (81%) were reported as elderly (>65 years) and/or suffering from an underlying illness which predisposed them to listeriosis.

In the same time period, there were ten pregnancy-associated cases and four neonatal cases - an average rate of 5.6 notifications per 100,000 live births, 2004-2007³. The increase in listeriosis notifications reported in 2007 was primarily among pregnancy-related and neonatal cases (table 3). Five of the pregnancy-related cases in 2007 were non-Irish-born women; three from Eastern Europe, one from Asia and one from Africa. In addition, one of the neonatal cases was born to an Eastern European mother.³ This increase in the number of pregnancy-associated cases in Ireland contrasts with recent rises in human listeriosis incidence noted in Germany and in England and Wales where the increases reported were in the numbers of non-pregnancy-associated adult cases.^{6,7}

³ Rate was calculated using CSO data on births for 2004-2006, and an estimate of 64,000 births for 2007 as data not yet published

Incidence, 2004-2007

Listeriosis notifications from 2004-2007 ranged between seven and 21 per annum (table 1). Cases were distributed throughout Ireland (table 2) with a slight seasonal summer peak in incidence most years (table 1). The highest incidence was in 2007, when the crude incidence rate (CIR) was 0.5 per 100,000 (table 1).³

A steady increase in reported cases of human listeriosis across the EU over the last eight years is believed to represent a true change in incidence.⁴ Overall the reported incidence of listeriosis across the EU in 2006 was 0.3 per 100,000 (range 0.0-1.0 per 100,000), with Denmark, Finland and Luxembourg reporting the highest incidences.⁵

Risk groups

It is well established that listeriosis occurs mainly in elderly individuals, immunocompromised persons, or other vulnerable groups such as pregnant women or neonates.

Epidemiology of Hepatitis C Infection in Ireland

Introduction

Hepatitis C infection is a major cause of chronic liver disease and death worldwide. Transmission of the virus is primarily through sharing contaminated equipment when injecting drugs or through receipt of unscreened blood or blood products. Sexual, occupational and perinatal transmission can also occur but are less common.^{1,2}

Most studies estimate that between 60 and 85% of those infected fail to clear the virus. According to the World Health Organization, there are approximately 170 million chronic carriers worldwide.^{1,2} Chronic infection can cause slowly progressing liver disease with the most serious effects usually seen after more than 20 years of infection. It is estimated that 10-20% of people who are chronically infected will develop cirrhosis or liver failure, with a median time from infection to cirrhosis of 30 years. The estimated annual risk of hepatocellular carcinoma (HCC) in patients with cirrhosis is between one and seven percent.³

Disease progression varies between individuals, with older age at infection, male sex, higher alcohol consumption and longer duration of infection all associated with faster progression.^{1,2}

Hepatitis C can be treated but success rates vary. One of the key factors affecting response to anti-viral treatment is the genotype of the virus. Sustained virologic response rates are lower for people with genotype 1 hepatitis C compared to people with genotypes 2 or 3. However, response rates have improved significantly in recent years with the advent of combination regimens of pegylated interferons and ribavirin. Sustained virologic response rates of up to 46% in genotype 1 patients and up to 82% in genotype 2/3 patients have been achieved with these therapies in clinical trials.⁴

Methods

Comprehensive data on the epidemiology of hepatitis C in Ireland are limited. Most of the available information comes from routine surveillance and from special studies in high prevalence groups such as injecting drug users (IDUs), prisoners and asylum seekers. The Irish Blood Transfusion Service (IBTS) also collects data on the prevalence of hepatitis C in blood donors.

Sources of information about the burden of hepatitis C disease in Ireland include the hospital inpatient enquiry system (HIPE), the national cancer registry (NCRI), Central Statistics Office (CSO) mortality data and liver transplantation data from the National Liver Transplant Centre in St Vincent's University Hospital. A national research database has also been set up to follow the natural history of infection in people infected through the administration of contaminated blood and blood products prior to the introduction of screening. The baseline report on this cohort was published in October 2007 (<http://www.ndsc.ie/hpsc/A-Z/HepatitisHIV/AIDSandSTIs/HepatitisC/HepatitisCDatabase/BaselineReport/>).⁵

Results

Hepatitis C notifications 2004-2007

Hepatitis C became a notifiable disease in Ireland in January 2004. Prior to this it could be notified as viral hepatitis, type unspecified, but most cases were not reported. Since it became notifiable, rates have been high with 5,357 cases of hepatitis C notified in Ireland between 2004 and 2007 (table 1).

The geographic distribution of cases has been fairly consistent over the

Table 1. Number of cases and age-standardised notification rates (ASR) per 100,000 population for hepatitis C, 2004-2007

Year	Number of cases	ASR per 100,000
2004	1,130	25.5
2005	1,433	33.4
2006	1,222	28.5
2007	1,572	36.8

past four years, with approximately three-quarters of cases notified by the HSE Eastern area (HSE E) (77%, n = 4,125) (figure 1).

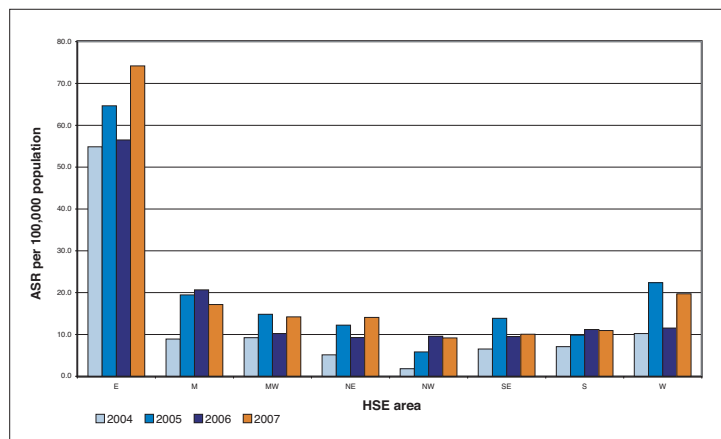


Figure 1. Annual ASR per 100,000 population by HSE area, 2004-2007

The age and sex distributions of cases have also been quite consistent between 2004 and 2007. Male cases predominated: 63% of cases were male (n = 3,387), 35% were female (n = 1,884) and sex was not known for the remaining 2%. The highest rates were among young to middle-aged adults, with 92% of cases aged between 20 and 54 years (figure 2). The median age at notification for females was slightly younger than that for males at 31 compared to 33 years.

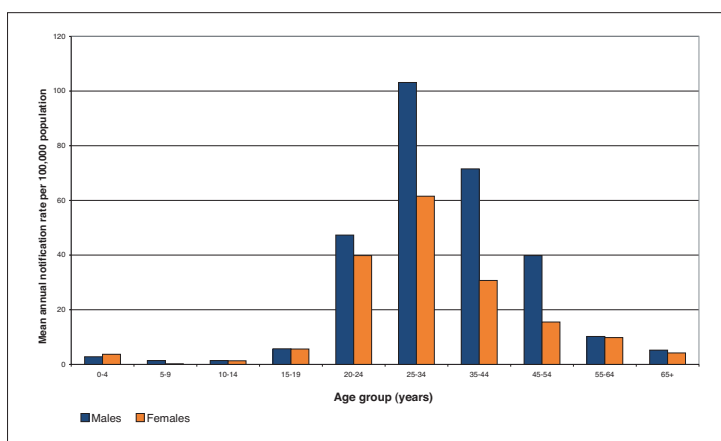


Figure 2. Mean annual age- and sex-specific notification rates per 100,000 population, 2004-2007

Hepatitis C prevalence data

Injecting drug users and prisoners

Studies of injecting drug users (IDUs) in prisons and IDUs attending methadone clinics, specialist addiction treatment centres and GPs have estimated the hepatitis C prevalence in this population to be between 62 and 81%.⁶⁻¹²

Asylum seekers

Thirty-five to forty percent of all new asylum applicants are screened for communicable disease in the HSE. A review of the screening service in this area was carried out in 2004 and found that over half of those who availed of screening were tested for hepatitis C antibodies and 1.5% were positive.¹³

Blood donor screening

The IBTS blood donor-screening programme detected a hepatitis C antibody prevalence of 0.02% (43/207,015) in new blood donors between 1997 and 2006 (personal communication, IBTS, February 2007). This low prevalence is to be expected as blood donors are unpaid volunteers, and individuals who are identified as having relevant risk factors are excluded prior to donation.

Burden of hepatitis C disease

Hepatitis C infection through blood and blood products

Approximately 1,700 people have been infected with hepatitis C through the administration of blood and blood products in Ireland.^{5 15 16} These include recipients of blood transfusions and blood clotting factors, women infected through anti-D immune globulin and people who received treatment for renal failure. People infected in this way are "one-off" cohorts as blood and blood products are now screened for hepatitis C.

Patients in these cohorts were invited to consent to be included in a national hepatitis C research database which involved the extraction of certain data from their medical charts. Participation in the baseline round of data collection was over 70% and the median time since infection at baseline was 27 years. Twenty percent of patients with positive confirmatory tests for hepatitis C antibodies had cleared the virus prior to testing and the remaining 80% had tested positive for circulating virus at some stage (PCR positive). Of the patients who tested PCR positive (n = 746), 9.7% had developed cirrhosis, 1.3% had developed liver tumours/HCC and 3.5% had died from liver-related disease. Alcohol consumption in excess of recommended limits was mentioned in the charts of over half of the patients who died from liver-related disease. Eighty percent of those who ever tested PCR positive remained PCR positive at last test.

National Cancer Registry of Ireland

HCC is the most common form of primary liver cancer. The most important causes worldwide of HCC are chronic infection with hepatitis B and hepatitis C. Three hundred and seventy-five cases of HCC were registered with the NCRI between 1994 and 2005 (figure 3) (personal communication: NCRI, May 2007).

A systematic review of all published data on the prevalence of chronic hepatitis B and C infection among HCC cases found a prevalence of hepatitis C antibody positivity of 34.3% from studies in nine European countries. An additional 6.5% of cases were positive for both hepatitis C antibodies and hepatitis B surface antigen.¹⁷ These prevalences were 27.5% and 2.5% respectively in a smaller study in the United Kingdom. Therefore, although NCRI data do not specify underlying cause, it is likely that somewhere in the region of one-third of HCC cases here are anti-HCV positive.

Central Statistics Office mortality data

The underlying cause of death was reported to be primary liver cancer for 288 people between 1994 and 2005 (figure 3) (personal communication: CSO, May 2007).

Hospital In-Patient Enquiry Data

The HIPE scheme is a computer-based health information system designed to collect medical and administrative data on discharges and deaths from acute hospitals (excluding private hospitals). Each discharge record represents one episode of care and patients may have been admitted more than once, or to more than one hospital, with the same diagnosis. HIPE coverage of acute hospitals was 95% between 1999 and 2004. During this period, there were 3,060 discharges with a principal diagnosis of 'other specified viral hepatitis without mention of hepatic coma'. Most of these are likely to have been due to hepatitis C. A further 778 discharges were associated with a principal diagnosis of primary liver cancer (personal communication: Economic and Social Research Institute, July 2007).

Liver transplants

The liver unit in St Vincent's University Hospital, Dublin carried out 311 liver transplants between 2000 and 2006. Twenty-five of these were known to be a consequence of HCV infection and a further seventeen were known to be due to hepatitis C plus another indication such as alcoholic liver disease or hepatocellular carcinoma (personal communication: Liver Transplant Unit, St Vincent's University Hospital Dublin, April 2007).

Discussion

Data on the epidemiology of hepatitis C in Ireland are available from a variety of sources including routine surveillance and special studies. These show a high prevalence of hepatitis C in certain populations, namely one-off cohorts of those infected in the past through administration of blood and blood products and the ongoing larger cohort of IDUs. The prevalence in the general population is unknown. Information on hepatitis C in Ireland is improving. Risk factor information is now being provided on some patients through the routine notification system. A national hepatitis C strategy is being developed by the HSE and will be published in 2008. Further studies and research are needed to address the gaps in our knowledge. It is hoped that these developments will lead to better prevention and control of hepatitis C and guide service planning for those with chronic disease.

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References available on request

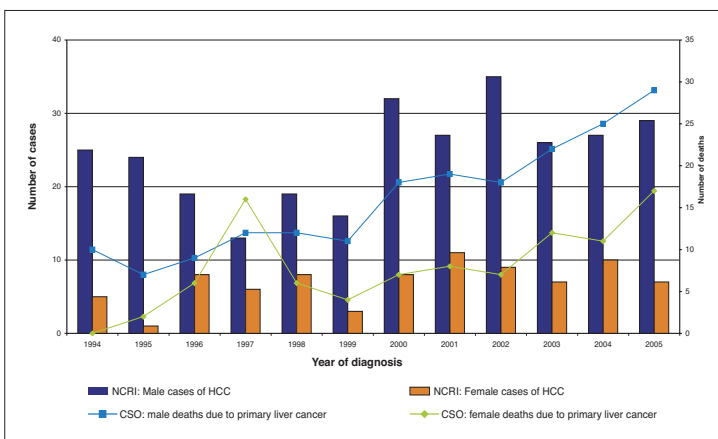


Figure 3. Number of cases of primary liver cancer registered with the NCRI by sex, and number of deaths coded to primary liver cancer by the CSO, 1994-2005

Morbidity and mortality

In Ireland, between 2004 and 2007, eighteen non-pregnancy-associated adult cases and three neonates (41%) were reported to have developed bloodstream infection and/or meningitis. There were two reported fatalities due to listeriosis (one in a non-pregnant adult and one neonate), and three intrauterine deaths.

Microbiology

The *L. monocytogenes* serovars most commonly reported as associated with human infection are serovars 1/2a, 1/2b and 4b. Isolates can be further characterised by molecular typing methods to investigate possible links between cases. In Ireland, there is no official reference laboratory service for human isolates of *Listeria*. In previous years, only a handful of human isolates were typed. Two hospital laboratories have a research interest in *Listeria* and during the upsurge in cases in 2007, twelve isolates were forwarded to the National Salmonella Reference Laboratory (NSRL) for serotyping and molecular typing by pulsed field gel electrophoresis (PFGE)⁸ and three to Waterford Regional Hospital (WRH) for ribotyping.

From the results obtained for these fifteen isolates, it appears that the upsurge in cases was not caused by a single common strain. Two isolates were indistinguishable both by ribotyping and PFGE providing support for a possible unrecognised common link. While the predominant serotype from patients was 4b, 1/2 was the predominant *L. monocytogenes* serotype from food (table 4).

Table 4: Serotypes of *L. monocytogenes* isolates referred to the NSRL, 2007

Source	1/2	4b	Untypeable	Total
Human	3	12	0	15
Food	15	3	1	19

Transmission

Transmission of human listeriosis is mainly foodborne (with onward vertical transmission to the foetus/neonate in the case of pregnancy-associated cases). The incubation period ranges from three days to ten weeks, with an average period of three weeks. *L. monocytogenes* is ubiquitous in the environment. It has been detected in a variety of raw foods such as uncooked meats and vegetables as well as in processed foods contaminated post-processing such as soft cheeses and ready-to-eat meats, both of which have been implicated internationally in outbreaks. The foods most often reported as associated with infection are ready-to-eat refrigerated and processed foods such as pre-prepared cooked and chilled meals, soft cheeses, cold cuts of meat, pâtés and smoked fish.

Reported consumption of high-risk foods among cases in Ireland

In Ireland, data on consumption of high-risk foods by listeriosis cases were collected where available through enhanced surveillance. However, recall can be poor among those who are very ill or elderly. The period investigated was four weeks before symptom onset, or in the case of neonatal cases, four weeks before the end of the pregnancy. In 2007, a number of patients reported recent consumption of foods considered high-risk for listeriosis, in particular soft cheese and sliced cooked meats. However, this information is difficult to interpret in the absence of control group data.

Prevention during pregnancy

As with other food borne illnesses, there are several steps that will help to reduce the risk of infection with *L. monocytogenes* during pregnancy:

- Keep foods for as short a time as possible and follow storage instructions including 'use by' and 'eat by' dates

- Cook food thoroughly, especially meat, ensuring that it is cooked through to the middle
- Keep uncooked meats separate from vegetables and from cooked and ready-to-eat foods
- Wash salads, fruit and raw vegetables thoroughly before eating, or peel if appropriate
- Wash hands, knives, and cutting boards after contact with uncooked food
- Make sure that the refrigerator is working correctly
- When heating food in a microwave, follow heating and standing times recommended by the manufacturer
- Throw away left-over reheated food. Cooked food which is not eaten immediately should be cooled as rapidly as possible and then stored in the refrigerator
- Avoid eating high-risk foods such as raw (unpasteurised) milk or foods made from raw milk, soft or mould-ripened cheeses (e.g. feta, Brie, Camembert, blue-veined cheeses), pâté, smoked salmon
- If contact with ewes at lambing time is unavoidable, wash hands after handling animals to reduce any possibility of infection.

Summary

Typing (serology and molecular typing) of human *L. monocytogenes* isolates during the upsurge in cases in 2007 was invaluable as it supported the results of public health investigations which suggested an increased incidence of sporadic disease rather than a large common source outbreak. The continued support of primary hospital laboratories in forwarding human *Listeria* isolates for further studies is appreciated. Typing of isolates from food or food premises may also be valuable, particularly in the context of a suspected common source outbreak.

A recent publication by Denny and McLauchlin (2008) highlighted an opportunity for the establishment of a formalised listeriosis network in Europe.⁴ The continued integration of epidemiological and microbiological information at national level in Ireland will be essential should such a network be established.

In consequence of the rise in the number of pregnancy-associated/neonatal cases in 2007, efforts are being made to develop appropriate messages for pregnant women, in particular those whose first language is not English. A leaflet highlighting ways to minimise their risk has been developed for pregnant women by Safefood and will be translated into several languages. Other useful resources are outlined below:

Useful links

HPSC factsheets on listeriosis at <http://www.ndsc.ie/hpsc/A-Z/Gastroenteric/Listeriosis/Factsheets/>
 Safefood leaflet for pregnant women at <http://www.safefoodonline.com/>
 FSAI report on *The control and management of L. monocytogenes contamination of food chain* at http://www.fsai.ie/publications/reports/listeria_report.pdf.

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References on request