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Changes to the Irish Primary Childhood Immunisation Programme

The National Immunisation Advisory Committee (NIAC) and the Department of Health and Children are recommending significant changes to the national childhood immunisation programme in 2008. These changes, which have just been published in the revised Immunisation Guidelines for Ireland, include the addition of two new vaccines, the pneumococcal conjugate vaccine (PCV) and hepatitis B vaccine, to the routine childhood programme.

The changes to the childhood immunisation programme include:

- Replacing the 5-in-1 vaccine with a 6-in-1 vaccine which includes hepatitis B vaccine (table 1)
- The addition of pneumococcal conjugate vaccine covering 7 serotypes (PCV7). Two doses will be given in the first year of life and a booster at 12 months of age
- A decrease in the number of doses of meningococcal C vaccine (MenC) given in the first year of life (two will be given rather than three)
- The addition of booster doses of PCV7 and MenC vaccine at 12 and 13 months respectively.

Table 1. Vaccine preventable diseases covered by routine childhood vaccines

Vaccine name commonly used	Specific vaccines included	Protects against
5-in-1	(D) Diphtheria toxoid (T) Tetanus toxoid (aP) Acellular pertussis components (Hib) Hib conjugate (IPV) Inactivated polio	Diphtheria Tetanus Pertussis (whooping cough) Hib disease Polio
6-in-1	5-in-1 + (Hep B) Hepatitis B recombinant vaccine	Diphtheria/tetanus/pertussis/ Hib disease/polio/hepatitis B
Pneumococcal conjugate vaccine	(PCV7) Pneumococcal saccharide conjugate with saccharide serotypes 4, 9V, 14, 18C, 19F, 23F, 6B	*Streptococcus pneumoniae* - 7 serotypes
MenC	Meningococcal C conjugate vaccine	Meningococcus serogroup C disease

Table 2. Early childhood immunisation programme, current and recommended schedule in 2008

Childhood immunisation programme Current (2002) and new schedule (September 2008)		
	Current schedule	**New schedule (September 2008)**
Birth	BCG	BCG
2 months	5-in-1 + Men C	6-in-1 + PCV C
4 months	5-in-1 + Men C	6-in-1 + Men C
6 months	5-in-1 + Men C	6-in-1 + PCV+MenC
12 months*	MMR + Hib	MMR + PCV
13 months	---	Men C+ Hib
Early school booster (4-5 years)	DTaP/IPV + MMR	DTaP/IPV +MMR

*In current schedule 12-15 months is identified as time for MMR + Hib booster

A pneumococcal conjugate vaccine catch-up programme is also planned to provide protection to young children (< 2 years of age) who are most at risk from invasive pneumococcal disease.

The proposed changes to the immunisation programme in 2008 will prevent unnecessary illness, hospitalisation, disability and deaths related to common vaccine preventable diseases. The introduction of routine vaccination against pneumococcal and hepatitis B infections is particularly welcome and will benefit the whole community.

The planning and implementation of these changes is being coordinated by the National Immunisation Office (NIO) of the Health Service Executive (HSE). The HSE has already started training staff and distributing information materials for all health professionals and parents of children who will start the new programme in September 2008.

Suzanne Cotter, HPSC

Serotype Distribution of *Streptococcus pneumoniae* in Ireland, prior to Introducing the Conjugate Vaccine to the Infant Schedule

Introduction

Streptococcus pneumoniae infections can result in serious invasive disease such as meningitis, pneumonia and blood stream infection. Invasive pneumococcal disease (IPD) is a significant cause of morbidity and mortality worldwide, especially in young children, elderly adults and those with predisposing risk factors. Antibiotics such as penicillin were once universally effective in treating IPD but with the emergence of resistant strains treatment is now more difficult. In 2006, 15.7% of invasive *S. pneumoniae* isolates in Ireland were non-susceptible to penicillin, having increased from 10.3% in 2004 and 11.7% in 2005.[1]

S. pneumoniae strains are divided into 91 serotypes based on the composition of their capsular polysaccharides. Although immunity is type specific, the most common serotypes associated with IPD are vaccine preventable. Two pneumococcal vaccines are licensed in Ireland; a 23-valent polysaccharide vaccine (PPV23; Pneumovax by Merck) and a 7-valent conjugate vaccine (PCV7, Prevenar by Wyeth). A third vaccine not yet licensed in Ireland, has recently been accepted for review by the European Medicines Agency (10-valent conjugate vaccine, PCV10; Synflorix by GlaxoSmithKline). PPV23 is safe and effective in older children and adults but poorly immunogenic in infants and covers approximately 90% of serotypes responsible for IPD. PCV7 is effective even in infancy and covers 65–80% of serotypes associated with IPD among young children in western industrialised countries.[2]

In 2000 PCV7 was licensed in the US. Following its introduction, substantial reductions in IPD incidence among the target population of children aged <5 years has been seen. IPD incidence rates in 2005 were 77% lower for children aged <5 years compared with average rates in 1998-1999.[3] A herd-immunity effect due to PCV7 has also been observed, where the incidence of IPD has been reduced in unvaccinated populations.[3] Increases in non-PCV7-type disease have been reported, predominantly due to serotype 19A. However, recent studies have indicated that in the general US population these increases have been small relative to the declines in PCV7-type disease.[3]

Since 2000, other countries including Canada, Australia and many of the western European countries have introduced PCV7. From 1st September 2008, PCV7 will be included in the Irish childhood immunisation schedule. Children born on or after 1st July 2008, will be offered PCV7 at 2, 6 and 12 months. A catch-up programme for children <2 years of age will also take place.[4] Prior to this, PCV7 was only recommended for children considered at increased risk of IPD. PPV23 vaccination continues to be recommended for all adults ≥65 years of age and anyone aged ≥2 years considered at increased risk of IPD.[4]

As no comprehensive IPD serotype distribution data were available for Ireland and with the introduction of PCV7 imminent it was important to establish this baseline to effectively monitor the impact of the vaccine following its introduction. A collaborative project between RCSI/Beaumont, the Children's University Hospital, Temple Street and the Health Protection Surveillance Centre (HPSC), commenced in April 2007 to obtain this vital typing information. The results from the first 12 months (April 2007 – March 2008) of this study are presented here.

Methods

Invasive *S. pneumoniae* isolates obtained by clinical microbiology laboratories between 01/04/2007 and 30/03/2008 were forwarded to the RCSI Education and Research Centre at Beaumont Hospital for typing. Typing was performed using multiplex PCR and serological methods. Penicillin susceptibility testing was assessed using the E-Test® method. Data were collated on an MS Access database at HPSC and analysis performed using MS Access and MS Excel.

To assess the completeness of the typing project dataset, IPD data (confirmed cases only) from infectious disease notifications as reported using the Computerised Infectious Disease Notification (CIDR) system and data from the European Antimicrobial Resistance Surveillance System (EARSS) collated on the WHONET database were used.

Results

Over the 12-month period, 347 isolates were collected by 29 laboratories and submitted to RCSI/Beaumont for typing. Results relating to 333 of these isolates have been included in the analysis and are presented here. Fourteen isolates were excluded: eight were non-recoverable, five were duplicates and one was an atypical *S. pneumoniae* isolate.

Serotype distribution

Among the 333 isolates included in the analysis, 37 different serotypes were identified. The five most common serotypes were 14, 4, 9V, 7F, 19A and these accounted for 45% of the isolates typed (figure 1). The seven serotypes contained in PCV7 occur in the top 10 most prevalent serotypes associated with IPD in Ireland (figure 1). Serotype 14 was also most commonly associated with invasive disease in children <2 years of age and accounted for 32% of isolates within this age group. This was followed by 18C which accounted for 16% of isolates.

Coverage by pneumococcal vaccines

Of the 333 isolates typed, 50% belonged to serotypes covered by PCV7, 62% by PCV10 and 90% by PPV23 (figure 2). In the <2 year olds, 84% of isolates had serotypes covered by PCV7 and 89% by PCV10. In the >65 year old adults, PPV23 would have covered 88% of isolates typed (figure 2).

Penicillin non-susceptible S. pneumoniae (PNSP)

Fifty of the isolates (15%) were PNSP. The serotype most commonly associated with penicillin non-susceptibility was 9V, accounting for 46% of the non-susceptible isolates. This was followed by serotype 14 (22%) and 19F (10%). All three serotypes are covered by PCV7.

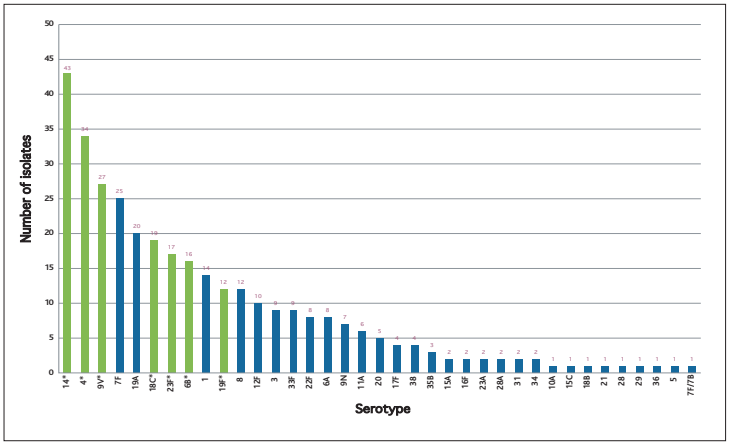

Figure 1. Serotype distribution of invasive S. pneumoniae isolates in Ireland, April 2007 – March 2008 (n=333 isolates)

* Bars highlighted in green indicate serotypes covered by PCV7

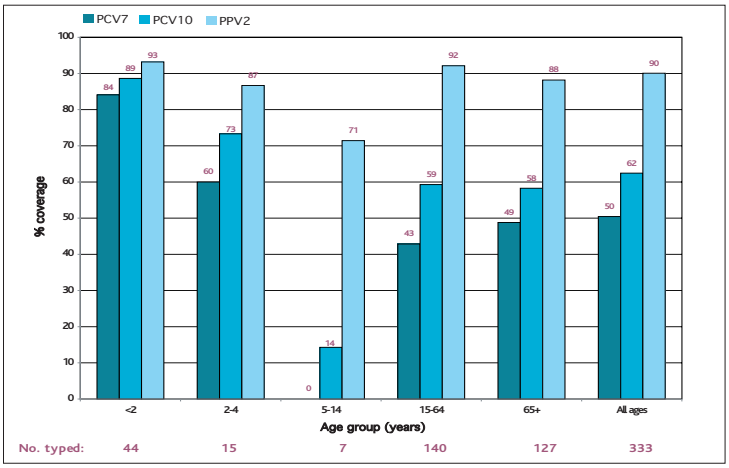

Figure 2. Proportion of typed S. pneumoniae isolates covered by pneumococcal vaccines
Note: PPV23 not effective in children <2 years of age; PCV10 not yet licensed in Ireland

Completeness of the typing dataset

To assess the completeness of the typing dataset the number of confirmed IPD cases reported through the infectious disease notification and the EARSS systems over the same 12-month period were compared. The highest number of IPD cases were reported through EARSS (n=402), while the lowest number were reported through the notification system (n=308 confirmed cases). Therefore, the EARSS dataset is considered to be the one that most accurately ascertains the burden of IPD in Ireland. The proportion of EARSS isolates submitted for typing improved over time; 76% were submitted during the first three months (April–June 2007) rising to 85-88% in the remaining nine months. Over the 12-months, 83% of the EARSS isolates were typed. Of the 333 isolates typed, 247 of these had actually been officially notified and thereby had a matching event on CIDR. However, not all confirmed IPD notifications on CIDR had an isolate submitted for typing (n=61) and not all isolates submitted for typing had been notified (n=86) (figure 3). The total number of unique IPD cases (n=394) ascertained through the two systems is very similar to that reported by EARSS (n=402).

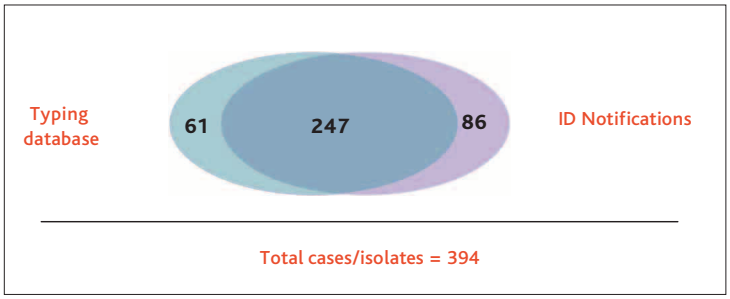

Figure 3. Number of IPD cases/isolates ascertained through the typing project alone, the infectious diseases notification system alone and both systems, April 2007 – March 2008

Discussion

Comprehensive data on the serotype distribution of invasive *S. pneumoniae* isolates in Ireland over a 12-month period are presented. The level of participation in the typing project was very good considering that this was a new initiative. Isolates were submitted by 29 out of 31 laboratories that reported *S. pneumoniae* isolates to EARSS over the same period. Based on the EARSS dataset, 83% of isolates available were typed and all age groups were represented. Although 37 different serotypes were identified, the serotypes contained in PCV7 occurred in the top 10 most prevalent serotypes associated with IPD. The three most common serotypes were 14, 4 and 9V (all contained in PCV7 and PPV23). Eighty-four percent of serotypes infecting children <2 years of age are covered by PCV7. This increased to 89% for PCV10. Therefore, successful implementation of PCV7 to the primary childhood immunisation schedule later this year should have a significant impact in reducing the burden of IPD in vaccinated children. Assuming the herd immunity effect seen in other countries post-PPV7 intervention also occurs then the incidence of disease in unvaccinated children and older adults should also decline.

Eighty-eight percent of serotypes associated with disease in adults ≥65 years are covered by PPV23. Serotype 9V, the type most commonly associated with non-susceptibility to penicillin is covered by both PCV7 and PPV23. Therefore, pneumococcal vaccination should also have an impact in reducing the rates of antimicrobial resistance associated with *S. pneumoniae*.

These results provide invaluable baseline data on serotype distribution and will be used in the continued surveillance of IPD after the introduction of PCV7. To successfully monitor the impact of this vaccination programme a number of key surveillance activities need to work efficiently. These activities include:

- **Notifications:** Clinicians and laboratories must notify all cases of IPD to public health
- **Typing:** Laboratories need to submit all invasive *S. pneumoniae* isolates for typing and report the results to public health
- **Enhanced surveillance:** Public health should perform enhanced surveillance on IPD cases (particularly in children) so that additional information is obtained on items such as clinical presentation, risk factors and vaccination status
- **Antimicrobial resistance:** Laboratories must report details of invasive isolates of *S. pneumoniae* (from blood and CSF) to EARSS.

The pilot typing project continues throughout 2008. The need for a permanently resourced reference facility is an absolute priority to ensure the continued monitoring of the *S. pneumoniae* serotype distribution, to assess the impact of introducing PCV7, to investigate vaccine failures and to inform future public health policy regarding immunisation schedules and the value of introducing expanded valency IPD conjugate vaccines as they become available.

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The Threat of Rabies in Ireland

Incident

In February 2008, a five month old 'British Blue' pedigree kitten purchased by a Polish couple over the internet from a Polish supplier presented to a veterinary practice with seizures, encephalitis and drooling. It inflicted significant bites on the attendant vet, nurse and owners, in each case drawing blood. A provisional diagnosis of rabies was made and notified to the Department of Agriculture and Food (DoAF) and to the local director of public health. There was concern as the couple were unable to provide the website address of the Polish supplier. The country of birth of the kitten was unknown and if born outside Ireland or the UK, the kitten was an illegal import. For this reason it was deemed a high risk exposure from a potential rabies source.

The four people exposed were referred urgently for post-exposure prophylaxis to the Chief Medical Officer, Cherry Orchard Hospital, to receive rabies-specific immunoglobulin and vaccination over a period of 21 days. No other human exposure was identified. HPSC was informed. The kitten was euthanised and brain tissue samples sent to the UK for direct fluorescent antibody tests (FAT). Tissue culture isolation tests and mouse inoculation tests were negative for the presence of rabies virus. At this stage, other diagnoses were thought to be more probable than rabies (including feline infectious peritonitis and feline leukaemia).

Clinical features of rabies

Rabies is a vaccine-preventable acute, progressive, viral infection that if left untreated leads to encephalomyelitis. Case fatality rate in humans and many animals is 100% if post-exposure treatment is not administered. Only six human cases are documented as having survived rabies following the onset of encephalomyelitis – five of these had received some vaccine prior to the onset of symptoms.

Rabies is transmitted by a bite or lick to mucous membranes or cornea, from an infected animal. The incubation period is usually 1-3 months but has been recorded as up to seven years. The closer the bite is to well innervated parts, nerve bundles or the brain, the deeper the wound, and the higher the viral load, the shorter the incubation period. The virus spreads along nerve bundles out of reach of circulating antibodies. It is communicable up to seven days before symptoms and during the course of the disease. Early symptoms are non-specific and include fever, headache and malaise. Other symptoms include anxiety, confusion, paralysis, agitation, hyper-salivation, difficulty swallowing and hydrophobia.

Epidemiology

Rabies is endemic in wild and domestic animals in many parts of the world. Most human deaths from rabies occur in countries with inadequate public health resources and limited access to preventive treatment, few diagnostic facilities and poor surveillance. WHO estimates that 55,000 people die each year of the disease.[1]

In Europe there has been a long-running campaign against rabies. In many countries the ground is seeded regularly with live attenuated vaccine pellets for foxes. Much of Europe is gaining rabies-free status. Between 1990 and 2004, the annual number of rabies cases fell from 21,000 to 5,400 due almost exclusively to control of rabies in foxes with targeted oral vaccination campaigns.

Ireland is considered rabies-free since 1903 and practices strict quarantine of imported animals. In Ireland, as with the UK, there is a requirement that all pets entering from countries other than the UK should have undergone vaccination and serological testing. Animals from the UK that satisfy the Pets Pilot Scheme can enter Ireland without quarantine. Illegal importation of pets continues to pose a threat for rabies in Ireland.

Bat rabies is an emerging threat to humans in Ireland. Bats are a reservoir for lyssaviruses (along with classic rabies virus, a member of the genus *Rhabdoviridae*). An ongoing survey in Ireland and the U.K. has shown that these viruses are likely to be endemic in the bat population. Sporadic human rabies cases following a bat bite have been described in Europe.[2]

Pre-exposure prevention

Vaccination is recommended for those at high risk, including laboratory workers; healthcare workers who have or are about to, come in contact with a patient with probable or confirmed rabies; those who are in direct contact with imported animals; zoo staff; vets in the DoAF; food safety inspection staff; dog wardens; those who handle exotic animals; those who may be exposed to bats; and anyone travelling to endemic countries who may be in contact with animals.

The schedule is 0, 7, 28 days. If exposure is significant, a further two boosters are recommended.[3]

Post-exposure management

Management advice is contained in NIAC[3] and WHO guidelines.[1] Clean the wound with copious soap and water and then iodine, seek specialist advice and contact the local health authorities. Make a risk assessment based on country of exposure, the severity and site of the wound, the circumstances of the bite, the species and behaviour of the animal, the immune status of the individual and the vaccination status of the animal. If the risk is assessed as low, the vaccine schedule is 0, 3, 7, 14, and 30 days. If the risk is high then human rabies immunoglobulin should be given into and around the wound to neutralise the virus and the vaccine given at a different site to induce active immunity. Tetanus toxoid should also be given as indicated.

A supply of human rabies immunoglobulin (HRIG) is maintained at Cherry Orchard hospital.

Rabies is a notifiable disease. The local medical officer of health, HPSC, the DoAF Senior Veterinary Inspector, Customs, and Gardai should be informed if there is a suspected case. Companion animals should be vaccinated.

Summary

Although this kitten did not have rabies, it highlights certain important issues. Rabies is a recurrent danger to European countries from endemic countries. The risk from illegal import of infected domestic animals exists. The recent illegal importation of an infected animal to France from the Gambia highlights this.[4] The recent case of the rabid dog from Sri Lanka who developed rabies in a quarantine centre in UK has reinforced the need for vigilance in this area.[5] Co-ordinated animal and human health responses are vital.

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