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Meningococcal C vaccine launched

E.coli O157 and HUS

Salmonella infections in Ireland

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IN THE NEWS!

Men C Immunisation Programme

This month the Department of Health & Children is introducing a National Immunisation Programme against Meningococcal Group C infection. This is one of the largest vaccination programmes ever introduced in this country and will be implemented on a phased basis. Meningococcal disease results from bacterial infection caused by the organism *Neisseria meningitidis*, and Group B & C are of major importance in Ireland. The epidemiology of meningococcal disease was described in the previous issue of EPI-INSIGHT.

Children and young people are at highest risk of the disease, hence the vaccination programme will target those at highest risk first. Phase 1 of the programme will commence in October 2000 and will include: children up to, and including 4 years, who will be vaccinated by their GP; all young people in school classes from Junior Certificate to Leaving Certificate inclusive; first year students in third level institutions; young people aged 15-18 years who are not in full time education, who will be vaccinated by GP/local health board arrangement. On completion of phase 1of the programme the second phase will commence during 2001. This will consist of vaccine being offered to children aged 5-6 years in school. On completion of phase two, phase three will commence and will consist of: children aged 7-14 years in school and young adults aged 19-22 years inclusive.

The number of doses of vaccine required is dependent on age. Infants under one year require three doses. Babies under six months will be called for vaccination at 2, 4 and 6 months, in line with the primary vaccination programme. Babies aged between 6-12 months will receive 3 doses of vaccine and will be called for vaccination as part of a special catch up programme. Children over 12 months of age require one dose of vaccination. Children will be called for vaccination at 15 months to coincide with their MMR vaccination, all parents of children aged 13 months to 4 years inclusive, will be encouraged to present to their GP for vaccination and will require one dose of vaccine. School going children and young people require just one dose of vaccine.

The vaccination campaign is being organised within each health board and is directed by a project manager. The Office for Health Gain is co-ordinating the programme nationally. Information leaflets for parents and young people have been prepared and are being distributed nation-wide. Leaflets for medical practitioners and nurses are being distributed: "Meningococcal C Vaccine, Guidelines for Healthcare Professionals" and "Meningococcal C Vaccine, Guidelines for Practitioners, including Standards for Practice" have been published by the Office for Health Gain. The latter includes good practice in giving vaccines, consent, guidelines on storage and distribution of vaccines and technical details on using the vaccine. In addition, the booklet gives advice on identification and management of anaphylactic reactions. These booklets are being distributed to healthcare practitioners involved in the vaccination programme nationwide and are also available from the Office for Health Gain.

Dr Orlaith O Reilly, FFPHMI

HUS link to Antibiotic Treatment in Children with *E.coli* O157:H7

E.coli O157:H7 is a cause of sporadic and epidemic gastrointestinal infection. In some cases haemolytic-uraemic syndrome (HUS) can develop. This is a serious illness characterised by thrombocytopenia, haemolytic anaemia and nephropathy. A prospective cohort study[1] in four states in the United States identified children less than 10 years of age who had *E.coli* O157:H7 infection between 1/4/97 and 31/8/1999. Ten of 71 children developed haemolytic-uraemic syndrome (HUS). The study concluded, "antibiotic treatment of children with *E.coli* O157:H7 infection increases the risk of the HUS". The authors recommend "against giving antibiotics to children who may be infected with *E.coli* O157:H7 until the results of a stool culture indicate that the pathogen responsible is one that is appropriately treated by an antibiotic". In 1999 there were 51 cases of *E.coli* O157:H7 in Ireland and 28 of these cases were in children under 10 years of age. Provisional data for the first six months of 2000, indicate there were 12 cases in total in Ireland, half of these in children under 10 years of age.

1. Wong CS, Jelacic S, Habeeb RL et al. The Risk of the Hemolytic-Uraemic Syndrome after Antibiotic Treatment of Escherichia coli O157:H7 Infections NEJM *2000; 342; 1930-6.*

SALMONELLA INFECTIONS IN IRELAND

Introduction

Salmonella is a bacterial pathogen that is a major cause of food borne illness in Ireland. It has been recognised as the causative organism in many outbreaks in Ireland, and prevention, surveillance and control of infection with salmonella is a public health priority. Most cases of human infection with salmonella are associated with an acute self-limiting gastrointestinal illness, characterised by diarrhoea, abdominal cramps, fever and vomiting, and occasionally bloody diarrhoea. In the immunocompromised, the elderly and in other vulnerable populations, it may pose a serious health risk. More unusually, *Salmonella* Typhi and *Salmonella* Paratyphi can cause enteric fever, a severe systemic life threatening condition, but this is very rare in Ireland

This article introduces the terminology and methods used in identification of salmonella, and reviews information available from the recently established Interim National Salmonella Reference Laboratory (INSRL) and other sources to provide an overview of the epidemiology and burden of disease caused by salmonella infection in Ireland today.

Nomenclature and identification methods

The system for naming salmonellae is particularly complex and so it is necessary to outline this system briefly. Despite the clear clinical distinction between those salmonella associated with enteric fever and those associated with gastroenteritis, all salmonella are now grouped together in a single species called *Salmonella enterica (S.enterica)*. This species is divided into groups based on detection of O antigens and H antigens on the surface of the bacterial cell. [The O antigens and H antigens present are detected using specific preparations of antibody (sera)]. The pattern of O and H antigens on the cell is called the serotype and for convenience each serotype is given an additional name, for example *Salmonella enterica* serotype Enteritidis or *Salmonella enterica* serotype Typhimurium. The names are frequently abbreviated, for example, *Salmonella* Enteritidis (*S.* Enteritidis) or *Salmonella* Typhimurium (*S.* Typhimurium).

Routine sub-classification of *S. enterica* serotypes is based on studying the ability of panels of anti-bacterial viruses (phages) to kill the particular strain. The well-known *Salmonella* Typhimurium DT 104, for example, refers to a subset of *S.* Typhimurium strains that are killed by three particular phages but are resistant to all of the other phages used. Standardised antimicrobial sensitivity testing (15 antimicrobial agents) is also performed to assist in sub-classification of all *S. enterica* serotypes. INSRL also has Pulsed Field Gel Electrophoresis available and additional molecular techniques for characterisation of salmonella isolates when appropriate.

Role of the INSRL

In 2000 the Department of Health and Children provided resources for establishment of an Interim National Salmonella Reference Laboratory (INSRL) in the Department of Medical Microbiology, University College Hospital, Galway. The reference laboratory will accept strains of *S. enterica* from all clinical and food microbiology laboratories for serotyping, phage typing, and antimicrobial sensitivity testing. With national analysis, INSRL can detect widely dispersed outbreaks that would otherwise escape attention and may give an early warning of a problem and prompt intervention to prevent further infection. Comprehensive standardised antimicrobial sensitivity testing and molecular techniques can be applied to all strains to determine how closely bacteria are related. Improved networking across the European Union over the next few years will increase the power and potential benefit of such an early alert mechanism and increase our obligation as a "good neighbour" to contribute to such an early detection system. Prior to the establishment of INSRL, data from many laboratories in Ireland were, for several years, made available to Professor Flynn at the Department of Medical Microbiology, University College Hospital, Galway for compilation to provide national data for the pan-European network, Enter-net[1].

Information from INSRL

Demographic information

From January to August 2000, 500 isolates were referred to INSRL. The male:female ratio was 1:1. The age groups of those affected was as follows:

Table 1: Age group of isolates of S. enterica *(n=368) referred to INSRL, Jan–Aug 2000*

Age group (yrs)	Number of cases (%)
<1	28 (7.6)
1-4	48 (13.0)
5-9	28 (7.6)
10-14	15 (4.1)
15-24	49 (13.3)
25-44	107 (29.1)
45-64	64 (17.4)
65+	29 (7.9)
Total	368

Serotyping, phagetyping and antibiotic susceptibility results

At present *S.* Typhimurium and *S.* Enteritidis are the predominant salmonella serotypes associated with human salmonellosis in Ireland. (Table 2). This table should be interpreted with caution as ascertainment has varied over this time period.

Table 2: Serotypes of S. enterica *referred to INSRL.*

Serotype	1998	1999	2000 Jan-Aug
S. Typhimurium	578	200	214
S. Enteritidis	60	155	175
S. Bredeney	15	55	25
S. Kentucky	14	12	5
All Other Serotypes	54	52	81
Total	721	474	500

As is the case elsewhere in Europe at present, the predominant *S.* Typhimurium phage type is DT104 (75.6%) and the predominant phage type of *S.* Enteritidis is PT4 (74.6%). *S.* Typhimurium DT104 is resistant to antibiotics, and is most commonly associated with resistance to Ampicillin, Chloramphenicol, Streptomycin, Sulphonamides, Tetracyclines and Spectinomycin. (ACSSuTSp), so called multidrug resistant DT104. Eighty five percent of all *S.* Typhimurium DT104 is multidrug resistant.

Other sources of information

Salmonellosis is a notifiable disease. Medical practitioners are legally obliged to report all suspected cases. Information on trends in salmonellosis notifications show that crude incidence rate of salmonellosis rose in the 1990s to peak in 1998, and dropped in 1999. To date in 2000 (weeks1-34, week ending 24/8/00), the number of notifications is 436 as compared with 526 in the same period in 1999, showing a continuing downward trend.

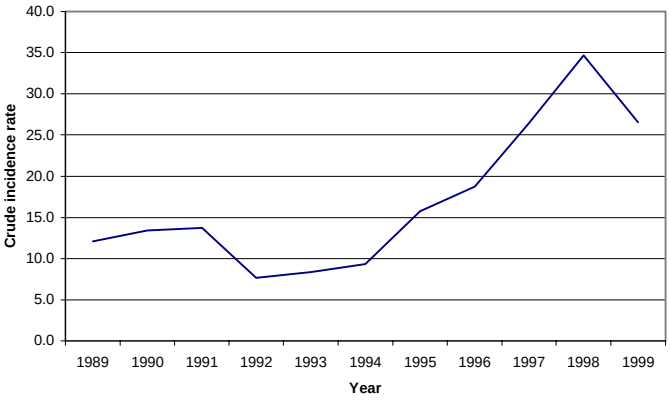

Figure 1: Crude incidence rate of salmonellosis per 100,000 population, 1989-1999. (Source: clinical notifications)

Outbreak surveillance information

The Food Safety Authority of Ireland operates an outbreak surveillance system for gastrointestinal illness. Of the 29 outbreaks reported in 1999 a pathogen was identified in 22 (76%). Salmonella was the causative organism in 13 outbreaks (59%). These outbreaks affected over 300 persons, of whom 65 were hospitalised. There were no reported deaths. The serotypes of *S. enterica* identified were *S.* Enteritidis (n= 7), *S.*Typhimurium (n=4), *S.* Bredeney (n=1) , *S.* Aberdeen (n=1).

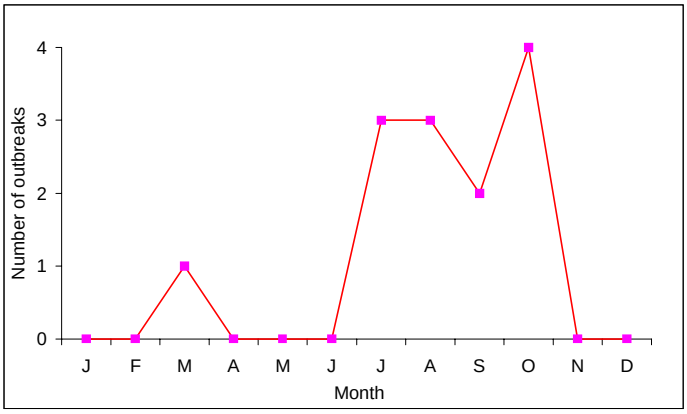

Figure 2: Seasonal distribution of Salmonella enterica *outbreaks in Ireland, 1999*

Salmonella outbreaks usually peak in the summer months but in 1999 the largest number of salmonella outbreaks occurred in October. A specific food was implicated in 11 outbreaks caused by Salmonella in 1999; eggs, chicken dishes (*S.* Enteritidis) and meat (*S.* Typhimurium). In four outbreaks which implicated *S.*Typhimurium, there was no definite food vehicle identified. The main factors contributing to outbreaks which are investigated by health boards are:

- contaminated raw product,
- inadequate cooking and reheating,
- poor storage / inadequate refrigeration,
- cross contamination,
- infected food workers
- poor hygiene practices in premises.

Discussion

Salmonella is a significant food borne pathogen in Ireland, as evidenced by the information presented. Looking at clinical notification data, there is a suggestion that the trend in incidence is downward, as has been observed recently in the UK. With the continuing participation and support of clinical laboratories for INSRL, it will be possible in the future to use laboratory confirmed data to determine the incidence of *S. enterica* more accurately.

INSRL is providing for the first time in Ireland comprehensive standardised antimicrobial sensitivity testing information on *S. enterica.* What has emerged so far is that multidrug resistant *S.* Typhimurium DT104 is the commonest type of salmonella identified in Ireland. The increase in prevalence of multidrug resistant strains is of public health concern; particularly as most of this resistance is not plasmid mediated and therefore not readily reversible.

The capacity of INSRL to identify clusters and unusual patterns of antimicrobial sensitivities has already been demonstrated. The emergence of a new sensitivity pattern seen with DT104 since June this year is currently under investigation in an effort to identify epidemiological links between apparently unrelated clinical cases.

The outbreak surveillance information has identified the main foods associated with salmonella outbreaks, and the predominant modes of transmission. This information is being used to target prevention and control strategies through the food chain for prevention of salmonella infection. *S.* Enteritidis is found in poultry, and hens that are infected lay contaminated eggs. Therefore, it is important that caterers receive assurance from their suppliers that the eggs they buy come from salmonella controlled flocks. Adequate cooking of food will kill all strains of *S. enterica,* and good hygiene and knowledge about handling food in the kitchen at home and in the catering industry will prevent cross contamination. Avoidance of high risk foods such as undercooked eggs, in vulnerable groups will also prevent infection. Following outbreaks in 1998 the FSAI worked with industry to bring in a safer eggs programme for Ireland. Eggs produced under the Egg Quality Assurance Scheme set up by An Bord Bia and the Irish Egg Association, are subject to enhanced Salmonella controls in addition to the regulatory requirements and are inkjet marked with the QA Logo.

There is worldwide concern about the increasing prevalence of multi-drug resistant strains such as *S.* Typhimurium DT104. Control measures at farm level include the avoidance of inappropriate use of antimicrobial agents. A national salmonella control programme in pig herds has recently been developed with FSAI, the Dept of Agriculture, food producers and processors. In this programme, pig herds are monitored and categorised according to the level of salmonella contamination present. Specific controls are put in place and advice is given to farmers depending on the results.

Definitive phage typing and antimicrobial sensitivity testing of all strains will identify outbreaks that would otherwise be missed, and provide an opportunity to prevent further cases.

Already the benefits of INSRL are apparent. This is of course due to the ongoing participation of laboratories in the system, and to public health who follow up links that are suggested by national analysis of all strains. By working together, it is likely that successful prevention and control measures will be put in place to combat this public health threat.

Prof Martin Cormican (INSRL), Dr Margaret Fitzgerald (FSAI) & Dr Derval Igoe (NDSC)

References:

1. http://www2.phls.co.uk/index.html

Vaccinations in Northern Ireland

The introduction of the new conjugate vaccine began in November 1999 in the United Kingdom. In Northern Ireland, the vaccination programme started in early November 1999 with the initial target group being children under 1 year and children 15-17 years. Children 1-4 year old were scheduled for vaccination in January 2000 with children 5-14 year old receiving vaccine from April.

From January to June 2000, the enhanced surveillance system identified 107 patients with confirmed or probable meningococcal disease. Twenty-nine (37%) of the 79 laboratory confirmed cases were group C. During the same period in 1999, the surveillance system identified 94 cases. Twenty (39%) of the 51 laboratory confirmed were group C. None of the group C cases had been previously vaccinated with the new conjugate vaccine.

Due to the small number, it is still difficult to measure the impact of the immunisation campaign in Northern Ireland. However, the results reported from other parts of the UK showed a marked reduction in group C infection.

Adverse Drug Reactions Monitored

During clinical trials, the most frequently observed adverse reactions (ADR) associated with use of meningococcal C vaccine included injection site reactions, rash, altered feeding habits, vomiting, diarrhoea, headache, irritability, unusual or persistant crying, myalgia and fever. In the majority of cases, symptoms were mild and resolved spontaneously. There have also been very rare reports of allergic reactions, including anaphylactoid reactions and seizure following vaccination, from which individuals have usually recovered rapidly.

Following vaccination, symptoms of meningism such as neck pain/stiffness or photophobia have also been reported rarely. These symptoms usually resolve spontaneously but clinical alertness to the possibility of co-incidental meningitis should always be maintained.

In order to effectively monitor the introduction of the new meningoccal vaccines and to confirm their expected safety profile, healthcare professionals are requested to report all suspected adverse drug reactions associated with their use to the IMB in the usual way.

Post-paid ADR report cards may be obtained from the IMB on request. In addition, a downloadable version of the report form may be obtained from the IMB's website and sent to the following freepost address:

Freepost, The IMB, Earlsfort Centre, Earlsfort Terrace, Dublin 2.

Cards can be downloaded directly from the website:

http://www.imb.ie/drug/drug.htm

Safety of Men C Meningococcal Conjugate Vaccine

There has been recent misinformation in the press in relation to 11 deaths in the UK alleged to be linked to administration of the Men C meningococcal vaccine during the implementation of the national vaccination campaign in the United Kingdom. These cases have been examined in the course of routine follow up of reporting of suspected adverse events by the Medicines Control Agency (MCA) and the Committee on Safety of Medicines (CSM) and were found unlikely to be associated with the use of the vaccine. Six cases were Sudden Infant Death Syndrome (SIDS), two had congenital heart disease, two died of Group B meningococcal disease and one had a convulsion 10 days after vaccination. All the deaths are regarded as coincidental rather than causally related to vaccination.

This vaccine does not contain any live bacteria and therefore cannot cause meningitis or septicaemia. To date over 15 million doses of the Men C vaccine have been distributed in the United Kingdom. Last winter there was approximately a 75% reduction in the numbers of confirmed cases of meningococcal C disease in 15-17 year olds and those under one year old (the first groups to be vaccinated) compared to the previous winter. The Committee on Safety of Medicines in the UK has concluded that vaccination provides clear benefit in terms of lives saved and disabilities prevented. There is no suggestion that the vaccine has led to any deaths.

It is important to maintain alertness in the general public and professional groups in relation to those presenting with signs and symptoms of meningococcal disease. The vaccine cannot offer immediate protection to someone who is already incubating the infection and can only protect against Group C meningococcal infection and not against other serogroups or species.

Further Information:
Safety of MenC meningococcal conjugate vaccine SCIEH Weekly Report 29 August 2000; Vol 34
Press Statement from the Committee on Safety of Medicines and Joint Committee on Vaccination and Immunisation 31st August 2000, UK

Salmonella Monthly Report:

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, INSRL.

Health Board	E	M	MW	NE	NW	SE	S	W	Total
S.Typhimurium	12	0	1	3	0	0	2	0	18
S.Enteritidis	24	2	1	6	3	4	8	1	49
S.Agona	0	0	0	0	0	0	0	1	1
S.Alachua	1	0	0	0	0	0	0	0	1
S.Blockley	0	0	0	0	0	0	1	0	1
S.Bredeney	4	1	0	0	1	0	4	1	11
S.Dublin	1	0	1	1	0	0	0	0	3
S.Hadar	0	0	0	0	0	0	0	1	1
S.Heidelberg	0	0	0	1	0	0	0	0	1
S.Infantis	1	0	0	0	0	1	0	1	3
S.Kentucky	3	0	0	0	0	0	1	0	4
S.Livingstone	1	0	0	0	0	0	0	0	1
S.Schwarzengrund	1	1	0	0	0	0	1	0	3
Unnamed	1	0	0	0	0	0	2	0	3
Total	49	4	3	11	4	5	20	5	101