July 2016

TARRANT VIRAL WATCH

IN THIS ISSUE

The influenza season is finally drawing to a close here in Alberta as evidenced by the steady decrease in most indicators over the last couple of months. We have summarized the season on page 2 of this newsletter.

The end of the season, however, doesn't mean the end of respiratory disease surveillance in the province. We continue data collection & analysis over the summer months as we look for indicators of early season outbreaks and develop a summer profile of influenza. We request TARRANT sentinels continue completing online reports indicating the total number of patients seen, and the number of patients with influenza-like illnesses (ILI) and lower respiratory tract illnesses (LRTI). The Vaccine Effectiveness Study will also continue over the summer, so please continue to obtain respiratory swabs from every consenting patient who presents with ILI. We will however, stop distributing our monthly bulletins until the fall.

We once again thank all of our dedicated sentinels and wish you all a wonderful summer!

TARRANT 2015-16 Season Highlights

- **Over 190,000** patients screened for ILI and LRTI through our weekly TARRANT reporting from the start of September to the end of May.
- **Over 800** samples collected for the Vaccine Effectiveness (VE) study.
- Contributed to **four** publications in peer reviewed journals through the Canadian Sentinel Physician Surveillance Network (SPSN).
    1. 2014-2015 End of Season Analysis
    2. 2015-2016 Mid Season Analysis
    3. Repeat Vaccination Effects
    4. Surveillance for Enterovirus-D68
- Attended **5** provincial conferences/CME events to share TARRANT data and recruit new sentinels.
- Enrolled **23 new** sentinel sites across the province
- Rolled-out RedCap, an online weekly reporting platform on January 3rd, 2016.
- Concluded the CPGS Study
- A Calgary based family physician was the highest submitting sentinel with 20 weekly TARRANT reports, 35 VE swabs, 14 Weekly CPGS Reports and 5 CPGS Swabs between joining our program in November 2015 and the end of March 2016.

TARRANT Viral Watch, Department of Family Medicine, University of Calgary
G012, Health Sciences Centre, 3330 Hospital Drive NW, Calgary, Alberta, T2N 4N1

Elaine Douglas (Program Coordinator): 403-210-9261 Dylan Kendrick (Research Assistant): 403-210-9261
Virginia Goetz (Research Assistant): 403-220-2750 Kinza Rizvi (Research Assistant): 403-210-7806
Fax: 403.270.4329 tarrant@ucalgary.ca www.tarrantviralwatch.ca

2015-2016 Influenza Season Summary

Alberta

Influenza: From the beginning of the season (Aug 30, 2015) until June 4, 2016, there have been 5310 laboratory-confirmed cases of influenza in the province. The majority (3706, 70%) of cases were influenza A, with A(H1N1)pdm09 predominating. Despite lower cumulative numbers for Influenza B, this virus comprised the majority of cases towards the end of the season. The influenza rate for influenza A peaked at week 7 at ~11.0 laboratory confirmed cases per 100,000 persons. The rate for influenza B peaked at week 11 at ~5.0 laboratory-confirmed cases per 100,000 persons.

During the 2015-16 Seasonal Influenza Immunization Program (Aug 30, 2016– June 4, 2016), over 1.1 million Alberta residents received an annual dose, an overall coverage rate of 26% for the province. The coverage rate for the 2014-15 seasonal influenza immunization program was 24%. Only 8% of Albertans aged 9-17 years were vaccinated, compared to 60% of Albertans over 65 years of age.

Other Infectious Respiratory Diseases Rhinovirus/enterovirus predominated at the start of the season, reaching a percent positive rate of just under 40% before dropping to under 10% by week 1. However, since then the positive rate has been steadily increasing, reaching almost 20% in week 25. Human metapneumovirus prevailed through the mid season (week 51-week 9), with the positive rate climbing to roughly 25%. Parainfluenza, adenovirus, coronavirus and mixed infections had low levels of detection throughout the season.

Data Source: AHS Public Surveillance

Canada

Influenza activity was high throughout Canada over the season, with over 33,000 laboratory-confirmed cases identified. Almost 21,000 of the confirmed cases tested positive for influenza A (62%), and over 9000 have tested positive for influenza B (28%). Of the influenza A positive specimens, 32% were A(H1N1)pdm09, 4.7% were A(H3N2) and 63% were unsubtyped. The 20-44 year age group represented the majority of influenza cases with 24% of total cases, with the 45-64 year age group close behind with 23% of the total confirmed cases. Over 250 influenza-associated deaths have been reported nationally: 52% in seniors 65+ years, 43% in adults 20-64 years and 5% in children 0-19 years.

Each year the National Microbiology Laboratory (NML) characterizes a proportion of positive influenza lab specimens to compare circulating strains to the seasonal vaccine. This season, 2678 isolates were tested. All A viruses were covered by the vaccine but only 79% of B viruses were covered. The NML also undertakes antiviral testing of a select number of specimens. Out of 968 tested A (H1N1)pdm09 specimens, nine were resistant to oseltamivir each showing a H275Y mutation. All A(H3N2) subtype and all B specimens were sensitive to oseltamivir and all influenza A and B specimens were sensitive to zanamivir.

Data Source: FluWatch

International

Internationally, influenza activity continues to decrease to inter-seasonal levels in the temperate northern hemisphere. In the Southern Hemisphere, South America and South Africa influenza activity has started to increase, with low overall activity in most of Oceania. Over the past season, influenza A(H1N1)pdm09 dominated in North America and Northern and Eastern Asia, as well as in Europe, North Africa, and the Middle East. Other key international developments included human infections with avian influenza A(H7N9) in China and the ongoing surveillance of the middle east respiratory syndrome coronavirus (MERS-CoV, see page 4).

Data Source: WHO

Repeat Vaccination Effects

After widely disappointing vaccine effectiveness with the 2014-15 annual influenza vaccine, many in the community and in health care professions seriously questioned how this could happen and why we are continually getting it wrong. Why the influenza vaccine is limited in protecting us from circulating influenza viruses is generating scientific interest. Our data enabled a recent publication in Clinical Infectious Diseases by Danuta Skowronski (PI of the Canadian Sentinel Physician Surveillance Network, SPSN), entitled *"A perfect storm: impact of genomic variation and serial vaccination on low influenza vaccine effectiveness during the 2014-2015 season,"* that helps us get closer to answering the question.

Viral isolates obtained from cases you (sentinels) saw and swabbed, were sequenced in Canadian labs. This revealed important mutations among circulating A(H3N2) strains from vaccine strains that reduced vaccine effectiveness (VE). Although it is commonly understood that when the circulating and vaccine strains are different VE is low, Skowronski and colleagues integrated information about influenza vaccination history of study participants in previous seasons. They found that serial vaccination can result in greater reduction of VE. Effects of prior immunization on VE depend on:

1. Antigenic distance between prior vaccine strain and current vaccine strain
2. Antigenic distance between epidemic strain and vaccine strain

Negative interference (=reduced VE) is greater when sequential vaccine strains are antigenically similar to each other and positive interference (=improved VE) is greater when the epidemic strain is similar to the prior vaccine strain. A more negative dose-response pattern was observed for A(H3N2) in those who had additionally received the 2012-2013 vaccine that was also antigenically related to the 2013-2014 and 2014-2015 A (H3N2) vaccine components. Figure 1 below (Skowronski et al. 2016) suggests that participants who were vaccinated every year since 2012-2013 were at a 1.54 times (54%) increased risk of A(H3N2) illness compared with those consistently unvaccinated.

Vaccination History (2012–2013, 2013–2014, and 2014–2015)	Case n (%)	Control n (%)
Unvaccinated all 3 seasons	238 (46)	465 (49)
Current but neither prior (2012–2013 nor 2013–2014)	9 (2)	48 (5)
No current but 1 prior (2012–2013 or 2013–2014)	29 (6)	60 (6)
No current but both prior (2012–2013 and 2013–2014)	44 (8)	75 (8)
Current and 1 prior (2012–2013 or 2013–2014)	7 (1)	38 (4)
Current and both prior (2012–2013 and 2013–2014)	193 (37)	268 (28)

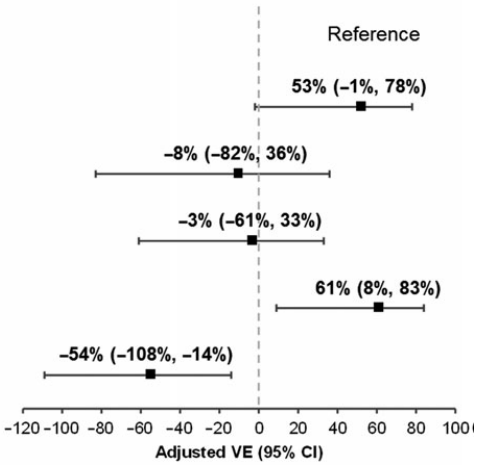

Figure 1.

Repeat vaccination effects are complex and we are still learning about what causes them. One possible biological/ immunological mechanism is the **infection block hypothesis**, the idea that repeat vaccination blocks cross-protective immunity from prior infection. Another theory is **antibody-dependent enhancement** in which low-level, non-neutralizing, cross-reactive antibodies form antigen-antibody complexes that facilitate virus uptake, replication and cytokine production.

The value added by linking your data from active surveillance, real-time measurement of VE and advanced viral characterization to identify and explain low vaccine effectiveness represents a collaboration across disciplines that is working answer these questions and improve future vaccines.

Figure 1. Effect of prior 2012–2013 and/or 2013–2014 season influenza vaccine receipt on current 2014–2015 influenza vaccine effectiveness for influenza A(H3N2). Calendar time was modeled by week of specimen collection using cubic B-spline functions with 3 equally spaced knots. The effect of prior 2013–2014 and/or 2012–2013 vaccine receipt in participants aged ≥3 years in 2014–2015 and those with complete data for 2012–2013, 2013–2014, and 2014–2015 influenza vaccine receipt. Abbreviations: CI, confidence interval; VE, vaccine effectiveness.

TARRANT and VE Updates

New Research Assistant TARRANT is very excited to announce that Dylan Kendrick has joined our program. Dylan completed his Bachelor of Science at the University of Calgary with a major in biology. He is now pursuing a Master of Science degree in Cardiovascular and Respiratory Sciences, with plans for medical school in which he hopes to combine clinical work with his research interests. Welcome Dylan!

Funding We are pleased to announce that both the TARRANT surveillance program and the Vaccine Effectiveness (VE) study have received funding to continue through the 2016-2017 season. New VE program materials for the 2016-2017 season will be mailed out in September. Until that time, please continue using materials from the 2015-2016 season.

Weekly Reporting For TARRANT weekly reporting, our primary stakeholder, (Alberta Health) requires that 90% of our sentinels report weekly. If a report is not received, we are required to contact you ensure reports are received over the subsequent weeks. In order to fulfill this mandate, we will be contacting sentinels over the next couple of months to confirm continued involvement with the program for the upcoming year. If there is anything preventing you from participating that we may assist with or should you be unable to continue with the program, please contact us by phone at 403-220-2750 or by email at tarrant@ucalgary.ca.

MERS-CoV Update

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a viral respiratory disease caused by a novel coronavirus that was identified in Saudi Arabia in 2012. Since September of 2012, there have been 1768 laboratory-confirmed cases, with 630 deaths related to MERS-CoV, a mortality rate of 35.6%. Twenty-seven countries have currently reported cases of MERS-CoV. The virus appears to be circulating throughout the Arabian Peninsula where camels are the primary reservoir, mainly in Saudi Arabia where greater than 85% of cases have been seen. Cases being reported outside of the Middle East, were contracted and exported outside the region. The Republic of Korea experienced an ongoing outbreak in 2015 that affected 186 of whom 32 died all from one camel.

The annual pilgrimage to Mecca in Saudi Arabia, known as the Hajj will take place September 9th—14th, 2016. With previous cases being reported in the Mecca region, the mass travel to and from the area presents a risk for travel related cases of MERS-CoV and the spread of the virus to other countries. Preparedness measures for MERS-CoV during and after the pilgrimage are ongoing as well as better ways in which to enhance surveillance and exchange information during the Hajj.

Person Under Investigation

1. A person with an acute respiratory infection, which may include history of fever and cough and indications of pulmonary parenchymal disease, based on clinical or radiological evidence of consolidation *and* any of the following:

- History of travel to/residence in the Arabian Peninsula/neighboring countries within 10 days before onset of illness.
- History of close contact with a person with acute respiratory illness of any degree who had a history of travel to, or residence in the Arabian Peninsula/neighbouring countries within 10 days before onset of illness.
- The disease occurs as part of a cluster that occurs within a 10-day period, without regard to place of residence or history of travel, unless another etiology has been identified.
- The disease occurs in a health care worker who has been working in an environment where patients with severe acute respiratory infections are being cared for, particularly patients requiring intensive care.
- Develops an unexpectedly severe clinical course despite appropriate treatment, even if another etiology has been identified, if that alternate etiology does not fully explain the presentation or clinical course of the patient.

2. A person with an acute respiratory illness of any degree of severity who, within 10 days before onset of illness, had close contact with a confirmed/probable case of MERS-CoV infection, while the case was ill.

Source: WHO, Public Health England, Public Health Agency of Canada