Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

April 2006

Volume 7 Issue 4

hpsc EPI-Insight

Disease Surveillance Report of HPSC, Ireland

ISSN: 1393-9548

Contents

hpsc
Health Protection Surveillance Centre
25-27 Middle Gardiner St
Dublin 1, Ireland
Ph +353 1 876 5300
Fx +353 1 856 1299
E info@mailx.hse.ie
www.hpsc.ie

The rise in antimicrobial resistance in invasive isolates of *Escherichia coli* and *Enterococcus faecium* in Ireland and comparisons with Europe

Antimicrobial resistance (AMR) amongst bacteria that cause disease in humans is a global public health problem. It is associated not only with increased morbidity and mortality, but also with significant healthcare costs associated with efforts to prevent its emergence and dissemination. In 2001, a Strategy for the control of Antimicrobial Resistance in Ireland (SARI) was published to address this growing threat.[1]

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a well-known example of a major AMR problem in Irish hospitals. Data on blood culture isolates of *S. aureus* reported to the European Antimicrobial Resistance Surveillance System (EARSS) indicate that Ireland has one of the highest proportions of MRSA in Europe.[2,3] Although significant increases in MRSA proportions have been reported from 14 of 29 countries reporting to EARSS, the proportion of MRSA isolates in Ireland has been stable at approximately 42% since 2001.

Increasing AMR amongst other pathogens surveyed as part of EARSS is of growing concern in Ireland, as well as in other European countries.

Expansion of EARSS in Ireland

In January 2002, Ireland extended its participation in EARSS to include surveillance of AMR in *Escherichia coli* and the enterococci, *E. faecalis* and *E. faecium*. Routine data are collected from participating laboratories on invasive isolates of these pathogens (*E. coli* from blood or CSF and the enterococci from blood only) on a quarterly basis. Although the number of laboratories participating in the surveillance of these pathogens increased from 21 in 2002 to 42 in 2005, similar trends in AMR to those described below were obtained when the analysis of the data were restricted to the original participants.

Results

E. coli data from Ireland and Europe

The proportion of *E. coli* isolates in Ireland with resistance to fluoroquinolones (ciprofloxacin or ofloxacin) increased significantly from 5.4% in 2002 to 12.5% in 2004 and 16.8% in 2005 (up to the end of Quarter 3) (see Figure 1). Increasing resistance over the period 2001-2004 was observed in 15 of 26 countries reporting to EARSS. In 2004, four countries (Italy, Malta, Portugal and Spain) reported proportions over 25%.[3]

Resistance to gentamicin also increased significantly from 2.7% in 2002 to 5.7% in 2004 and 8.7% in 2005 (up to the end of Quarter 3) (see Figure 1). Increasing resistance over the period 2001-2004 was observed in 8 of 26 countries. In 2004, six countries (including Israel, Malta, Portugal and Romania) reported proportions over 10%.

Between 2001 and 2004, the proportion of *E. coli* isolates in Ireland with resistance to 3rd-generation cephalosporins (3GCs), e.g. cefotaxime or ceftazidime, was relatively stable at 2-3%, however, this increased to almost 4.5% up to

Continued page 4

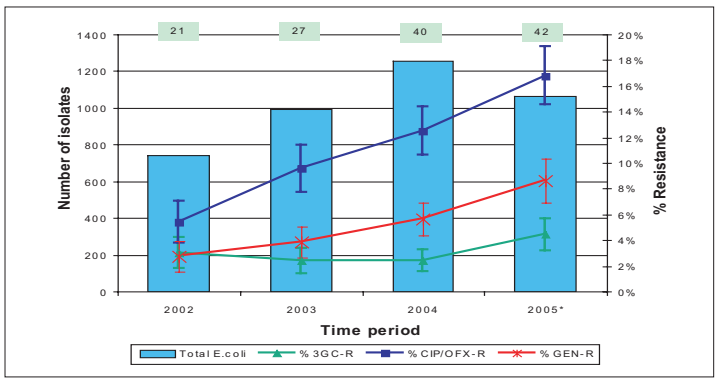

Figure 1. Antimicrobial resistance trends for E. coli – total numbers of E. coli and percentage resistance, with 95% confidence intervals, to third-generation cephalosporins (3GC), ciprofloxacin/ofloxacin (CIP/OFX) and gentamicin (GEN).

* Data for 2005 up to Q3 only; the numbers of participating laboratories by year-end are indicated above the bars.

Infectious Disease Outbreaks in Ireland, 2004

Introduction

Outbreak investigations aim to identify the source of the outbreak, institute control measures and prevent additional cases. Information gathered during outbreak investigations can be used to determine possible ways of preventing future outbreaks.

The principal objective of the national outbreak surveillance system is to gain information on the epidemiology of all outbreaks of infectious disease in Ireland.

More specific objectives include measuring the burden of illness caused by outbreaks, identifying high-risk groups in the population and estimating the workload involved in the management of outbreaks. The information gathered can be used to inform public health professionals on the causes and factors contributing to outbreaks, to target prevention strategies and to monitor the effectiveness of prevention programmes.

Outbreak definition

An outbreak of infection or foodborne illness may be defined as two or more linked cases of the same illness or the situation where the observed number of cases exceeds the expected number, or a single case of disease caused by a significant pathogen. Outbreaks may be confined to some of the members of one family or may be more widespread and involve cases either locally, nationally or internationally.

Methods

Since 1st January 2004, outbreaks or "unusual clusters or changing patterns of illness" have been notifiable under the Amendment to the Infectious Diseases Regulations.[1] (see outbreak definition in box above). Since that date, medical practitioners and clinical directors of diagnostic laboratories are required to notify to the medical officer of health any unusual clusters or changing patterns of illness, and individual cases thereof, that may be of public health concern.

In addition, since 1st January 2004, all outbreak data are being entered into the CIDR system database either directly by the HSE-region, (if that region has gone live onto CIDR) or indirectly by staff in HPSC.

Table 1. All outbreaks of ID, number of IID outbreaks and total numbers ill in IID outbreaks reported by health board (2004).

Health Board	Number of Outbreaks	Outbreak rate per 100,000 pop.	No. ill in all outbreaks	No. of IID outbreaks
ERHA	67	4.8	1949	61
MHB	9	4.0	218	9
MWHB	8	2.4	290	8
NEHB	21	6.1	315	19
NWHB	12	5.4	336	8
SEHB	23	5.4	390	21
SHB	40	6.9	569	36
WHB	7	1.8	85	7
Total	**187**	**4.8**	**4152**	**169**

Table 2. Pathogens associated with IID outbreaks notified in 2004.

Disease	Number of outbreaks	Number ill
Noroviral Infection	78	2838
Suspect norovirus	59	1038
VTEC Escherichia coli	10	17
Salmonellosis	8	30
Cryptosporidiosis	5	25
Shigellosis	2	15
Campylobacter infection	1	2
Giardiasis	1	2
Rotavirus	1	5
C. difficile	1	11
Unknown	3	25
Total	**169**	**4008**

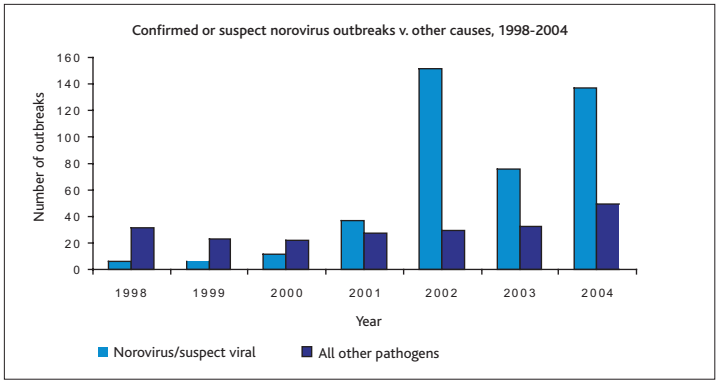

Figure 1. Number of outbreaks by year and by pathogen, 1998-2004 (Data prior to July 2001 provided by FSAI)

Results

During 2004, 187 outbreaks of infectious disease were reported to HPSC, of which 169 were gastrointestinal/ infectious intestinal disease (IID) outbreaks. The IID outbreaks were responsible for at least 4,008 people becoming ill, and there were 115 reported hospitalisations. The regional distribution of all outbreaks of infectious disease, and those specifically IID are detailed in Table 1. The highest number of outbreaks was reported from the ERHA region (n=67), although the highest outbreak rates were in the SHB and NEHB (both 6.9/100,000). The lowest rate was reported from the Western health board region (1.8/100,000).

Causative Pathogen

The breakdown of IID and non-IID outbreaks by pathogen are outlined in Tables 2 and 3 respectively. In 2004, as has been the trend since the year 2000, the IID outbreaks have been dominated by noroviral/ suspect viral outbreaks, comprising 81% of all IID outbreaks in 2004 (Figure 1). The overall numbers of IID outbreaks reported increased compared with 2003.

After norovirus, the next most commonly reported cause of outbreaks was VTEC *E. coli* and *Salmonella enterica*.

There were ten outbreaks of VTEC reported in 2004, one general and nine family outbreaks. The general outbreak involved a significant investigation and occurred at a sports event in June 2004. Four cases were confirmed as *E. coli O157* (VT1 and VT 2 positive) infection. Three cases were hospitalised. Cases ranged in age from twelve to forty-nine years.

Epidemiological, environmental and microbiological investigations implicated the consumption of water from the sports club as the cause of the outbreak. Consumption of this water was prohibited as soon as it was confirmed as a possible source of infection and this action effectively ended the outbreak.

Table 3. Non–IID outbreaks notified in 2004

Disease	Number of outbreaks	Number ill
Hepatitis A (acute)	3	8
Measles	2	7
Mumps	2	16
Hepatitis B (acute and chronic)	1	3
Leptospirosis	1	5
Vancomycin Resistant Enterococci	1	n/a
Meningococcal disease	1	3
Tuberculosis	1	3
Chickenpox	1	3
MRSA	1	4
Respiratory suspected viral	1	65
Suspected Rubella/Parvovirus	1	11
Suspected Scabies	1	5
Not identified	1	11
Total	**18**	**144**

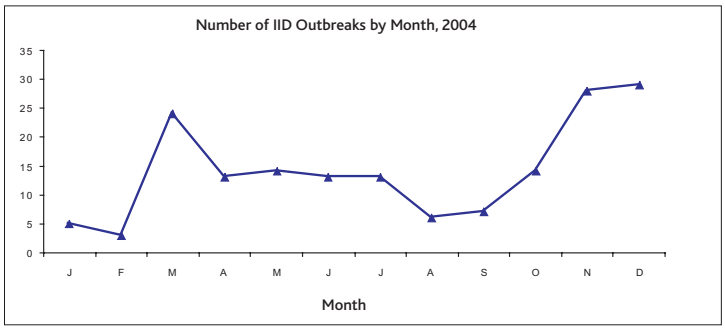

Figure 2. Seasonal distribution of IID outbreaks, 2004.

Interestingly, a microbiological and/or epidemiological link with waterborne transmission was also found for a number of the family outbreaks/clusters of VTEC in 2004. In addition, contact with animals was also suspected for a number of the waterborne outbreaks.

Eight outbreaks of *S. enterica* were reported, including one general and six family outbreaks; one small outbreak was deemed to be travel-associated. The general outbreak was caused by *S.* Typhimurium and occurred in a restaurant in the WHB region. Ten persons became ill, and a tiramisu dessert was implicated epidemiologically in the outbreak. The restaurant was closed during the investigation and subsequently no additional cases were identified.

Five outbreaks of cryptosporidiosis were reported in 2004: four general and one family outbreak. All the general outbreaks were reported as waterborne.

Two outbreaks of shigellosis were notified, one general and one family outbreak. The general outbreak occurred in a crèche and eleven children were reported ill.

Eighteen outbreaks of non-IID/gastroenteric diseases were notified in 2004, which is the highest numbers reported since we initiated surveillance of all infectious disease outbreaks. Table 3 outlines the pathogens implicated and numbers ill.

Mode of Transmission

Similar to previous years, person-to-person spread was the principal mode of transmission reported in the majority of outbreaks of IID reported in 2004 (Table 4). Most of these outbreaks were due to noroviral/ suspect viral.

Table 4. Principal mode of transmission reported in outbreaks of IID (2004).

Primary Mode of Transmission	Number of IID Outbreaks
Person to person	136
Foodborne	12
Waterborne	6
Animal contact	3
Not Specified	12
Total	**169**

Table 5. IID Outbreaks by location, 2004.

Location	Number of IID Outbreaks
Hospital	68
Residential institution	49
Private house	17
Hotel	12
Not Specified	7
Other	6
School	4
Restaurant / Cafe	3
Crèche	1
Public house	1
Travel related	1
Total	**169**

There were twelve outbreaks where the primary mode of transmission was described as food borne, and six outbreaks were deemed to be waterborne in 2004, compared to 2003 when no waterborne outbreaks were reported. There was also an increase in the number of outbreaks reported to be due to contact with livestock compared with 2003.

Location

Similar to the trend, which first emerged in 2002, the commonest location in which outbreaks occurred in 2004 was healthcare settings (Table 5). 69% of all reported outbreaks occurred in these settings. The greatest number of people ill was also associated with outbreaks in the health-care sector.

Seasonal distribution

When the IID outbreaks in 2004 are analysed by month of onset of illness of first case, it is seen that the majority of outbreaks occurred in the winter months of November and December (Figure 2). This is not surprising as the majority of outbreaks of norovirus occur during the winter season.

Discussion

In 2004, all outbreaks of infectious diseases became notifiable for the first time, under the new Infectious Diseases Legislation.[1] There was an increase in the overall number of outbreaks reported nationally in 2004, with 169 outbreaks of IID notified, compared to 102 in 2003. In addition, the highest number of non-IID outbreaks since the surveillance system commenced was notified in 2004 (n=18).

The 2004 outbreak data continue the trend in recent years of a predominance of outbreaks of viral gastroenteritis, principally caused by norovirus (NV) (81% of IID outbreaks confirmed/suspected NV). Detailed molecular detection and typing of norovirus isolates was introduced by the National Virus Reference Laboratory (NVRL) in 2003, which has enabled us to study in much greater detail the molecular epidemiology of strains causing outbreaks in Ireland.

A one-year North-South study funded by Food Safety Promotion Board, coordinated jointly between HPSC and NVRL in the Republic of Ireland, commenced in 2004. The aim of this study was to merge epidemiological and virological data on norovirus outbreaks on the island of Ireland by genotyping and obtaining sequence date from one sample of every outbreak detected North and South for a one-year period. The study was completed in October 2005 and is due to be published in the coming months. Some interesting trends emerged from analysis of the data North and South, such as the emergence of the GII-4 (2004 variant) of NV, the so-called "Jam" strain in the winter season of 2004.[2]

This strain was originally detected in Europe at an outbreak of NV at an international scout jamboree held in the Netherlands in the summer of 2004[3], but has subsequently been detected across Europe and in Japan and Taiwan. This variant had been recognised in Australia during the 2004 southern hemisphere winter season.[4]

In 2004, Ireland also joined the European network 'Divine-net', which is an extension of the previous EU project entitled "Foodborne Viruses in Europe".[5] This network aims to merge epidemiological and virological data on outbreaks of viral gastroenteritis, including norovirus, across Europe. The data-sharing agreement between NVRL and HPSC, which commenced for the North-South study, has been extended to fulfil the requirements of the Divine-net project and serves to provide continued valuable data on the molecular epidemiology of NV in Ireland.

Water was seen to be an important mode of transmission from analysis of the 2004 data, with a general across-health board outbreak of VTEC O157, as well as a number of smaller family outbreaks confirmed/ suspected to be waterborne. In addition, four small general outbreaks of cryptosporidiosis were considered to be waterborne. With the potential for a substantial number of people to be exposed in such outbreaks, the message must be reinforced that untreated water supplies, particularly from private wells, may pose a significant risk to public health.

Outbreak data have been entered into the CIDR system since the beginning of 2004, therefore real time data on outbreaks are available to all CIDR users nationally as they go live on the system. It is hoped that as national roll-out on CIDR is achieved, enhanced surveillance data on all outbreaks of infectious disease will be even more timely and complete as users enter their own outbreak data.

This will enable epidemiological, microbiological and environmental data relating to the outbreak to be shared locally and nationally, and should greatly assist in the management and control of outbreaks, as well as allowing analysis of the national data to inform future public health policies.

Barbara Foley, Fiona Cloak and Paul McKeown, HPSC

References on request

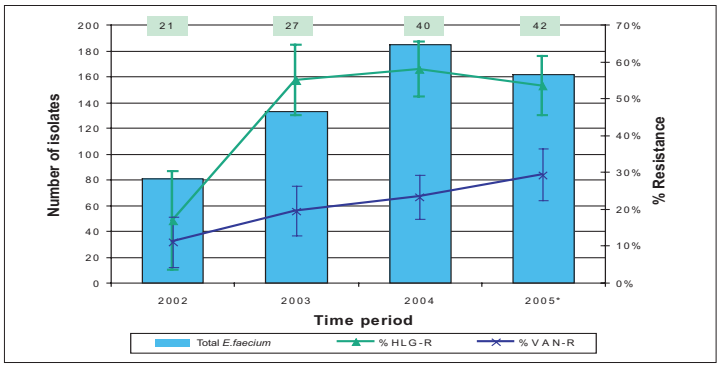

Figure 2. Antimicrobial resistance trends for E. faecium – total numbers of E. faecium and percentage resistance, with 95% confidence intervals, to high-level gentamicin (HLG) and vancomycin (VAN).

* Data for 2005 up to Q3 only; the numbers of participating laboratories by year-end are indicated above the bars.

the end of Quarter 3 2005 (see Figure 1). Significant increases in 3GC-resistance were reported from 10 of 26 countries between 2001 and 2004. The rapid spread of *E. coli* strains producing extended-spectrum beta-lactamases (ESBLs) is considered to be the most likely explanation for the increases observed.[3]

E. faecium data from Ireland and Europe

The proportion of vancomycin-resistant *E. faecium* (VREfm) isolates in Ireland increased from 11.1% in 2002 to 23.2% in 2004 and 29.3% in 2005 (up to the end of Quarter 3) (see Figure 2). Although this increase does not reach statistical significance due to the small numbers of isolates reported, the trend is a cause for concern. Significant increases in VREfm were reported in France (from 1.6% in 2002 to 5% in 2004) and Germany (from 1.4% in 2001 to 10.6% in 2004). In 2004, Ireland had the second highest proportion of VREfm in Europe after Portugal (with 42.3%). According to EARSS, the most likely explanation for the overall increase in VREfm throughout Europe is the spread of the hospital-adapted clonal complex 17 strain.[3]

Multi-drug resistance in *E. coli* and *E. faecium* in Ireland

Growing resistance among invasive isolates of *E. coli* and *E. faecium* in Ireland means that the options for treatment of such infections are becoming more limited. This is further emphasised by the increasing proportion of multi-drug resistant (MDR) *E. coli* isolates [defined as resistant to three of more of the four antibiotics (ampicillin, 3GCs, ciprofloxacin and gentamicin) for which the EARSS *E. coli* protocol requires mandatory reporting]. In 2004, 5.6% of blood culture isolates of *E. coli* were MDR compared to 2.4% in 2003.[2] By comparison, the proportion of *E. faecium* isolates that was MDR (defined as resistant to ampicillin, high-level gentamicin and vancomycin) was higher in 2004 (18%), although this was only a slight increase compared to 2003 (17%).

Discussion

Inappropriate and excessive use of antibiotics in hospital and community settings is considered to be the major driving force behind the emergence and spread of resistance to antimicrobial agents. Data on community antibiotic consumption in Ireland show a steadily increasing level of consumption over the past decade, including increasing use of "broad spectrum" antibiotics.[4] Preliminary data also suggest that hospital antibiotic consumption in Ireland is higher than the European average. As more consumption data become available, it will be possible to examine the relationship between the use of different classes of antimicrobial agents, such as fluoroquinolones and glycopeptides, and trends in AMR, including ciprofloxacin-resistant *E. coli* and VREfm. However, it is clear that measures to limit inappropriate use of antibiotics in both community and hospital settings are urgently required. In addition to reducing inappropriate use of antibiotics, other interventions are required to prevent the spread of AMR in healthcare settings, including local screening and surveillance programmes, provision of isolation facilities, promotion of hand hygiene and ensuring minimum levels of infection control staffing.[5] It is clear from the data presented here that AMR among bacterial pathogens, including but not restricted to *E. coli* and *E. faecium*, continues to pose a significant challenge to patient care in Ireland, as well as in other European countries. Continuous monitoring, including enhanced surveillance, is essential in order to inform appropriate prevention and control measures.

Stephen Murchan and Robert Cunney on behalf of the Irish EARSS Steering Group

Acknowledgements

We would like to thank all consultant microbiologists, surveillance scientists and medical scientists in Irish microbiology laboratories for their continued support and dedication to the EARSS project.

References

1. A Strategy for the Control of Antimicrobial Resistance in Ireland, 2001. Available at: http://www.hpsc.ie/A-Z/MicrobiologyAntimicrobialResistance/Strategyforthecontrolof AntimicrobialResistanceinIrelandSARI/
2. HPSC Annual Report 2004. Available at: http://www.hpsc.ie/AboutHPSC/AnnualReports/File,1438,en.pdf
3. EARSS Annual Report 2004. Available at: http://www.rivm.nl/earss/Images/EARSS%20annual%20report%202004%20webversie_tcm61-25345.pdf
4. Antibiotic Consumption in Ireland, 1993 to 2002. Epi-Insight Volume 5, Issue 4, April 2004. Available at: http://www.hpsc.ie/EPI-Insight/Volume52004/File,681,en.PDF
5. Spread of MRSA determined by antibiotic use and infection control, highlights European-wide study. HPA Press Release, 13 September 2005. Available at: http://www.hpa.org.uk/hpa/news/articles/press_releases/2005/050913_mrsa.htm

Influenza vaccine composition for the 2006/2007 season.

WHO has recommended that vaccines to be used in the 2006-7 season (northern hemisphere winter) contain the following:

- an A/New Caledonian/20/99(H1N1) - like virus
- an A/Wisconsin/67/2005(H3N2) - like virus[a]
- a B/Malaysian/2506/2004 - like virus[b]

Candidate vaccine viruses include:

[a] A/Wisconsin / 67/2005(H3N2) virus and A/Hiroshima/52/2005

[b] B/Malaysian/2506/2004 virus and B/Ohio / 1/2005

More information may be obtained at the following:
http://www.who.int/csr/disease/influenza/2007northreport.pdf