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Contents

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Enhanced Surveillance of Invasive Group A Streptococcal Infection in Ireland

Group A streptococcus (GAS - *Streptococcus pyogenes*) causes a range of diseases in humans including pharyngitis, soft tissue infection, scarlet fever, septicaemia, rheumatic fever and post streptococcal glomerulonephritis. Invasive group A streptococcal infection (iGAS) covers infections associated with the isolation of the bacterium *S. pyogenes* from normally sterile body sites or from a nonsterile site in the presence of streptococcal toxic shock syndrome (STSS), and may be life-threatening. The clinical presentation of iGAS may include: STSS, necrotising fasciitis (NF), bacteraemia with no identified focus, cellulitis, myonecrosis or focal iGAS (pneumonia, puerperal sepsis, osteomyelitis, or surgical wound infections).[1]

Method

In Ireland, iGAS is a notifiable disease since 2004,[2] and Irish guidelines for the surveillance, diagnosis and management of iGAS were published by HPSC in 2006.[3] Most departments of public health use the Computerised Infectious Disease Reporting (CIDR) system to notify iGAS cases. Enhanced surveillance of iGAS commenced in 2005.[4] In December 2006, iGAS enhanced fields relating to isolate details, risk factors, and clinical and epidemiological features were added to the CIDR system. Many HSE departments of public health provided backdated information via this system. This article describes the enhanced iGAS data received by HPSC for 2005-2006.

Results

There were 61 cases (1.4/100,000 population) of iGAS notified in 2006, a rise of 20% on the 49 cases (1.2/100,000) notified in 2005. There was no seasonal pattern to the notifications. A regional cluster of iGAS was seen in the HSE Western area during the early part of 2005. However, no epidemiological link was established among the cases, as previously reported.[5] The age breakdown for the two years 2005 and 2006 combined shows that iGAS affects all age groups but the incidence is higher among the elderly; 26% of all infections occurred in those aged 65 years or over (figure 1). Overall, slightly more males (52%) were affected than females.

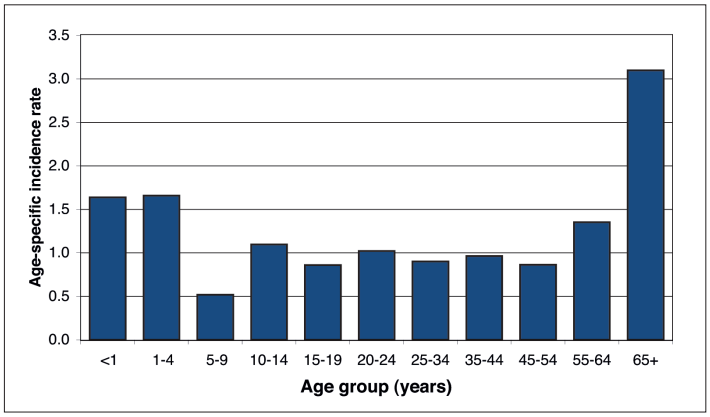

Fig 1. Age-specific incidence rate per 100,000 population of iGAS cases for 2005 and 2006 combined

There was an increase in enhanced data received in 2006. One or more enhanced data fields were entered for 41 (67.2%) of the 61 cases reported in 2006, and for 28 (57.1%) of the 49 cases reported in 2005 (table 1). The source of the isolate was known for 35 (85.4%) cases in 2006 and for 26 (89.3%) in 2005, with *S. pyogenes* isolated from blood in the majority.

Only two cases had typing data for 2006: both were serotype M-1. For 2005, typing data were available for 13 isolates, all from the HSE West cluster: serotype M-1 (six isolates), M-12 (two isolates), M-87 (two isolates) and one isolate each of M-3, M-5 and M-28 were reported. These types are commonly reported internationally.

In 2006, bacteraemia was present in eight cases, cellulitis in six, STSS in three, pneumonia in three and NF in two cases. In 2005, three cases had bacteraemia, one STSS and three NF. Skin lesions or wounds were known to be risk factors in seven cases in 2006 and two in 2005. Three cases were recorded as injecting drug users (IDUs) in 2006. Other clinical features and risk factors are outlined in table 1. Note that a patient could have more than one clinical feature and risk factor. One case was recorded as hospital-acquired in 2006. No cases were known to have travelled abroad.

Continued page 4

Epidemiology of Influenza in Ireland, 2006/2007 Season

Introduction

The 2006/2007 influenza season was the seventh year of influenza surveillance using sentinel general practices in Ireland. The Health Protection Surveillance Centre (HPSC) is working in collaboration with the National Virus Reference Laboratory (NVRL) and the Irish College of General Practitioners (ICGP) on this project.

Influenza activity was mild to moderate in Ireland for most of the 2006/2007 season, with the peak of activity occurring during week 7 2007. Influenza A(H3) was the dominant subtype circulating. Influenza activity mainly affected 15 to 64 year olds.

The most significant global event during the 2006/2007 influenza season was the continuing global spread of poultry outbreaks of avian influenza A(H5N1) associated with sporadic cases/clusters of human infection and a significant proportion of human deaths.[1,2]

Materials and Methods

Clinical data

Forty-eight general practices (located in all HSE areas and representing 4.0% of the national population) were recruited to report electronically, on a weekly basis, the number of patients who consulted with influenza-like illness (ILI). ILI is defined as the sudden onset of symptoms with a temperature of 38°C or higher, with two or more of the following: headache, sore throat, dry cough and myalgia. Cases were those attending for the first time with these symptoms.

Virological data

Sentinel GPs were requested to send a combined nasal and throat swab on at least one ILI patient per week to the NVRL. Swabs were tested for influenza using immunofluorescence and PCR techniques and results were reported to HPSC. The NVRL also tested respiratory specimens (predominantly paediatric) referred mainly from hospitals.

Other indicators of influenza activity

The departments of public health reported an influenza activity index every week to HPSC. The activity index is analogous to that used by the WHO global influenza surveillance system and the European Influenza Surveillance Scheme (EISS).[3,4] Each department of public health also established one sentinel hospital in each HSE area, reporting total, accident and emergency, and respiratory admissions data on a weekly basis. Sentinel primary and secondary schools were also located in each HSE area in close proximity to the sentinel GPs, reporting weekly absenteeism data.

The departments of public health also notified HPSC weekly of all cases of influenza and all influenza/ILI outbreaks. An enhanced dataset on all hospitalised influenza cases aged between 0 and 14 years of age was also reported to HPSC from the departments of public health. From January 2005, HPSC was notified of all registered deaths on a weekly basis from the General Register Office.

Results

It should be noted that hospital admissions data and enhanced surveillance data for the 2006/2007 season are provisional.

Clinical data

Influenza activity in Ireland peaked slightly earlier in the 2006/2007 season compared to the previous season. Activity was moderate for most of the season, with a peak during week 7 2007 at 67.6 per 100,000 population (figure 1). During the peak of activity, the majority of ILI cases reported were in the 0-4 and 15-64 year age groups.

Virological data

The NVRL tested 351 sentinel specimens for influenza virus during the 2006/2007 season. One hundred and twenty-six (35.9%) sentinel specimens were positive for influenza: 124 influenza A (119 A(H3), 2 A(H1) and 3 A unsubtyped) and 2 influenza B. The predominant influenza virus subtype identified was influenza A(H3), accounting for 96% of positive influenza A sentinel specimens. The majority of positive influenza sentinel cases were in the 15-64 year age group (82.3%).

The NVRL also tested 1,824 non-sentinel respiratory specimens, 43 (2.4%) of which were positive for influenza A and 340 (18.6%) were positive for RSV. The majority of non-sentinel influenza (65.1%) and RSV (93.1%) positive specimens were in the 0-4 year age group.

Vaccination status and antigenic characterisation

Of the 126 positive influenza virus detections from sentinel specimens, 106(84.1%) were unvaccinated, 3(2.4%) were vaccinated and vaccination status was unknown in 17(13.5%) cases. Influenza A(H3) was detected in the three cases that were vaccinated.

Four influenza A(H3) specimens were sequenced at the NVRL and antigenic characterisation was undertaken at the WHO laboratory (Mill Hill) in London. All four influenza A(H3) strains were antigenically similar to the current vaccine strains A/Wisconsin/67/2005 and A/Hiroshima/52/2005.

Regional influenza activity

Regional influenza activity peaked during week 7 2007, with HSE East, Mid-West and South East all reporting localised influenza activity. Overall, influenza activity was most intense in HSE E, MW and SE during the 2006/2007 season. The highest ILI consultation rates were observed in HSE Midlands, peaking during week 6 2007.

Outbreaks

During the 2006/2007 season, no ILI/influenza outbreaks were reported to HPSC.

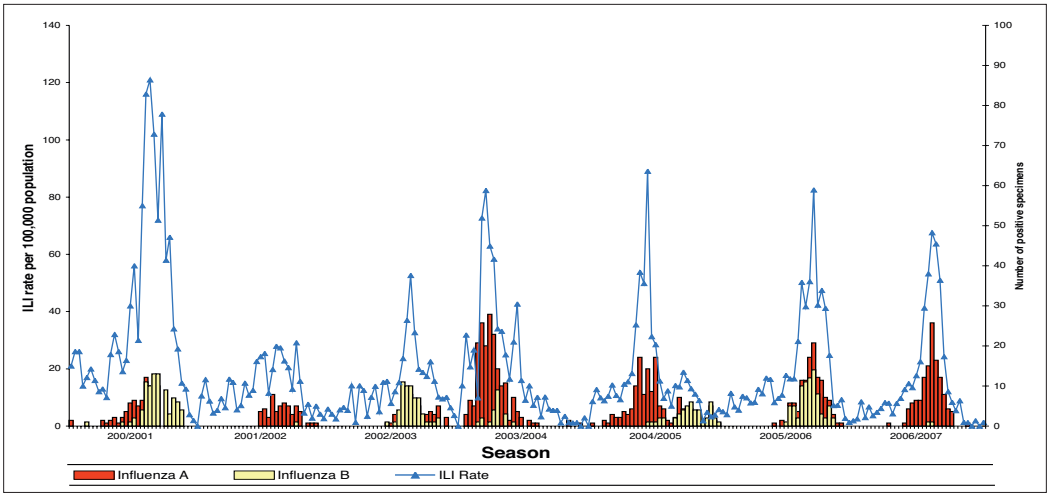

Figure 1. ILI rate per 100,000 population and the number of positive influenza specimens detected by the NVRL during the 2000/2001, 2001/2002, 2002/2003, 2003/2004, 2004/2005, 2005/2006 & 2006/2007 seasons.

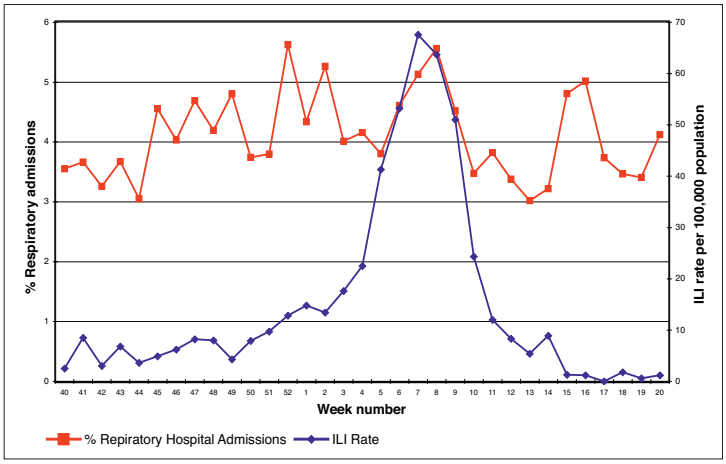

Figure 2. Respiratory admissions as a percentage of total hospital admissions in eight sentinel hospitals and ILI rates per 100,000 population by week for the 2006/2007 influenza season

Sentinel hospitals and sentinel schools

Hospital respiratory admissions (as a proportion of total hospital admissions) in sentinel hospitals peaked during week 52 2006 (figure 2). A similar peak occurred during week 8 2007, one week after the peak in sentinel GP ILI consultation rates. Absenteeism in several sentinel schools was also at elevated levels during the peak in ILI consultation rates.

Enhanced influenza surveillance (for hospitalised 0-14 year olds)

During 2006/2007 season, the Computerised Infectious Disease Reporting (CIDR) system was updated to include the influenza enhanced dataset. A total of 268 influenza notifications were reported on CIDR during 2006/2007. Twenty-nine of these notifications were patients aged between 0 to 14 years who had been hospitalised. Of these 29 notifications, enhanced data were completed for 27 (93%). Five cases were hospitalised in January 2007, 14 in February, six in March and two in April 2007. ILI GP consultation rates were at elevated levels during February 2007. One case was in the 5-14 year age group and 26 were in the 0-4 year age group, 19 of which were under one year of age and seven were in the 1-4 year age group. Ten cases were notified from HSE E, four cases from HSE M, 12 cases from HSE NW and one case from HSE SE. This compares to 10 hospitalised influenza cases in 0-14 year olds reported during the 2005/2006 season, all from HSE E. Twenty-six cases were positive for influenza A and one stated organism unknown. Symptoms included fever (22/27), cough (19/27), gastrointestinal manifestations (12/27), fatigue (11/27) and sore throat (8/27). Complications included bronchitis, acute otitis media, secondary bacterial pneumonia, primary viral pneumonia, croup, liver dysfunction and other respiratory complications. The mean number of days in hospital was 5.3 (ranging from 1-32 days). Five cases were in at-risk categories for influenza, none of whom were vaccinated. Outcome was recorded in 21 cases, 16 of whom recovered and five where outcome was unknown.

Mortality data

One death attributed to influenza was registered with the General Register Office during week 3 2007 (from HSE MW). Influenza was the secondary cause of death and not the primary cause in this case. This death was registered during January 2007 but occurred during January 2006.

Influenza activity worldwide

The United Kingdom experienced the seventh consecutive year of low levels of influenza activity during the 2006/2007 season. ILI rates peaked in February in all regions except Scotland where the ILI peak occurred in January. Peak levels were above baseline but within normal seasonal activity. A/Wisconsin/67/2005 (H3N2)-like virus was identified as the dominant circulating strain.[5] Influenza activity was medium in the majority of European countries this season, with influenza A virus identified as the dominant virus circulating.[4] In Canada and the US, influenza activity peaked in February, with influenza A(H3N2) predominating in Canada (where the majority of strains were identified as A/Wisconsin/67/05(H3N2)-like) and A(H1) in the US (where the majority of strains were identified as A/New Caledonia/20/99-like).[6, 7]

Discussion

Influenza activity was moderate and peaked late in Ireland during the 2006/2007-influenza season, with influenza A(H3) as the dominant circulating subtype. The A(H3) strains circulating matched the strains contained in this season's vaccine. Influenza activity also started later in most of Europe, Canada and the US, with medium levels of activity reported.

The high rate of completion, at 93%, of enhanced data for hospitalised influenza cases aged 0-14 years was very encouraging and highlighted the significant morbidity associated with influenza in children e.g. otitis media, pneumonia and liver dysfunction. None of the cases occurring in children in at-risk groups were vaccinated, re-iterating the need for health care professionals to promote influenza vaccine uptake in these groups.

The small number of influenza-attributed deaths reported to HPSC for the last few seasons is not unexpected. Excess deaths due to influenza are often not registered as influenza deaths. Monitoring influenza and pneumonia deaths is one method of identifying these influenza-non-attributed deaths and from this, estimating the mortality burden caused by influenza each season. A system that monitors influenza and pneumonia deaths in Ireland is currently being developed which could prove to be a significant early warning tool and would be invaluable for health system response planning in the event of an influenza pandemic.

Avian influenza A(H5N1) outbreaks have posed a significant threat to human health since 2003. Of greatest concern is the risk that continuing transmission of the virus to humans will give avian and human influenza viruses an opportunity to reassort their genes, thereby acquiring the ability to transmit easily from human-to-human and thus triggering a pandemic. To date, 15 EU Member States (Austria, Bulgaria, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Poland, Slovakia, Slovenia, Spain, Sweden and the UK) have reported cases of highly pathogenic avian influenza A (H5N1) in wild birds. As of 28 August 2007, avian influenza H5N1 was confirmed in poultry in seven EU Member States: Czech Republic, Denmark, France, Germany, Hungary, Romania and the UK.[1] Avian influenza A(H5N1) remains predominantly a disease of birds. From November 2003 to 23 August 2007, 322 human cases and 195 deaths have been reported in South East Asia, Africa and Eastern Europe, all of which have been associated with close contact with dead or dying poultry.[2] In all human cases to date, there has been no evidence of efficient human-to-human transmission. Human infections remain a rare event.

However, with the ever-greater threat of a pandemic posed by influenza A(H5N1), EU Member States are strengthening their preparedness for a potential human influenza pandemic. As a result of this threat, a number of additional measures have been put in place in Ireland to improve surveillance of ILI/influenza. Work is in progress to increase the number of sentinel GPs, thereby improving geographical and population representation. Sentinel GPs are also currently monitoring ILI on a year-round basis. In addition, influenza and all outbreaks became notifiable in Ireland on 1 January 2004 and an ILI/influenza specific outbreak reporting form was piloted during the 2006/2007 season. Reporting of such events is critical to early detection of influenza activity. Other activities that are being

Continued page 4

Enhanced Surveillance of Invasive Group A Streptococcal Infection in Ireland (cont.)

Table 1. iGAS enhanced surveillance data 2005-2006

Year	2005	2006
Total iGAS cases notified	49	61
Enhanced data received	28 (57.1%)	41 (67.2%)
Source of isolate known†	25 (89.3%)	35 (85.4%)
• Blood	17	31
• CSF	1	1
• Deep tissue	4	3
• Joint fluid	1	-
• Sputum	1	-
• Abscess	1	-
iGAS risk factors*		
• Wound/skin lesion	2	7
• IDUs	1	3
• Steroid use	1	3
• Alcoholism	1	2
• Malignancy	-	2
• NSAID use‡	1	2
• Diabetes mellitus	1	1
• Varicella infection	-	1
Clinical presentation*		
• Bacteraemia	3	8
• STSS	1	3
• Cellulitis	3	6
• Myositis	-	1
• NF	3	2
• Osteomyelitis	1	-
• Septic arthritis	1	1
• Pneumonia	1	3
• Meningitis	1	1
• Peritonitis	1	-
• Abscess	2	-
• Puerperal sepsis	-	1
• Unknown	8	25
Hospital acquired case	-	1
Recent travel	-	-
Management		
• ICU admission	7	5
• Surgical intervention	6	10
Total patients where outcome known	15 (54%)	22 (54%)
• Recovered	11	12
• Died	4	10

† Percentages of cases with enhanced data
* A patient could have more than one clinical feature and risk factor
‡ NSAID use (Non-steroidal anti-inflammatory drug use)

As in other countries, iGAS leads to severe disease and a poor outcome in patients. Ten patients required surgical intervention in 2006 and six in 2005. Five patients were admitted to the intensive care unit (ICU) in 2006 and seven in 2005. Outcome was known in 22 (54%) patients in 2006 and 15 (54%) in 2005. In 2006, ten patients were known to have died. In 2005, four patients died.

Conclusions

In summary, enhanced surveillance of iGAS has demonstrated the morbidity and mortality associated with the infection. iGAS also presents a cross-infection risk, with one hospital-acquired case reported in 2006. Typing of *S. pyogenes* isolates is essential in order to enable international comparisons of isolates, to link cases, and to determine evolutionary trends and the emergence of virulent strains. The Irish guidelines recommend that all iGAS isolates should be sent for strain typing. However, the low rate of isolate typing may be due to a lack of appropriate Irish reference facilities. An increase in the supply of enhanced data should provide a clearer epidemiological picture and help to control iGAS in Ireland in the future.

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Epidemiology of Influenza in Ireland, 2006/2007 Season (cont.)

implemented to improve the surveillance of influenza include weekly surveillance of influenza and pneumonia registered deaths, monthly surveillance of influenza vaccine uptake data in those aged 65 years and older, and the construction of baseline and epidemic threshold levels for influenza activity in Ireland. An evaluation of sentinel hospital admissions and school absenteeism data has been completed and recommendations are currently being implemented. Contact and attendance data are also currently being collated from GP co-operatives, to act as a crude indicator of influenza activity and a pilot project assessing the feasibility of using these data as an early warning tool has been completed by HSE NE. A national tele-survey to estimate influenza and pneumococcal vaccine uptake and morbidity from ILI was carried out for the 2005/2006 influenza season. Case based reporting of avian influenza is now operational on CIDR and an interim MS Access database is being developed for contacts of avian influenza cases. Data from these projects will in turn inform continuing national progress on pandemic preparedness and will be vital in the event of an influenza pandemic for planning and control measures.

Further information on influenza is available on the HPSC website at http://www.ndsc.ie/hpsc/A-Z/Respiratory/Influenza/.

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References on request