September 2016

TARRANT VIRAL WATCH

IN THIS ISSUE

We hope that all of our sentinels had a great summer and are getting prepared for the upcoming influenza season. As the influenza season draws closer, we want to remind everyone that we'll continue both the influenza Vaccine Effectiveness (VE) study and the TARRANT weekly ILI surveillance program in the upcoming year.

Last season we collected over 800 samples for the VE study and screened over 160,000 patients for ILI/LRTI. Alberta was one of the largest contributors to the national VE study and our data played an important role in determining the composition of this season's vaccine.

This work would not be possible without our extensive sentinel network and we thank you all for your ongoing contributions to the TARRANT program. We look forward to our continued collaboration in the upcoming season.

News and Updates

Since October 2015, Kim Le has been away on her maternity leave and we are excited to announce she recently rejoined the team as our Research Administrative Assistant.

In July, we wished farewell to one of our research assistants over the summer. Kinza Rizvi has completed her MSc and moved home to Ontario to pursue further research opportunities. We wish her the very best.

We are also very excited to give our congratulations to two of our current Research Assistants. Virginia Goetz has begun her Master's degree in Biomedical Technology and Dylan Kendrick has begun his Master's degree in the Cardiovascular and Respiratory Sciences program.

Update:

Swab kits and requisition forms for the new 2016-2017 season will be sent out shortly and can be expected to arrive at your clinic for the start of the flu season. This year we will be using **PINK** requisition forms and we ask that only the new forms are used when submitting samples.

We will not be providing compensation for VE submissions if the forms are not fully completed. Unfortunately, incomplete forms prevent us from using your data in our studies.

Lastly, we have moved to a new website, with all of our information now found at www.calgaryfamilymedicine.ca/tarrant

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2016-2017 Influenza Season

Trends seen during the current influenza season in the Southern Hemisphere can predict what to expect for the upcoming flu season in the Northern Hemisphere. Currently, the Southern Hemisphere, (such as South Africa, Australia and New Caledonia) has seen a recent increase in influenza activity with a notable shift from influenza B to influenza A(H3N2). It is expected that the predominating A(H3N2) influenza virus will be the dominant strain as we enter the 2016-2017 influenza season.

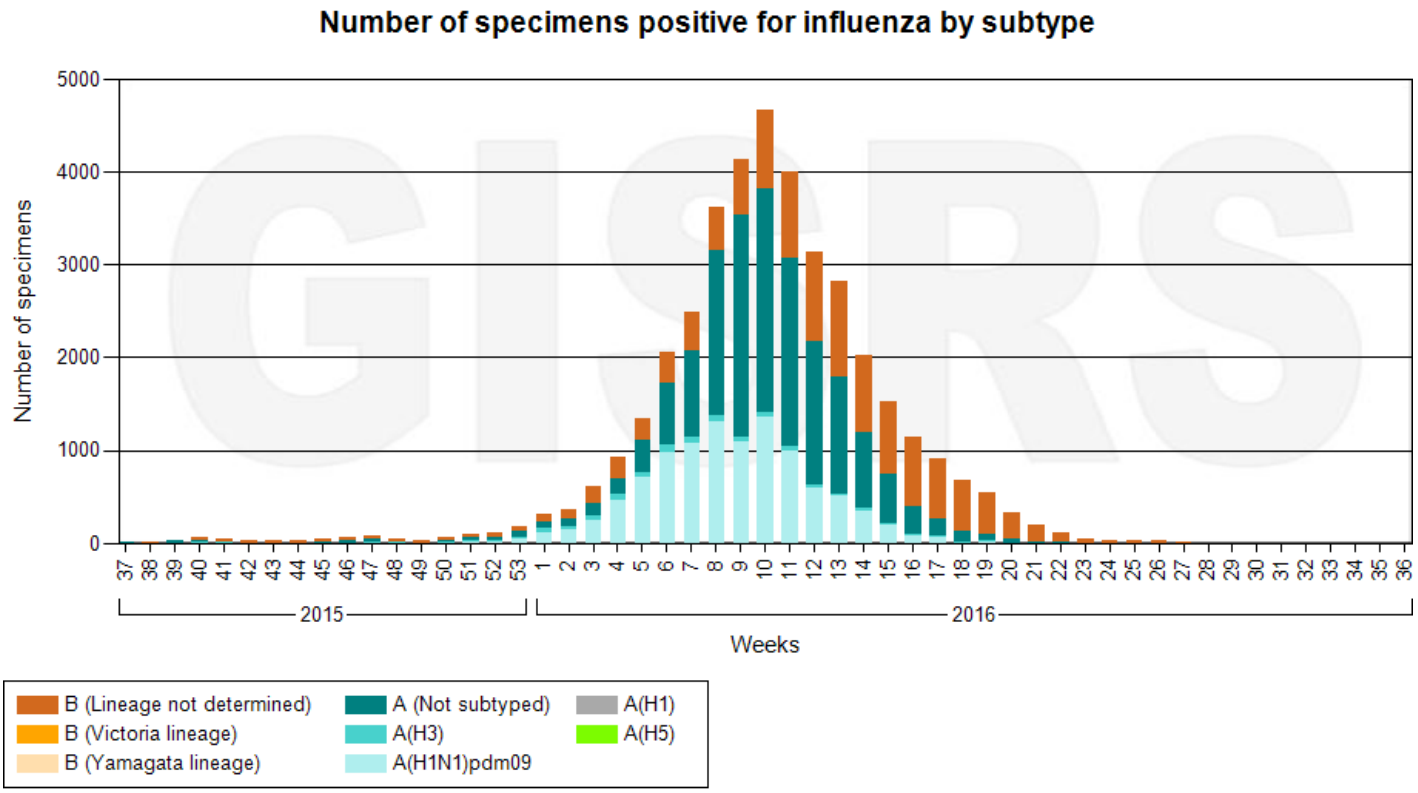
The 2016-17 Influenza Vaccine

This year, the seasonal trivalent vaccine for the northern hemisphere will contain:

- An A/California/7/2009 (H1N1)pdm09-like virus,
- An A/Hong Kong/4801/2014 (H3N2)-like virus (new this season)
- A B/Brisbane/60/2008-like virus (new this season)
- A B/Phuket/3073/2013-like virus (present in quadrivalent vaccines)

Among circulating influenza B viruses, there are two distinct lineages. The B/Brisbane/60/2008-like viruses are from the influenza B/Victoria lineage and represent the predominant circulating influenza B virus. Quadrivalent influenza vaccines contain both a B/Victoria lineage and a B/Yamagata lineage vaccine. viruses.

The following graph shows the influenza laboratory surveillance information for Canada over the past year's influenza season:



Source: WHO

Reversion of Live Attenuated Influenza Vaccine

Live Attenuated Influenza Vaccine (LAIV) (known as FluMist) contains live, weakened influenza viruses. Vaccines containing live viruses can cause a stronger immune response than vaccines with inactivated virus. Previously, scientific and clinical evidence had proven FluMist to be safe and effective. However, more recent studies conducted by sentinel networks across the globe are beginning to cast doubt on the effectiveness of LAIV. This controversy leads many physicians to wonder what vaccine they should recommend and many patients confused as to what's best for them.

In late May 2016, data on the effectiveness of LAIV among children 2 through 17 years during the 2015-2016 influenza season became available from the U.S. Influenza Vaccine Effectiveness Network. The data showed the estimate for LAIV vaccine effectiveness (VE) among study participants in that age group against any flu virus was 3 percent (95% CI of -49 percent to 37 percent). This 3 percent estimate means essentially no protective benefit could be measured. In comparison, Inactive Influenza Vaccine (IIV, flu shots) had a VE estimate of 63 percent (95% CI of 52 percent to 72 percent) against any flu virus among children 2 years through 17 years. Other (non-CDC) studies support the conclusion that LAIV worked less well than IIV this season. Unfortunately, our Canadian Sentinel Surveillance Network did not have sufficient sample size from the LAIV population to contribute to this conclusion. The US data from 2015-2016 follows two previous seasons (2013-2014 and 2014-2015) showing poor and/or lower than expected vaccine effectiveness (VE) for LAIV.

LAIV is currently sold as FluMist Quadrivalent was initially licensed in 2003 as a trivalent (three-component) vaccine. LAIV is currently the only non-injection-based flu vaccine available on the market. Until the 2013-2014 influenza season, LAIV VE data had suggested it was either comparable to, or better than, IIV. The reason for the recent poor performance of LAIV is not known, however it has been hypothesized that the attenuating temperature sensitive phenotype can revert and the vaccine backbone could regain virulence and cause disease. Given this information, for the 2016-2017 season, CDC is recommending the use of the flu shot (inactivated influenza vaccine or IIV) and recommending against the nasal spray flu.

However, soon after the U.S CDC stopped endorsing the spray, a large Canadian study published results showing that children vaccinated against influenza using a nasal spray appear to be equally protected from the flu as those vaccinated by injection. Dr. Mark Loeb (lead author) of McMaster University conducted a three-year cluster randomized double blinded trial involving giving vaccines by one method or the other to 1,186 children living in isolated Hutterite communities. There was also a control group of children and all children were tested for Influenza A and B. The researchers found 5.2% of those who received the nasal spray (LIAV) tested positive for influenza while 5.3% who received the injection (IIV) tested positive. Therefore, this study (in opposition to the CDC) found no difference in protection offered by the LAIV vs IIV during the 12-13, 13-14 and 14-15 seasons. Differences in outcomes are not fully understood but may be based on the fact the LAIV offered in the Canadian study was trivalent and in the U.S was qudravalent. Secondly, two of the seasons were predominantly A(H1N1), which showed high protection, whereas the 2013-2014 season was predominantly A(H3N2) , with low FluMist protection.

The controversy among these differing study results highlights the importance of measuring and evaluating the effectiveness of public health interventions, which can have significant implications for public health policy. Vaccine effectiveness studies continually move us closer to using new available data to ensure public health actions are most beneficial. It is our hope that the Canadian Sentinel Network to which you belong will collect enough LAIV samples over the 2016-2017 season and will therefore be able to contribute our data to answering this question.

References:

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Effects of Statin Use and Cell Autonomous Regulation

Effect of Statin Use on Vaccine Effectiveness

Older adults have the highest risk of influenza related complications. These individuals also commonly take statins to reduce cholesterol and manage cardiovascular risks. Statins have been seen to have anti-inflammatory effects, however recent published reports indicate that the use of statins may also impair the antibody response to vaccination and can reduce vaccine-induced protection.

Annual studies of influenza effectiveness have been conducted since 2004-05 by the Marshfield Clinic Research Foundation, where researchers analyzed the impact of chronic statin use on influenza VE. Their results indicate that statin use modified the effect of influenza vaccination for A(H3N2), with no effect observed for A(H1N1) or type B influenza strains. For A(H3N2), the use of statins was associated with a significantly reduced vaccine-induce protection for the individual. Interestingly, statin use alone without vaccination was associated with greatly reduced odds of A(H3N2) infection when compared to unvaccinated and non-statin individuals.

Evaluations regarding statin effects should explore the potential interference of statins with vaccine-induced protection, along with a potential protective effect from statin use that may reduce the risk of influenza in unvaccinated populations.

With the expected dominance of influenza A(H3N2) for the upcoming season, the effect of statins can have major implications on this season's vaccine effectiveness and the trends of influenza season as a whole.

Cell Autonomous Regulation of Influenza Virus by the Circadian Clock

Cell autonomous clocks drive circadian rhythms observed at the whole organism level. These circadian oscillations are thought to be generated through a number of genetic feedback loops, as well as confer competitive advantages to organisms. Disruption of these clocks can result in fitness costs as well as influence aspects of human health and disease, including immune response to influenza viruses.

Reports have shown that by simply altering the time in which the hosts are infected, there is a significant change in the extent of the virus infection and dissemination in vivo, reflecting the profound change in physiology that occurs throughout the day. It is expected that the virus has coevolved with its host's clock in order to take advantage of the predictability of the daily rhythms driven by cell autonomous molecular clocks.

It is also suggested that influenza replication increases in arrhythmic cells, shown through virus-induced disruptions at certain circadian times or loss of BMAL1, which is a transcription factor involved in generating circadian oscillations. The low levels of BMAL1 has been seen to lead to increased influenza viral infections, and interestingly, gene expression levels undergo seasonal variations in blood samples, showing a significant decrease in the winter months, which can be a factor contributing to the increase in viral infection in the winter months.

Understanding the interactions between the circadian clock, the onset of viral infection, and subsequent acute manipulations of the molecular circadian rhythm may provide alternate novel antiviral therapies.

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