

December
2011

TARRANT VIRAL WATCH

IN THIS ISSUE

~Season's Greetings from the TARRANT Team~

TARRANT News	1
Human-animal Health Interface in Influenza Surveillance	2
Is a Universal Influenza Vaccine In Our Future?	3
Staff News	
Sentinel Compensation	4
How to Avoid Rejection!	

For most people in Alberta, this time of year is considered the start of the Holiday Season. At TARRANT, we also consider it the real start of the Influenza Season. Where families & friends gather to celebrate, influenza & other respiratory viruses also gather and we start to see their effects in our communities.

It has been a fairly typical fall in Alberta for infectious respiratory diseases where non-influenza respiratory viruses have comprised the majority of infections. However, 16 laboratory-confirmed cases of influenza have been reported since the official start of the season in October. Fourteen have been influenza A and two have been the B strain. Five patients in the province have been hospitalized with influenza, all of whom were infected with the A/H3N2 subtype. Testing of 13 influenza isolates (7 A/H3N2, 1 H1N1 & 5 B samples) at the NML has shown all of the A strains have been compatible with the current season vaccine but two out of the five B samples were antigenically dissimilar to the vaccine. Antiviral testing of a mixed sample of thirteen A and B isolates showed no resistance to oseltamivir or zanamivir but all A/H3N2 samples tested were resistant to amantadine.

Elsewhere, the influenza season is also fairly quiet but the U.S. CDC continues to closely monitor the novel swine-origin influenza A virus mentioned in our last newsletter. The infection has now spread to 2 more states (Maine & Iowa) with a current total of ten confirmed patients --nine children & one adult. Three patients have required hospitalization but all have recovered uneventfully. The last 3 patients were in-contact children and this appears to be the first proven incidence of human-to-human transmission where there was no documented swine exposure. The virus is related to human H3N2 that circulated about 20 years ago so it is expected that most adults will have some immunity. A seed strain has been provided to vaccine manufacturers in case the need arises and antiviral testing has been undertaken showing no resistance to either oseltamivir or zanamivir.

In addition to surveillance, another important role our sentinels can play is to encourage all eligible patients to get their influenza vaccine. Although the VE study is test-negative case control in design and doesn't rely entirely on vaccine coverage rates, the more people that are vaccinated, the greater the opportunity to compare vaccine status between cases & controls. Early indicators show low influenza vaccine uptake in Alberta, so it will be interesting to see what impact this will have on our studies as well as the infection rates in the province. We are also still looking to increase VE Study submissions from patients 65+ years of age. So far, only 7.5% of submissions cover this age group & we are looking to double this number. Please continue to swab as many patients as possible & especially remember the seniors!

Our office will be closed December 24th until January 1st inclusive, but if your office is open during that time, please continue to send in your weekly reports. We look forward to another great year in 2012 collaborating with our dedicated sentinels & study colleagues. All the very best to you & your families!



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

403.220.2750: Karen Rivera
403.210.9261: Elaine Douglas

403.210.9258: Quynh Le
403.210.7806: Tova Dybvig

Fax: 403.270.4329

tarrant@ucalgary.ca

www.tarrantviralwatch.ca



Human-animal Health Interface in Influenza Surveillance

A variety of influenza viruses circulating within different species of animals have the potential to threaten human health (e.g. avian influenza virus subtypes H5N1 & H9N2 and swine influenza virus subtypes H1N1 & H3N2). Humans can be directly or indirectly exposed to these viruses so there is rising interest and need for transdisciplinary approaches with close monitoring & collaboration among experts from various disciplines to address this complex human-animal interface. Avian influenza (particularly H5N1) is one important example where a multifaceted approach would be beneficial.

Highly pathogenic H5N1 circulating in birds from south-east Asia & northern Africa is occasionally transferred to humans but is not currently easily transmitted between people; however recent reports indicate that only a few mutations are required to increase transmissibility in humans. With a mortality rate of greater than 50% in humans, any increase in infectiousness of this virus is of great concern so surveillance is of utmost importance.

Alberta has surveillance networks that target influenza in humans (e.g. TARRANT Viral Watch, Pediatric Infection Program, FluWatch) & these networks have strong vertical collaboration within the human health sector. Horizontal collaboration for H5N1 surveillance could include interfacing with the three major Avian Influenza (AI) surveillance networks which are outlined below:

The Canadian Notifiable Avian Influenza Surveillance System (CanNAISS) which is set up for detecting the presence of notifiable AI in live Canadian poultry, and enhancing Canada's surveillance efforts through:

- a) Wild bird surveillance
- b) Passive surveillance in domestic poultry when clinical signs suggestive of notifiable AI viruses are reported and targeted surveillance when notifiable AI is detected
- c) Pre-slaughter surveillance in commercial poultry
- d) Hatchery supply flock surveillance
- e) Voluntary enhanced surveillance in the poultry genetic exporters sector

The Canada's Inter-Agency Wild Bird Influenza Survey (CIAWIS) is a nation-wide survey for AI viruses in wild birds with two components:

- a) a seasonal survey of live wild waterfowl species from selected geographic regions across Canada
- b) an ongoing survey of deceased birds submitted to regional diagnostic laboratories (swabs from the cloaca & oropharynx are screened and all RRT-PCR samples positive for H5 or H7 are sent immediately for test confirmation & further characterization)

The Alberta Veterinary Surveillance Network (AVSN) is a comprehensive integrated surveillance program supporting producers, private-practice veterinarians and a team of animal disease experts to address livestock and poultry disease issues (e.g. AI) that affect industry, food safety and public health. AVSN is comprised of:

- a) Veterinary Practice Surveillance (VPS)
- b) Livestock Pathology Consultation Program (LPCP) & Livestock Disease Investigation Network (LDIN)

Over the last 8 years, over 300 people have died from H5N1 and that number could increase in an astounding manner if human-to-human transmissibility increases. Fortunately, there are some exciting developments in the human-animal health interface which may help to quickly identify & mitigate this threat. The recent emergence of the One Health Initiative which involves synergistic relationships amongst physicians, veterinarians, biologists, and public health officials will hopefully take disease surveillance to the next level by developing partnerships around the globe amongst those with interest in infectious disease.

Our TARRANT sentinels can play an important role in this partnership by immediately alerting public health officials when they see ill patients who have had contact with livestock, especially when the livestock are also ill.

Is a Universal Influenza Vaccine in Our Future?

Immunization is required yearly for protection against seasonal influenza strains such as H1N1, H3N2, and B type. One reason the vaccine is required annually is because influenza viruses are constantly changing their surface structures which allows them to evade the immune system. The influenza virus envelope is made up of hemagglutinin (HA) and neuraminidase proteins. Normally annual vaccines target HA surface proteins which are highly immunogenic and have a great affinity for binding antibodies but these proteins are extremely variable. The HA protein has 16 distinct antigenic subtypes, therefore developing an annual vaccine that binds to the highly variable head of the HA surface protein results in the need for frequent reformulation.

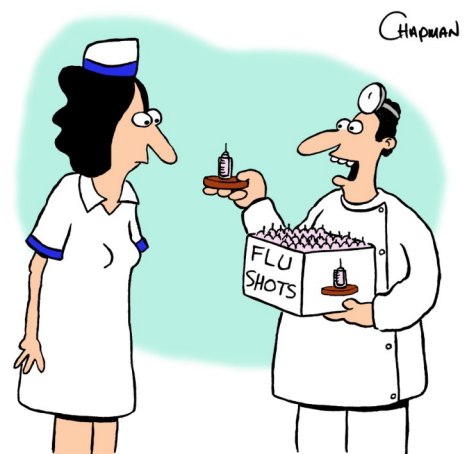
Recently, scientists have discovered universal influenza antibodies that could possibly protect the population from most types of influenza strains. The neutralizing antibodies bind to the conserved region of the virus' HA protein otherwise known as the stem. This region is similar across many different HA subtypes. The problem is that neutralizing antibodies have low affinity for this region. Unlike the variable head region which has many cavities that allow antibodies to bind with high affinity, the conserved stem region of HA has a flat surface and is therefore poorly immunogenic. There is evidence that immunization with DNA-based vaccines, or live attenuated viral vaccines elicit greater expression of neutralizing antibodies compared to the inactivated viral vaccines. Therefore designing a vaccine that is effective using neutralizing antibodies requires research in developing new influenza immunogens (adjuvants) that can elicit enough neutralizing antibodies for protection against influenza infection.

An alternative solution for developing a universal flu vaccine is to use conserved influenza matrix 2 proteins (M2). M2 is essential for normal functioning of the influenza virus. This protein is already a target of therapeutic anti-viral drugs such as adamantanes (M2 inhibitors), which prevent the virus from replicating by blocking the M2 protein. The first human phase 1 clinical trials have already been done using a fusion protein comprised of M2e and another conserved nuclear protein (NP). These influenza antigens are then linked to a toll-like receptor-9 (TLR9) agonist (adjuvant). This vaccine formulation has proven to be well tolerated and provide protection against divergent strains of flu.

Another reason for developing a universal flu vaccine is to extend duration of immunity so the population would not require annual vaccinations. Even though most of the population is asked to get vaccinated each year, uptake is low. A universal vaccine that provides long term protection (greater than 5 years) would have the potential to significantly increase immunization rates. Current vaccines only provide 1 year of protection while universal vaccines may potentially provide greater than 3 years of immunity to more than 3 strains of influenza.

A public health concern to be considered while introducing universal vaccines is society's behavior, particularly complacency regarding vaccination. Measles, for example, has been a vaccine preventable disease for years but has recently increased globally possibly due to increased inappropriate concern about vaccine safety. Also, the drive for immunization is often diminished once there is perception of eradication. To counter these concerns, the introduction of universal vaccines will require enhanced risk awareness programs to prevent outbreaks of influenza in non-vaccinated populations and those with waning immunity.

Currently, only small-scale clinical trials have been performed involving universal influenza vaccines but there are some promising results. We will keep an eye on this interesting research & provide updates as they develop.



"All we have to do is place them on the waiting room chairs!"

A FOND FAREWELL TO KAREN RIVERA

Karen has been the Research Administrative Assistant at TARRANT for over 8 years and will be leaving her position in early January, 2012 to pursue studies in the medical field.

We know many of you have gotten to know Karen well and we hope you will join us in wishing Karen all the very best in her future endeavours.



TARRANT & VACCINE EFFECTIVENESS STUDY COMPENSATION

We are now sending out invoices to our sentinels twice yearly with compensation periods ending in May & November. We have just sent out the November invoices to all sentinels who accrued a minimum of \$20.00 in either study & will process your payment upon receipt. If you qualified for compensation in the last payment period but did not submit your invoice, we have rolled any outstanding amounts into the most recent invoices. Please let us know if you do not receive an invoice or payment and we will ensure any concerns are addressed.

TOP 5 REASONS WHY VACCINE EFFECTIVENESS (VE) STUDY SUBMISSIONS ARE REJECTED

You assess your patient. Fever –check. Coughing –check. Sore throat, myalgia, arthralgia or prostration –check. Great, another patient to enrol in the VE Study! You go over the Verbal Consent script & receive consent. You grab a swab & complete a VE Study Requisition form. Off go the sample & the requisition...but you later receive word from ProvLab that sample wasn't processed or you receive word from us that the submission didn't qualify for the study. What went wrong??!

- 1. Missing patient identification.** ProvLab will not process submissions that are missing patient first & last name, DOB or PHN. Most sentinels use printed labels for this information but if you or your staff prefer to hand-write this section, please complete all requested information.
- 2. Missing specimen information.** AHS has recently instituted a policy requiring sample rejection if this important information is omitted. Please use the check boxes in the "Specimen Information" box to indicate specimen source and please remember to complete the "Date Collected" section as well.
- 3. Missing patient verbal consent.** As per study protocol, if affirmative patient consent is missing, the submission cannot be included in the study. If the patient (or guardian) consents to take part in the study, please ensure the "Yes" check-box is marked.
- 4. Not using a current-year Virology Test Requisition Form.** Each year the study questions change so we cannot enter submissions into the database when older forms are used. For the 2011-12 influenza season, you should only use blue forms; please immediately discard all others.
- 5. Improper sample handling.** Several submissions are omitted each year because diagnostics could not be performed on the sample. The most common problems are use of incorrect swab type, leaking specimens or incorrectly labelled specimens. Please use the swab kits we send to you, ensure the cap is tightened to prevent leakage & the sample labelled appropriately.

We greatly appreciate the time each sentinel takes to take part in the VE Study. Taking a moment or two to fully complete the requisition form & make certain the sample is handled properly will ensure your valuable time & effort has resulted in a qualifying submission. So far this season, **5% of submissions have been rejected** and we will be undertaking increased effort to contact sentinels when a rejection occurs to avoid future issues. If you ever need any assistance regarding your VE submissions, please contact us & we would be very happy to help.