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Increase in Hantavirus Infection in Europe, 2005

A significant increase in hantavirus infections has been reported in Belgium, Germany and France since spring 2005. During the period 1 January to 15 June 2005, 120 cases were reported in Belgium (total number of cases for 2004 was 47), and 115 cases in France (total number of cases for 2004 was 55). In Germany, 258 laboratory-confirmed cases were reported between 1 January and 30 June 2005 (64 for the same period in 2004) and the increase in cases occurred earlier in the year than in previous years. In 2005, most cases occurred in men, and the mean age was around 41 years in all three countries. In Germany 82% of cases were caused by the hantavirus species Puumala, 2% were caused by Dobrava, and the virus species was not specified in the remainder.[1]

Epidemiology

Hantaviruses are RNA viruses that infect rodents worldwide. More than 25 antigenically distinguishable species exist, each associated primarily with a single rodent species. Several species are known to infect humans resulting in haemorrhagic fevers with renal syndrome (HFRS) of varying severity. Severe illness is associated with Hantaan (HTN) viruses (primarily in Asia) and Dobrava viruses in the Balkans. The Puumala viruses which are endemic in Central and Northern Europe cause a less severe HFRS called nephropathia epidemica.[2]

The reservoir of infection for the Puumala virus is the bank vole which is found in forests and agricultural hedgerows. The voles have highly fluctuating populations which move into urban and rural gardens and dwellings particularly in the autumn and winter of years when their populations reach peaks. Most hantavirus epidemics have been associated with increased rodent populations.[3] Occupational and recreational activities may influence the risk of exposure.

Mode of transmission

The virus is found in the urine, faeces and saliva of infected rodents. Transmission is thought to occur through inhalation of aerosolised excreta from these rodents. Disease has also followed the bite of an infected rodent.[3]

Incubation period

The incubation period varies from a few days to nearly two months, usually 2-4 weeks.[2]

Clinical features

The illness presents with sudden onset of fever, headache, backache, abdominal pain and varying degrees of haemorrhagic manifestations and renal involvement. The severe form of HFRS caused by the HTN and Dobrava viruses has a case fatality rate ranging from 5% to 15%. The case fatality rate in nephropathia epidemica is <1%.[2]

Diagnosis

Diagnosis is made by demonstrating specific antibodies using ELISA or IFA. Most patients have IgM antibodies at the time of hospital admission. Hantaviruses are difficult to recover from cell-culture or animal hosts but can be detected by reverse transcription-polymerase chain reaction or in tissues by immunohistochemical staining.[3]

Treatment

Supportive therapy is critical and renal dialysis may be necessary in severe cases. IV ribavirin may be of benefit if given early enough.[2]

Prevention

In endemic areas avoid contact with wild rodents as much as possible. Rodents should be prevented from accessing houses and other buildings. Food that could attract rodents should be stored in rodent-proof conditions. Areas/surfaces that may have been contaminated with rodent excreta should be sprayed with a disinfectant prior to cleaning. Avoid aerosolisation of contaminated dust.[2]

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Ireland to Participate in WHO European Immunisation Week

This year Ireland, together with six other countries, has committed to piloting European Immunisation Week - 17 to 24 October 2005. This is a WHO initiative aimed at increasing vaccination coverage through enhanced awareness of the importance of immunisation in protecting lives and preventing disease. The HSE Programme of Action for Children has been asked to take the lead role in the preparation for this week supported by a WHO communications consultant. Various activities are being planned around the country with the theme "*Prevent, Protect, Immunise*". In addition a new website www.immunisation.ie will be launched. This will contain useful up-to-date information on childhood and adult immunisations for the general public and health care professionals as well as information leaflets which can be downloaded in several languages.

For more information please contact the HSE Programme of Action for Children at 01 876 7108.

Enhanced Bacteraemia Surveillance in Ireland, 2004

Introduction

The rise in antibiotic resistance in clinically important bacteria is a worldwide problem that has led to diminished therapeutic choice and poorer outcomes in patients. The European Antimicrobial Resistance Surveillance System (EARSS) aims to monitor the occurrence of antibiotic resistance in major pathogens causing invasive infections (bacteraemia and meningitis) by collating data from microbiology laboratories across Europe.[1]

In Ireland, the level of methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the highest among countries reporting to EARSS. Levels of penicillin-non-susceptible *Streptococcus pneumoniae* (PNSP) and vancomycin-resistant enterococci (VRE) are moderately high. And while resistance levels in invasive isolates of *Escherichia coli* to third-generation cephalosporins are comparatively low, fluoroquinolone resistance in this organism still remains problematic.[2]

As well as resistance data, collection of additional information, both clinical and demographic, was identified as vital in understanding the factors affecting the acquisition of these invasive isolates in Ireland, as has been the case elsewhere.[3, 4] This in turn could offer input into future infection control measures both nationally and in those hospitals that participate in the surveillance scheme.

This report covers the first year (2004) of enhanced data collected on EARSS pathogens causing bloodstream infections in Ireland.

Method

Hospitals voluntarily contributing to the enhanced survey were asked to supply a completed questionnaire for the first isolate per patient per quarter from blood-culture under the EARSS protocol. The fields included were patient age/sex, admission and specimen dates, transfers, clinical significance, risk factors, primary source and secondary foci.[5] Clinical and scientific staff at the microbiology departments of contributing institutions completed the forms after obtaining the data from a variety of hospital systems.

The questionnaires were designed and scanned using Cardiff Teleform™ software, and the data were managed on an MS Access database where corresponding records were linked to the isolates' antimicrobial sensitivities as present on the EARSS dataset. Chi-square tests were used for statistical inference and the findings were considered significant at $P<0.05$.

Results

Seven laboratories contributed to the enhanced surveillance on 985 matched records. The resistance profiles of the isolates were found to be representative of equivalent blood-culture isolate data for all the EARSS participating hospitals for 2004 (table 1).

Length of stay (LOS) before culture is here defined as the number of days spent by a patient in the hospital before a positive specimen is taken (specimen date minus admission date).[6] The proportion of cumulative frequency over total number of isolates for each organism was plotted against LOS before culture for the first seven days of the data as shown in figure 1. Nearly 90% of all *S. pneumoniae* (SPN) isolates were sampled by day two. That is, very few new cases arose in patients who had been in the hospital for more than two days, thus reflecting the community-acquired nature of this organism. By contrast, it took 63 days before 90% of all enterococci (EFF) isolates were sampled, thus reflecting their hospital-acquired nature. Data points for *E. coli* (ECO) and methicillin-sensitive *Staphylococcus aureus* (MSSA) fell between these two extremes reflecting a complex situation. The curve for MRSA was parallel to that for enterococci but higher, so while most MRSA infections are hospital-acquired, the organism would already have been acquired at the time of admission in a number of patients.

Half of all infections were in patients aged 65 years or over. The proportion of MRSA in patients in the age group >65 years (59%) was significantly higher ($P<0.001$, relative risk 1.79) than in the <65 years age group (33%).

Table 2 shows factors affecting each organism. Respiratory tract infection was usually the primary source for *S. pneumoniae* bacteraemia. Urinary tract infection with or without catheter, and the intra-abdominal/GI tract were commonly the sources for *E. coli* bacteraemia. The intra-abdominal/GI tract was also a common source of enterococcal blood-stream infections. Furthermore, central venous catheters (CVCs) were frequently noted as a source for these organisms. Among primary sources of *S. aureus* bacteraemia, CVCs were by far the most commonly noted, followed by respiratory tract and skin/soft tissue infections. The proportion of isolates that were MRSA among these three main sources of *S. aureus* bacteraemia was widely different: CVCs were the source in 48% of isolates (which is close to the overall level), the respiratory tract in 61% (which is higher although without reaching statistical significance at $P=0.08$) and skin/soft tissue infections in 29% (which is significantly lower than the overall level with $P=0.005$).

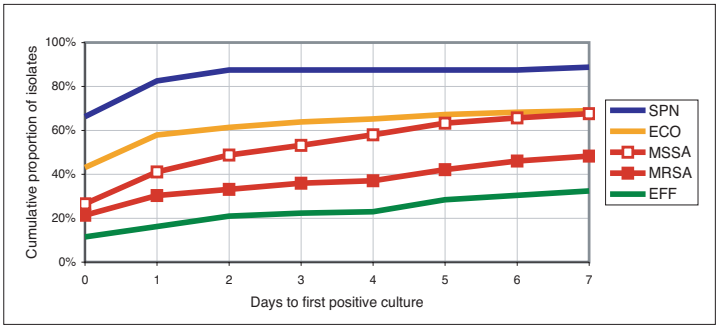

Figure 1. Proportionate cumulative frequencies of pathogens isolated by days to first positive culture (or length of stay before culture) for days 0-7.

One or more known risk factors were noted for each infection. Malignancies and immunosuppression were collectively by far the most common risk factors associated with the acquisition of EARSS pathogens. For *E. coli* and enterococci, stay in an intensive care unit (ICU stay) and recent surgery were frequently recorded. Major factors affecting *S. aureus* blood culture isolates, with varied proportions of MRSA, were: haemodialysis (52%, $P=0.09$), recent surgery (49%, $P=0.4$) and ICU stay (58%, $P=0.02$).

Secondary foci were largely non-identifiable. However, bone/joints and the cardiovascular system (endocarditis) for *S. aureus* were noted in a number of cases.

Discussion

The number of hospitals participating in this enhanced bacteraemia survey appears to be small, although the number of records examined represents 29% of all isolates investigated under the EARSS protocol in Ireland, in 2004. This probably reflects an overrepresentation by larger hospitals and the surveillance scheme would benefit by the addition of smaller institutions.

Plotting LOS before culture is a useful method for determining a particular strains' tendency to be either hospital- or community-acquired. Such analyses here indicate that in Ireland there may be a small proportion of MRSA isolates that are community-acquired and a better estimate of the number of true community-acquired MRSA bacteraemia episodes within the EARSS dataset could be ascertained using these analyses along with strain-typing data.

The age distribution analysis shows that the burden of infection is on older people. The probability of isolating MRSA as opposed to MSSA in blood-

Table 1. Breakdown by organism and major resistance groups for the 985 isolates in the enhanced bacteraemia surveillance and the equivalent results from the complete EARSS dataset for 2004. (Provisional data).

Organism	This study	EARSS
Streptococcus pneumoniae	90	400
penicillin non-susceptible	13 (14%)	41 (10%)
Escherichia coli	311	1244
Enterococci	158	424
Enterococcus faecalis	81	239
vancomycin resistant	1 (1%)	3 (1%)
Enterococcus faecium	77	185
vancomycin resistant	21 (27%)	43 (23%)
Staphylococcus aureus	426	1323
methicillin/oxacillin resistant	193 (45%)	553 (42%)
TOTAL	**985**	**3391**

Table 2. All factors associated with important bacteraemia-causing pathogens in Irish hospitals taking part in the enhanced surveillance.

Factor		*S.pneumoniae*	PNSP	*E.coli*	Enterococci	VRE	*S. aureus*	MRSA
Age category	<65	56	5	131	92	14	229	76
	65+	34	8	180	66	8	197	117
Primary source	Central venous catheter (CVC)	0	0	13	40	6	132	64
	Intra-abdominal / GI tract	1	0	71	40	7	5	5
	Non-surgical wound	0	0	0	3	0	7	6
	Other source	0	0	3	5	1	9	1
	Peripheral venous catheter	0	0	1	0	0	18	9
	Respiratory tract infection	59	8	6	4	0	33	20
	Skin or soft tissue infection	1	0	2	5	0	52	15
	Surgical wound	0	0	7	3	1	17	6
	Unknown	29	5	52	47	7	133	57
	Urinary catheter	0	0	131	7	0	9	5
	Urinary tract w/o catheter	0	0	25	4	0	11	5
Risk factor	Bone marrow transplant	12	2	30	22	7	28	10
	Diabetes	2	1	12	11	1	19	11
	Haemodialysis	1	0	14	18	3	82	43
	Immunosuppressive drugs	3	1	28	18	4	25	11
	IV drug use	3	0	0	1	0	18	3
	Major trauma	0	0	1	4	0	6	2
	Other immunosuppressive illness	4	2	8	7	2	14	6
	Other malignancies	9	0	58	23	2	51	25
	Other risk factors	4	1	28	22	2	40	17
	Recent surgery	0	0	37	41	3	69	34
	Solid organ transplant	0	0	9	4	1	8	5
	Stay in intensive care unit (ICU)	5	0	33	44	7	57	33
Secondary focus	Abscess	0	0	1	3	0	3	0
	Bone or joint	0	0	0	2	0	9	3
	Cardiovascular system	0	0	0	2	0	9	4
	Central nervous system	1	0	0	0	0	1	1
	Other foci	0	0	2	2	1	8	3

cultures from patients aged 65 years or over is nearly twice that in younger patients. This indicates that there is a sub-population of older patients who are more frequently administered healthcare and thus their chances of exposure to MRSA is increased.

The proportion of *S. aureus* bacteraemia isolates resistant to methicillin has reached equilibrium over the last three years and remains stable at around 42%, as measured under the EARSS protocol in Ireland.[7] Furthermore, the rates of *S. aureus* and MRSA bacteraemias, as expressed in counts per 1000 bed-days used, in most hospitals have also remained stable. This situation is probably a reflection of hospitals regularly treating patients with certain case-mix profiles and can lead to the following scenarios (figure 2):

- Those centres routinely admitting older patients, large number of patients with respiratory infections and/or greater use of ICU wards would be expected to consistently have a higher than the national average proportion of MRSA.

- Centres routinely admitting patients with skin/soft tissues infections and mainly younger patients would be expected to have a lower than the national average proportion of MRSA, but their *S. aureus* rate would remain high.

- Those centres with larger oncology/haematological departments carrying out high numbers of surgical procedures and/or having high CVC usage would be expected to have higher rates of both MRSA and *S. aureus* bacteraemias.

- In contrast to the other scenarios, single-speciality centres would be expected to have lower rates.

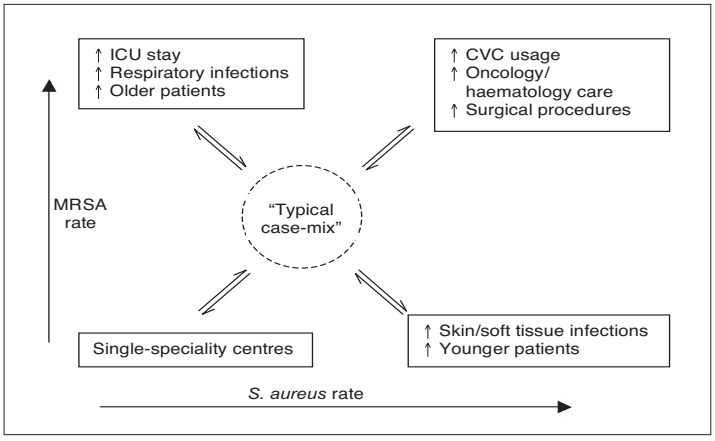

Figure 2. Schematic representation of major factors affecting S. aureus and MRSA rates.

Once the forces driving the very high and the very low levels are understood, then areas can be recognised for improvement in order to reduce the overall levels of nosocomial infections.

The above-mentioned scenarios only serve to illustrate the extreme circumstances of how the breakdown of results from this survey can explain the dynamics of the rates of *S. aureus* and MRSA in a hospital over time. An examination of the wider range of issues is beyond the scope of this study alone. The Strategy for the Control of Antimicrobial Resistance in Ireland (SARI) has launched a number of initiatives to address the levels of MRSA through hand-hygiene guidelines, recognition of shortfalls in key staffing levels, structural and environmental guidelines, as well as local antibiotic stewardship proposals. In order to effectively target and monitor these infection control programmes the National SARI Committee has identified EARSS enhanced bacteraemia surveillance as a priority and is encouraging hospitals to participate.

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Acknowledgments
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Invasive *Haemophilus influenzae* in Ireland, 2004/2005

Background

Invasive disease due to *H. influenzae* type b (Hib) infection is much less common in children following the introduction of Hib vaccination, which has been available routinely in Ireland since 1992. Uptake of Hib vaccine (three dose schedule) at 24 months currently stands at 90%. However, Hib disease has not disappeared completely and cases continue to occur.

A resurgence in the incidence of Hib infections in the UK, especially in children <5 years of age, was seen from 1998, peaking in 2002 with an incidence of 4.63 per 100,000 population in this age group.[1] Hib cases occurred there predominantly in vaccinated children. A similar situation did not emerge in Ireland at the time. Although a slight increase was seen in 2003 in children <15 years of age, the number of Hib vaccine failures remained unchanged and Hib disease was occurring predominantly in unvaccinated children.[2]

However, a changing trend in the epidemiology of this disease has recently emerged in Ireland. A rise in the numbers of invasive *H. influenzae* infections, Hib infections and vaccine failures was seen in the latter half of 2004 and has continued on into early 2005. To examine these trends, the data presented in this article, obtained from the national enhanced surveillance system for Hib, were analysed by the epidemiological years July to June.

Results

Invasive H. influenzae disease

In total, 43 cases of invasive *H. influenzae* infection were notified between July 2004 and June 2005 (2004/05). This represents more than a two-fold rise when compared with 2003/04, when 19 cases were notified (figure 1). The highest number of cases previously notified in any one epidemiological year was in 2002/03, when 30 cases were reported. Of the 43 cases notified in 2004/05, 16 occurred in children <5 years of age, four in 5-14 year olds, and 23 in those >15 years of age.

Invasive H. influenzae type b disease

The number of invasive Hib cases also increased in 2004/05, with 23 cases reported compared to just nine in 2003/04 and 17 in 2002/2003 (figure 2). Sixty-five percent of the Hib cases (15/23) notified in 2004/05 occurred in children <15 years of age. Only four Hib cases occurred in this age group the previous year whereas 13 cases occurred in 2002/03 (figure 2). There was a slight increase of Hib cases in adults in 2004/05, when 8 cases occurred. The range in previous years was from one to five cases per year (figure 2).

Hib disease manifested itself clinically in the <15 year age group in 2004/05 as meningitis (n=5), septicaemia (n=3), meningitis and septicaemia (n=1), septic arthritis/osteomyelitis (n=2), epiglottis (n=1), cellulitis (n=1) and clinical diagnosis unknown (n=2). No deaths were reported in this age group, but one child had serious adverse sequelae.

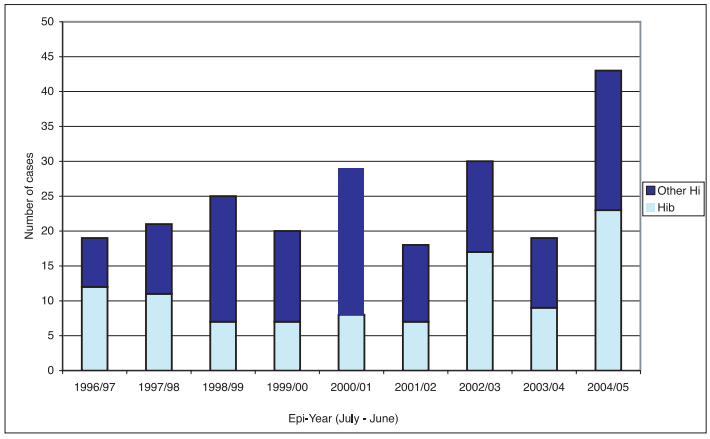

Figure 1. Number of invasive Haemophilus influenzae cases notified in Ireland by epidemiological year, July to June

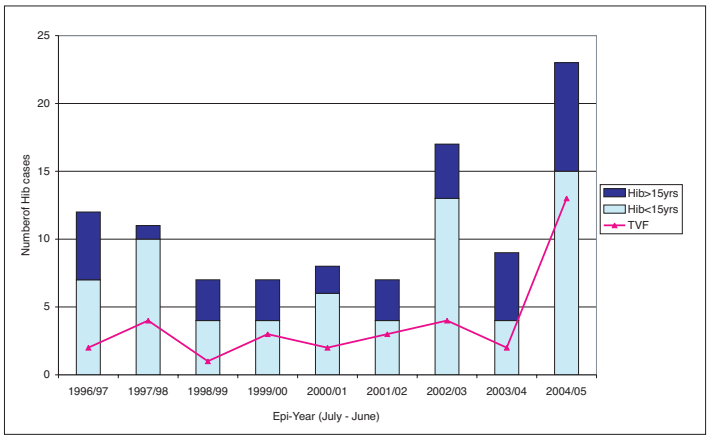

Figure 2. Number of invasive H. influenzae type b cases notified in Ireland by epidemiological year (July – June), in those under and over 15 years of age and the number of true Hib vaccine failures reported

Hib vaccine failures

The majority (87%) of Hib cases in 2004/05 were in fully vaccinated children <15 yeas old, compared to just half in 2003/04. The number of true Hib vaccine failures more than trebled in 2004/05 (n=13) compared with previous years when the numbers ranged between one and four failures per year (figure 2). A statistically significant increase in Hib vaccine failures was seen in 2004/2005 compared with 2003/04 when two failures occurred ($p = 0.0098$, Chi Square analysis, Yates corrected). The escalation in the number of true vaccine failures has been seen predominantly since the end of 2004 and has continued on into 2005. Four failures occurred in Q4-2004, five in Q1-2005, and three further failures in Q2-2005. The increase in Hib vaccine failures have not been linked to one particular brand of Hib vaccine.

A feature of these recent Hib cases and associated vaccine failures is that onset of illness has been at a younger age in recent birth cohorts. In 2004/05, nine (69%) of the 13 Hib vaccine failures occurred in children under three years of age (range 13 – 34 months).

Discussion

Over the past 12 months (July 2004 – June 2005) there has been an increase in the incidence of invasive *Haemophilus influenzae* disease in Ireland. A cause for concern is the increase in the number of Hib cases in children <15 years of age and the fact that these cases have occurred predominantly in vaccinated children. A similar trend occurred in the UK between 1999-2002 and the Department of Health there responded to this increase by launching a Hib catch up programme in early 2003, offering an additional dose of Hib vaccine to children aged between six months and four years.

The Irish National Immunisation Advisory Committee is closely monitoring this recent emerging trend in Ireland and the options available to address this issue are being actively investigated.

Margaret Fitzgerald, Suzanne Cotter, Darina O'Flanagan, HPSC

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