Increased prevalence of influenza B/Victoria lineage viruses during early stages of the 2015 influenza season in New South Wales, Australia: implications for vaccination and planning

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Citation style for this article:
Jennings Z, Carter I, McPhie K, Kok J, Dwyer DE. Increased prevalence of influenza B/Victoria lineage viruses during early stages of the 2015 influenza season in New South Wales, Australia: implications for vaccination and planning. Euro Surveill. 2015;20(31):pii=21201. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21201

Article submitted on 22 July 2015 / published on 06 August 2015

During the early weeks of the 2015 Australian influenza season, influenza B accounted for 67% (821/1,234) of all positive influenza tests in New South Wales. Of 81 successive influenza B viruses characterised, 33 (41%) were from children aged < 16 years; 23/81 (28%) belonged to the B/Victoria lineage. This lineage is not contained in the southern hemisphere's 2015 trivalent influenza vaccine. The significant B/Victoria lineage activity in the southern hemisphere suggests that the quadrivalent vaccine should be considered for the northern hemisphere.

The first four weeks of the 2015 influenza season in New South Wales, Australia (15 June to 12 July) have shown substantial early influenza B activity, with frequent detection of influenza B/Victoria lineage viruses, including in children (aged under 16 years). This lineage is not contained in the southern hemisphere's 2015 [1] or the northern hemisphere's 2015/16 trivalent influenza vaccine [2].

Prevalence of influenza B viruses in New South Wales, Australia

Data from 13 sentinel laboratories in New South Wales, Australia's most populous state, showed that influenza B viruses accounted for 67% (821/1,234) of positive influenza tests from 15 June to 12 July 2015 [1]. Of the 1,234 subjects with laboratory-confirmed influenza, 35% (432/1,234) were children (aged under 16 years). Of the 821 influenza B cases, 336 (41%) were children (Robin Gilmour, personal communication, 4 August 2015). This is significantly greater than the overall rate of influenza in children (41% vs 35%; p = 0.007, Fisher's exact test). Influenza B viruses detected from samples collected from individuals with an influenza-like illness were then characterised at our laboratory (one of three World Health Organization National Influenza Centres in Australia). Of the first successive 81 influenza B viruses characterised, 58 (72%) belonged to the B/Yamagata lineage. Half of 28 influenza B viruses that we characterised from 1 to 14 July belonged to the B/Yamagata lineage. This is significantly lower than the 89/94 (95%) ($p<0.0001$, Fisher's exact test) observed globally for influenza B viruses characterised from 29 June to 12 July 2015 [3].

Of the 81 characterised influenza B viruses, 33 (41%) were collected from children under 16 years of age (median age: 4 years; range: 0–13) and 13 of the infections in this age group were caused by B/Victoria lineage viruses. The ages of cases from whom the virus was characterised were representative of the age distribution of all cases of confirmed influenza infection. The median age for those aged 16 or older was 56 years (range: 17–94).

We have no data on the proportion vaccinated among the cases reported in this study.

At four predominantly adult hospitals within our local health district in western Sydney, there were 88 emergency department presentations with laboratory-confirmed influenza from 1 April to 18 July 2015. Of the 88 patients, 82 (93%) were adults and six (7%) were children. A total of 41 (47%) infections were caused by influenza B; 19 (22%) were due to influenza A(H1N1), 9 (10%) to A(H3) and 19 (22%) were untyped A. Influenza B virus was detected in 37 adults and four children.

A total of 26 patients (30%) required hospital admission (22 adults and four children), including seven into high-dependency or intensive-care units. Of the 26, 16 had influenza A (including four A(H1N1), six A(H3) and six that were not subtyped) and 10 had influenza B (five B/Victoria, three B/Yamagata and two that were not characterised). Of the seven patients admitted to high-dependency or intensive-care units, five had influenza A (including two A(H1N1), one A(H3) and two untyped) and two had influenza B/Yamagata. There has been one death (due to A(H3)), and as at 23 July, three patients (two B/Yamagata and one influenza A (not subtyped)) remain mechanically ventilated. Outbreaks of influenza B virus infection belonging to both the B/Yamagata and B/Victoria lineages have also been observed in care facilities for elderly people in New South Wales [1].

This early influenza B activity in New South Wales (the Australian influenza season generally runs from June to September and peaks in August) is in contrast to the 2014/15 northern hemisphere influenza season. In Europe, influenza B occurred later in the season and was detected in 168/810 (21%) of characterised viruses: B/Victoria lineage was identified in 3/168 (2%) of influenza B viruses [4]. In the United States, influenza B viruses also appeared late in the 2014/15 season, were detected in 810/2,193 (37%) of viruses and 228/810 (28%) of the influenza B viruses typed as B/Victoria lineage [5]. This is similar to our data before but not after 1 July, although the sample size (n = 28) after that date is small.

Background

Influenza B virus infection causes considerable morbidity and mortality, including acute respiratory distress syndrome, encephalopathy, acute renal failure and myocarditis [6,7]. Two antigenically distinct influenza B virus lineages, B/Yamagata and B/Victoria, are currently co-circulating globally [3-5]. Although clinical studies have not demonstrated any major differences in disease outcomes or antiviral susceptibility [8], in vitro studies have found up to 1,000-fold difference in neuraminidase inhibitor susceptibility in viruses of the two lineages (substantially greater in B/Victoria compared with B/Yamagata lineage) [9].

Vaccination remains key in protecting the general population against influenza virus infection. Seasonal trivalent influenza vaccines contain two influenza A virus subtypes and one influenza B virus. The southern hemisphere's trivalent influenza vaccine for the 2015 season contains A/California/7/2009 (H1N1)-like, A/Switzerland/9715293/2013 (H3N2)-like and influenza B/Phuket/3073/2013-like (B/Yamagata lineage) viruses [1]. For the first time, a quadrivalent influenza vaccine that also contains the B/Brisbane/60/2008-like virus (B/Victoria lineage) is available for the 2015 Australian influenza season [1] (but not through the Australian Government's National Immunisation Program).

Discussion

Several hypotheses may explain the early increased detection of B/Victoria lineage viruses in Australia. There may be an absence of cross-protective antibodies against B/Victoria lineage viruses in those who have received the trivalent influenza vaccine, and there may be reduced population immunity given that B/Yamagata lineage viruses have been the predominant circulating lineage in the World Health Organization Western Pacific Region in the past few years [10]. We observed a significant proportion of influenza B virus infection in children in our study. It has been reported that children accumulate natural immunity to influenza B more slowly than to influenza A [11]. In the same seroprevalence study [11], antibodies against only a single influenza B lineage were detected in young children, suggesting that they were susceptible to viruses of the other B lineage in the absence of protective antibodies. The high proportion of B/Victoria lineage infections detected in children in New South Wales (13/33) may amplify community transmission of influenza B virus as children shed more virus and for longer periods of time than do adults [12].

The predominant circulating influenza B lineage has been different from that chosen in the trivalent vaccine in five of 10 influenza seasons from 2001 to 2010 [13]. Reduced vaccine effectiveness during influenza seasons where there has been vaccine mismatch has resulted in a greater burden of influenza B virus infection (including influenza illness, influenza-associated hospitalisations and deaths) [13]. The quadrivalent influenza vaccine has demonstrated superior immunogenicity for the influenza B lineage not contained in the trivalent influenza vaccine in children and adults [14,15], and has been shown to be cost-effective [16,17]. It remains unclear if vaccination with the trivalent vaccine offers cross-protection against the influenza B virus lineage not contained in the vaccine. Some studies, including a meta-analysis, have shown significant cross-lineage protection [18-20], while others have found little or no cross-lineage protection [21]. The methods employed to estimate vaccine effectiveness and the participants included have varied in previous studies in several ways including the following: use of different influenza vaccines (inactivated and live attenuated); use of test-negative or people with other virus diseases as controls; inclusion of individuals previously vaccinated against the other influenza B lineage not currently contained in the present season's trivalent vaccine; and the exclusion of children. Data on influenza B lineages were not available for all participants in the studies above [19-21].

Although the sample size of the present study is small, our preliminary data suggest early and significant B/Victoria lineage virus activity in children and adults in New South Wales. The recommended influenza B component of the 2015/16 northern hemisphere's trivalent influenza vaccine is the B/Phuket/3073/2013-like virus (B/Yamagata lineage). As there may be incomplete

protection against B/Victoria lineage infection for those receiving the trivalent vaccine, our early data would suggest that a quadrivalent vaccine should be considered for the upcoming northern hemisphere influenza season (and for travellers to the southern hemisphere). This will be especially relevant if the northern hemisphere experiences early and widespread influenza B/Victoria activity similar to that being observed in the current southern hemisphere winter.

Acknowledgements

The authors would like to thank Robin Gilmour, Respiratory Epidemiologist, Health Protection NSW for supplementing epidemiological data not available in the public domain.

Conflict of interest

None declared.

Authors' contributions

ZJ, JK, DED: data analysis, preparation and editing of manuscript; IC: characterised influenza B viruses; KM: data analysis.

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