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National Disease Surveillance Centre,

25-27 Middle Gardiner St
Dublin 1,
Ireland

Tel: +353 (0)1 876 5300
Fax: +353 (0)1 856 1299
info@ndsc.ie
www.ndsc.ie

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Avian Influenza in Humans and Poultry in South East Asia

Human and poultry outbreaks

As of 27th January, 2004 seven laboratory-confirmed cases of avian influenza A (H5N1) and six deaths have been reported from Vietnam, with three cases and two deaths from Thailand. To date there are no reports of human-to-human transmission. The cases coincide with an unprecedented spread of highly pathogenic H5N1 avian influenza in poultry in several Asian countries, including Vietnam, Thailand, South Korea, Japan, Cambodia and China. Thousands of chickens have died and millions have been culled.

Human infection with avian influenza strains was first reported in 1997 in Hong Kong SAR, when influenza A (H5N1) infected 18 people, causing 6 deaths. Genetic studies linked the outbreak in humans to an outbreak of highly pathogenic avian influenza in poultry. The rapid destruction of the entire Hong Kong poultry population may have averted a pandemic. In February 2003, there were two cases of avian influenza A (H5N1) in a family in Hong Kong. An outbreak of H7N7 avian influenza in the Netherlands in April 2003 caused the death of a veterinarian and mild illness in 83 people. In Hong Kong, mild cases of avian influenza A (H9N2) occurred in two children in 1999 and in one child in December 2003.

Discussion

Avian influenza normally infects only birds. It is caused by type A strains of the influenza virus. Influenza A viruses are divided into subtypes on the basis of two surface glycoproteins, haemagglutinin (H) and neuraminidase (N). Fifteen avian influenza virus subtypes are known to circulate in the bird population providing an extensive reservoir of potential infection. Minor changes in the surface glycoproteins result in antigenic drift, while major changes in the surface glycoproteins lead to antigenic shift. Antigenic shift leads to the emergence of new subtypes and because populations have no immunity to these new subtypes, highly lethal pandemics can occur. However, for these new subtypes to spread disease in humans they need to have genes from human influenza viruses to facilitate person-to-person transmission. It had been thought that it was necessary for humans to be living in close proximity to domestic poultry and pigs for the conditions necessary for antigenic shift to occur. The rationale for this was that, because pigs are susceptible to avian and mammalian viruses, they served as a 'mixing vessel' for human and avian genetic material allowing the emergence of new subtypes. However, recent studies have indicated that humans themselves may act as 'mixing vessels'. Investigations by WHO of the virus strain isolated from the human cases found that all the genes were of avian origin and there has been no acquisition of human genes.

H5N1 is of particular concern. It mutates rapidly and is capable of acquiring genes from viruses infecting other species. It is known to be highly pathogenic in humans. The present epidemics in poultry increase the opportunity for spread to humans. Rapid elimination of the virus from animal populations is necessary to prevent this happening.

Control measures

WHO is currently helping the health authorities in the affected countries to control the outbreaks. Intensive surveillance, quarantining of infected farms, destruction of infected or potentially infected flocks, stringent sanitary measures and vaccination of persons at high risk of exposure to infected poultry are some of the measures undertaken to halt the outbreaks.

WHO has recommended that travellers to areas experiencing outbreaks should avoid contact with live animal markets and poultry farms. They also recommend that all poultry and eggs should be cooked thoroughly. Countries in the global influenza network have been alerted to increase surveillance of respiratory disease in humans and animals.

Urgent international and national research is being undertaken to allow a better assessment of the significance to human health of ongoing epidemics in birds in affected countries and elsewhere. Molecular studies from human and poultry cases help identify the origins of the viruses, how they might be related and how they are evolving. Initial results from studies comparing the H5N1 strains isolated from humans and poultry from the present outbreaks with those from previous outbreaks in Hong Kong in 1997 and 2003, found significant differences between the strains, indicating that the virus has mutated. Efforts are ongoing to develop an effective vaccine.

WHO, the UN Food and Agriculture Organisation and the World Organisation for Animal Health have called on all countries to work together to control this threat to public health and to provide funds to countries struggling to control the outbreaks.

All the above information is available on the WHO website at www.who.int/
References on request.

Epidemiology of Human Salmonellosis in Ireland, 2002

Introduction

Salmonella species is a bacterial zoonotic pathogen that is a relatively common cause of foodborne illness in Ireland and worldwide. At present there are over 2,500 known serotypes of salmonella. In recent years, two serotypes, namely, *S. enterica* serotype Enteritidis and *S. enterica* serotype Typhimurium have accounted for the majority of cases of human salmonellosis in Ireland.

Salmonellosis presents as an acute enterocolitis, with sudden onset of headache, abdominal pain, diarrhoea, nausea and occasionally vomiting. Fever is almost always present. Dehydration, especially amongst vulnerable populations such as infants, the immunocompromised and the elderly, may be severe. A wide range of domestic and wild animals can act as the reservoir for most common types of salmonella.

The serotypes *S. Typhi* and *S. Paratyphi* can cause enteric fever, a severe systemic life threatening condition. *S. Typhi* and *S. Paratyphi* are not endemic in Ireland, these serotypes do not occur in animals and infection is almost always associated with travel to areas in which human infection is endemic.

Prevention, surveillance and control of salmonella infections is of major public health importance. Measures have been implemented from farm to fork in an attempt to control spread of this zoonotic agent.

Materials and Methods

The National Salmonella Reference Laboratory (NSRL) was established in 2000 in the Department of Medical Microbiology, University College Hospital, Galway. This laboratory accepts *S. enterica* isolates from all clinical and food laboratories for serotyping, phage typing and antimicrobial susceptibility testing. This report reviews data available from the NSRL and weekly clinical notifications for the year 2002. These data enable us to provide an overview of the epidemiology and burden of disease caused by salmonella infections in Ireland.

Results

NSRL data

Demographic information

There were 416 human isolates of *S. enterica* referred to NSRL in 2002. The male: female ratio was 1.05:1. The high incidence in the 0-4 year age group is evident from figure 1 displaying age-specific incidence rates.

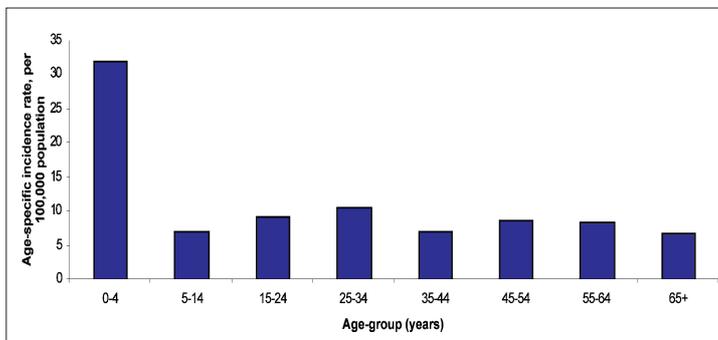


Figure 1. Age-specific incidence rates of human isolates of *S. Enterica* (n=416) referred to NSRL (2002).

Seasonality

There was a marked seasonality in the overall number of human cases of *S. enterica* reported in 2002, with a peak seen in both July and October 2002 (Figure 2). The seasonal peak was observed with *S. Enteritidis* but not with *S. Typhimurium*.

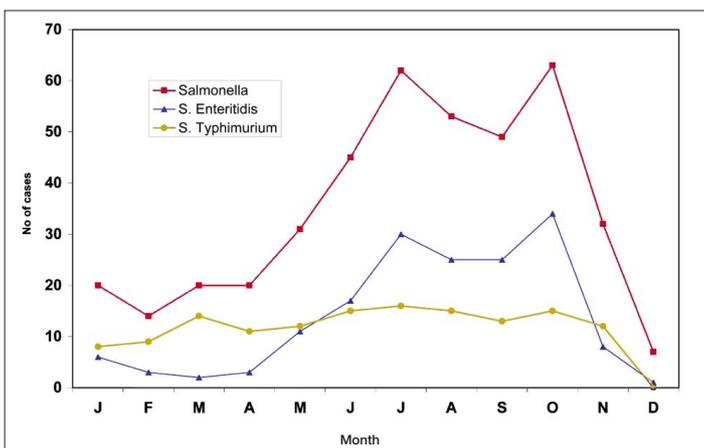


Figure 2. Isolates of *Salmonella enterica* (all serotypes), *S. Enteritidis* and *S. Typhimurium* referred to NSRL by month, 2002.

(Note: month refers to the date the isolate was received in the reference laboratory).

Serotyping, phage typing and antibiotic susceptibility results

The breakdown of the most commonly detected salmonella serotypes by health board is shown in Table 1. The trend that began in 2001 of *S. Enteritidis* taking over from *S. Typhimurium* as the predominant serotype was again continued in 2002. The next most commonly isolated serotypes were *S. Bredeney* and *S. Kentucky*. There were 5 isolates of *S. Typhi* detected. Three of these were known to be travel-associated.

Table 1. Serotypes of *S. enterica* referred to NSRL by year, 1998-2002.

Serotype	1998	1999	2000	2001	2002
	No. (%)				
<i>S. Enteritidis</i>	60 (8)	155 (33)	239 (36)	248 (46)	165 (40)
<i>S. Typhimurium</i>	578 (80)	200 (42)	286 (43)	165 (30)	140 (34)
<i>S. Bredeney</i>	15 (2)	55 (12)	24 (4)	11 (2)	2 (0.5)
<i>S. Kentucky</i>	14 (2)	12 (3)	15 (3)	4 (1)	1 (0.2)
All other serotypes	54 (7)	52 (11)	101 (15)	115 (21)	108 (26)
Total	721	474	665	543	416

Antimicrobial resistance

The antimicrobial susceptibility results of the most commonly isolated serotypes in 2002 are presented in Table 2. High levels of resistance were again found amongst *S. Typhimurium* isolates, particularly *S. Typhimurium* DT104. Many of these isolates were resistant to at least five antimicrobial agents, viz. ampicillin, chloramphenicol, streptomycin, sulphonamide and tetracycline (ACSSuT).

Table 2. Antimicrobial susceptibilities of human *Salmonella enterica* serotypes isolated in Ireland in 2002

Serotype	N	% Resistance						
		Amp	Chl	Strep	Sulph	Tet	Trim	Nal
<i>S. Enteritidis</i>	165	8	0	2	2	4	1	31
<i>S. Typhimurium</i>	140	72	56	74	78	79	17	4
<i>S. Virchow</i>	10	30	0	0	40	40	40	90
<i>S. Dublin</i>	9	0	0	0	11	0	0	0
<i>S. Stanley</i>	7	0	28	57	57	71	28	28
<i>S. Heidelberg</i>	2	0	0	50	0	50	0	0
<i>S. Bredeney</i>	2	50	0	50	0	50	0	0

Amp = ampicillin, Chl = chloramphenicol, Strep = streptomycin, Sulph = sulphonamide, Tet = tetracycline, Trim = trimethoprim, Nal = naladixic acid

Travel-association

In 2002, 82 isolates (19.7%) reported to NSRL were reported as travel-associated. The majority of these cases were associated with travel to Spain (n=26). The next most common country reported was Tunisia (n=6), followed by Thailand (n=5), Pakistan (n=4) and Portugal (n=4). Further analysis of the 26 cases associated with travel to Spain, revealed that 19 of these were *S. Enteritidis*. A variety of different phage types of *S. Enteritidis* were reported viz., 7 of PT1, 4 of PT6, 2 of PT4 and one each of PT12, PT14b, PT3, PT5a, and PT8.

Results

Clinical notification data

Salmonellosis is a notifiable disease. Medical practitioners are legally obliged to report all suspected and confirmed cases. Information on trends in salmonellosis notifications shows that the crude incidence rate rose in the 1990s to peak in 1998, and has been steadily decreasing since then (Figure 3). The total number of notifications in 2002 was 369 compared to 433 in 2001, and 640 in 2000.

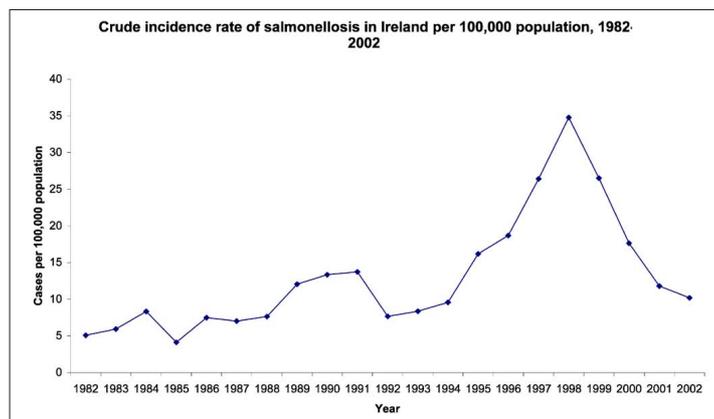


Figure 3. Crude incidence rate of clinical notifications of salmonellosis in Ireland per 100,000 population, 1982-2002.

Outbreak surveillance

There were three general outbreaks and five household outbreaks of salmonellosis reported to NDSC in 2002. The general outbreaks were small in size (ranging from two to eleven persons ill) and all occurred in healthcare settings; one in a residential institution and two in hospitals. In one of the hospital outbreaks there was co-infection with *C. difficile*.

Discussion

The importance of *Salmonella enterica* as an enteric pathogen and the significant burden of human illness for which it continues to be responsible, is evident from the data presented in this report. It must be emphasised that the laboratory-confirmed cases summarised in the data of the NSRL most likely represent only a small fraction of the actual cases of salmonellosis as most patients may not seek medical attention or may not have a specimen of faeces submitted if they do seek medical attention.

Similar trends regarding the epidemiology of this pathogen were noted in 2002 as in previous years. All age-groups were seen to be affected but the highest incidence was again noted in the 0-4 age-group. However, specimens are probably most likely to be submitted from infants and young children. The pattern of distribution by age-specific incidence rates (Figure 1) should be interpreted with this in mind. Both males and females were equally affected. There was a marked seasonality as reported in previous years with a peak in cases noted in July and October 2002. Interestingly, when the two commonest serotypes are compared in terms of seasonality, *S. Enteritidis* is seen to follow this pattern, but such a pattern is not evident for *S. Typhimurium*.

Analyses of the serotyping results revealed that in 2002, *S. Enteritidis* was the predominant serotype, followed by *S. Typhimurium*. This followed the change in trend that was first seen in 2001. Data have only been available since 1998 and from 1998-2000 *S. Typhimurium* had been the commonest serotype in Ireland.

Improvements and advances in the detailed laboratory typing data being generated by NSRL are enabling us to monitor salmonella trends more accurately and are providing us with comprehensive information regarding the epidemiology of this pathogen in Ireland. In particular, the advent of molecular typing methods being employed by NSRL such as plasmid profiling and PFGE has greatly enhanced our ability to identify clusters and outbreaks and examine trends in human, food and veterinary isolates to track this zoonotic agent through the food chain.

On a European and international level, the European-based network Enter-net has proven in recent years to be invaluable in terms of sharing knowledge and expertise in order to enable ourselves and our international colleagues to track clusters and epidemics of salmonellosis and trace back through a complex global food chain to identify the source of outbreaks.

When the antimicrobial susceptibilities of the various serotypes isolated in 2002 were examined, high levels of resistance were again found among *S. Typhimurium* isolates, particularly *S. Typhimurium* DT104. Many of these isolates have the penta-resistance phenotype (ACSSuT) that was reported in previous years. This continues to be a worrying trend.

One of the more notable features of the data reported to NSRL in 2002 has been the emergence of travel-associated cases with almost 20% of the cases identified by NSRL reported as having acquired the illness outside of Ireland. The majority of cases were associated with travel to Spain and the serotype most commonly linked with Spain was *S. Enteritidis*. The high number of cases associated with travel to Spain must be viewed in the context of the large volume of holiday travel to that destination. A wide variety of phage types of *S. Enteritidis* were reported in these travel-associated cases. It is quite probable that the overall proportion of travel-associated cases will increase further in coming years and a greater diversity of serotypes and sub-types will be detected.

In conclusion, although the overall incidence of human salmonellosis has decreased in Ireland over the past number of years (in line with the control programmes in place for *S. Enteritidis* and *S. Typhimurium*), there is still no room for complacency regarding this pathogen as it is quite likely that the relative importance of other serotypes will increase, and the burden of illness due to this pathogen remains very significant. Five cases of *S. Typhi* infection in 2002 represents an increase on previous years and there is a need for increased awareness of the risk of typhoid among people returning from endemic areas.

**Dr Barbara Foley and Dr Paul McKeown, NDSC;
Prof Martin Cormican, NSRL**

Acknowledgements

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Invasive *Haemophilus Influenzae* Type B Disease in Ireland

Introduction

Before the introduction of effective vaccines, *Haemophilus influenzae* type b (Hib) was the leading cause of bacterial meningitis and other invasive bacterial diseases among children less than five years of age. The Hib conjugate vaccine was introduced in Ireland in October 1992 as part of the primary immunisation schedule at 2, 4 and 6 months and a catch-up campaign was also launched at the time offering the vaccine to those under five years of age. Since introducing the vaccine, Hib disease has declined from approximately 100 cases per year in the late 1980s to approximately 10 cases per year by the mid-1990s (Figure 1). Between January 1996 and November 2003, 74 cases of invasive Hib have been reported in Ireland. Sixty two percent (n=46) of these occurred in children <5 years of age. Clinical manifestations of Hib disease in this age group were: meningitis (n=15), meningitis and septicaemia (n=9), septicaemia (n=7), pneumonia (n=5), epiglottitis (n=4), osteomyelitis (n=3), cellulitis (n=2) and leg abscess (n=1). In that period 21 true vaccine failures have occurred (i.e. invasive disease occurring in fully vaccinated individuals), ranging from 2-4 cases per annum. Nineteen of these failures occurred in children 1-4 years of age and in two aged 5-9 years.

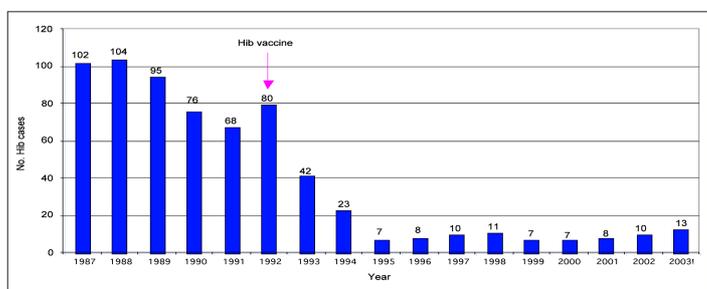


Figure 1. Number of invasive *H. influenzae* type b (Hib) cases in Ireland, 1987-2003

! Based on reports received at NDSC up to 28/11/2003

An increase in Hib disease has been observed since July 2002 with double the number of cases seen over the last two six-monthly periods (Figure 2). This increase has predominantly been in children less than five years of age (Figure 2). A similar increase due to other serogroups of *H. influenzae* has not been observed. No increase in Hib vaccine failures has been observed over the same period. Approximately half the Hib cases in children less than five years of age since July 2002 occurred in unvaccinated children.

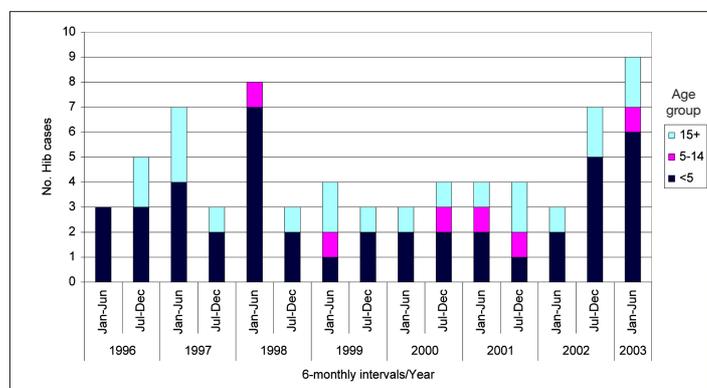


Figure 2. Number of invasive Hib cases by age group over six-monthly intervals, 1996-2003

There have been concerns in the UK recently regarding the efficacy of the Hib vaccine, following on from the steady increase

in the disease seen there since 1999 in 1-4 year old children and the fact that 90% of these cases occurred in fully vaccinated children.¹ A number of factors may have contributed to this decline in population immunity over time, the main ones being a waning of the effect of the catch-up campaign, the lower efficacy of the Hib vaccine when combined with DTaP rather than DTwP and the use of an accelerated immunisation schedule without a Hib booster.² In order to halt and reverse this gradual increase in Hib disease in the UK, a catch-up campaign commenced in May 2003 offering a booster dose of Hib vaccine to all children between six months and four years of age.¹

Based on the Hib data currently available in Ireland, there is no evidence to suggest that the effectiveness of the Hib vaccine has declined. This is reflected in the fact that the number of Hib vaccine failures has not increased recently, despite an increase in the number of Hib cases. Since 50% of the Hib cases in the less than five year olds were unvaccinated, poor uptake of the Hib vaccine in Ireland is more of an issue than any particular issue with the Hib vaccine.

For now it is vital in Ireland that we continue to monitor the situation closely and prioritise improving uptake of the Hib vaccine. Good quality Hib surveillance will ensure that any changes in the trends of the disease can be detected in a timely manner, and reasons for such changes identified, which in turn can be used to inform the appropriate public health decisions and prompt action.

Margaret Fitzgerald, Joan O'Donnell
and Darina O'Flanagan, NDSC

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2. Steinhoff M, Goldblatt D. Conjugate Hib vaccines. *Lancet* 2003; **361**: 360-361.

Guidelines on the Management of Outbreaks of Norovirus Infection in Healthcare Settings

The National Disease Surveillance Centre Guidelines on the Management of Outbreaks of Norovirus Infection in Healthcare Settings were recently launched by the Minister for Health and Children, Mr Micheal Martin. The guidelines provide a framework to address the challenge of outbreaks of illness due to norovirus in hospitals and other healthcare settings. A copy of these guidelines is available on the NDSC website at www.ndsc.ie

Salmonella Monthly Report (November 2003):

Strains are allocated to months based on the date of receipt of the isolate from the referring laboratory. These figures are provisional as work may not be finished on particular strains at the time of publication. Data are provided courtesy of Prof Martin Cormican and Dr Geraldine Corbett-Feeney, NSRL.

Health Board	E	M	MW	NE	NW	SE	S	W	Total
S. Bredaney	1	0	0	0	0	0	0	0	1
S. Enteritidis	1	0	0	0	1	0	0	0	2
S. Kentucky	1	0	0	0	0	0	0	0	1
S. Kottbus	0	0	0	0	0	1	0	0	1
S. Litchfield	1	0	0	0	0	0	0	0	1
Paratyphi A	0	0	0	2	0	0	0	0	2
S. Stanley	0	0	0	1	0	0	0	0	1
S. Typhimurium	1	0	0	0	0	1	1	0	3
S. Welikade	1	0	0	0	0	0	0	0	1
Unnamed	1	0	0	0	0	0	0	0	1
Total	7	0	0	3	1	2	1	0	14

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