In this bulletin:

Dear colleagues,

As we enter the summer months and our human influenza surveillance indicators decline to inter-seasonal levels, we would like to update you on recent global trends related to emerging respiratory pathogens, including novel influenza A viruses and MERS-CoV.

A. HIGHLIGHTS

- **Human Infections with Avian Influenza**
  - Avian Influenza A(H5N1). Egypt continues to experience a large-scale outbreak of avian influenza A(H5N1), with year-to-date case counts (n=132) exceeding prior yearly totals in that country by more than three times. In fact, the number of cases occurring between November 2014 and February 2015 in Egypt has exceeded the number of cases ever found in any country since 2003. A recent joint high-level mission, including representatives of human and animal health organizations, has assessed the current situation in Egypt and concluded based on epidemiologic and virologic features that the risk of an H5N1 pandemic has not changed appreciably, but warrants ongoing monitoring.
  - Avian Influenza A(H7N9). A third wave of human infections with avian influenza A(H7N9) appears to have subsided in China, following an expected seasonal peak in January-February. The peak of the third epidemic wave in 2014-15 was smaller in scale than the prior year's wave in 2013-14, but the epidemiological features of cases remain similar.

- **Other Influenza**
  - Swine-origin Influenza A(H1N1) variant (H1N1v). A fatal case of swine-origin influenza A(H1N1) variant (H1N1v) was reported in the United States last week. This is the second human case of H1N1v in 2015.
  - H5 Avian Influenza Outbreaks. Multiple outbreaks of highly pathogenic avian influenza (HPAI) due to H5 subtype viruses (e.g. H5N2, H5N8, H5N1) continue to be reported in domestic poultry, with 29 countries (including Canada and the Unites States) reporting HPAI H5 detections so far in 2015.

- **MERS-CoV.** Sporadic MERS-CoV activity continues in Saudi Arabia and affected regions in the Middle East, driven by small-scale nosocomial outbreaks, mostly in the Riyadh region.

Although the risk to Canadians for these emerging respiratory pathogens remains low, clinicians should remain vigilant and consult their local Medical Health Officer for advice related to diagnostic testing, infection control and follow up where a novel emerging pathogen may be suspected.

More detailed epidemiologic information, risk assessment and action and advice are provided below.

B. EPIDEMIOLOGICAL SUMMARY

1. Human Infections with Avian Influenza

i. Avian Influenza A(H5N1)

As of May 1, 2015, 132 human cases of avian influenza A(H5N1), including 37 deaths (case fatality: 28%), have been reported in Egypt so far in 2015, more than three times as many cases as any prior year in that country. In fact, the number of cases occurring between November 2014 and February 2015 has exceeded the number of cases ever found in any country since 2003. Of the 132 cases in Egypt so far in 2015, 115/132 (87%) were newly reported since our last bulletin to you on February 27, 2015, and covering the period January 26 to May 1, 2015.

Of these latest 115 cases, ages range from <1 to 77 years (median: 27 years), with 40 (35%) reported in children <10 years of age; 45 (39%) are male. All cases with known exposure history reported contact with poultry or poultry markets and all were hospitalized. Twenty-two deaths were reported during this period, but none occurred in children <10 years of age. Two family clusters, each comprised of two cases, are included in this total.

Although Egypt continues to report sporadic human cases of H5N1, the number of laboratory-confirmed cases decreased in April compared to the previous five months, according to the latest WHO risk assessment. The recent surge of cases since November 2014 has been attributed to a mixture of factors, including increased circulation of H5N1 in poultry compared to previous periods, lower public health risk awareness, and greater opportunities for poultry exposure due to increases in the number of small poultry farms and backyard poultry flocks and seasonality.

Preliminary laboratory investigations do not suggest any genetic changes in the virus that would increase the likelihood of transmission from animals to humans, and sustained human-to-human transmission in the community has not been observed. A recent joint high-level mission to assess the current situation in Egypt, including representatives of human and animal health organizations, has concluded that the pandemic risk from H5N1 has not appreciably changed.

Additionally in 2015 (as of May 1, 2015), 7 human cases of H5N1 have been further reported in China (n=5) and Indonesia (n=2, family cluster), for a global year-to-date tally of 139 cases, including 40 deaths (case fatality: 29%). Since 2003, a total of 840 laboratory-confirmed cases, including 447 deaths (case fatality: 53%), have been reported from 16 countries.

For an infographic of H5N1 activity (March 31), see: www.emro.who.int/images/stories/egypt/h5n1-infographic-march-2015.pdf?ua=1.

For the latest WHO risk assessment on influenza at the human-animal interface (May 1), see: www.who.int/influenza/human_animal_interface/Influenza_Summary_IRA_HA_interface_1_May_2015.pdf?ua=1.

For an executive summary of the joint high-level mission on the current H5N1 situation in Egypt, see: www.emro.who.int/images/stories/Executive_Summary_14_May_2015.pdf?ua=1.

ii. Avian Influenza A(H7N9)

Since our last bulletin to you on February 27, 2015, 85 new cases of human infection with avian influenza A(H7N9) have been reported in China, including 23 deaths (case fatality: 27%) at the time of reporting. Affected provinces include Guangdong (39), Zhejiang (23), Anhui (8), Fujian (4), Jiangsu (4), Hunan (2), Shanghai (2), Guizhou (1), Jiangxi (1), and Shandong (1). Among these recent cases, the epidemiologic profile remains similar to previous summaries. Ages range from 1 to 82 years (median: 55 years) and 63/85 (74%) are male. Of the cases with known exposure history, almost all (71/77, 92%) reported exposure to live poultry or live poultry markets. Three family clusters, each comprised of two cases, were reported, of whom four of six cases had exposure to live poultry or live poultry markets. Most cases were in severe/critical condition at the time of report; accordingly, the case fatality may increase as reporting becomes more complete.

Symptom onset dates of these latest cases range from January 21 to April 12, 2015. More than 80% of cases had onset in January-February (69/85, 81%), suggesting that the third seasonal wave of infections has subsided. Human cases of H7N9 continue to show a seasonal pattern, with case reports peaking from January to March.

As of May 1, 2015, a total of 657 laboratory-confirmed human cases and at least 261 deaths (case fatality: 40%) due to H7N9 have been reported since the start of the outbreak in February 2013. Case reports span three seasonal waves: the first wave of 135 cases (February 2013 to September 2013); a second, more substantial wave of 320 cases (October 2013 to September 2014); and an ongoing third wave of 202 cases (starting October 2014). Outside of the primarily affected area of China there have also been four imported cases reported from Taipei CDC, 13 from Hong Kong CHP, one from Malaysia MoH, and two from Canada. The majority of cases continue to be associated with exposure to infected live poultry or contaminated environments, although multiple clusters of probable close household or family transmission have also been identified. The risk of sustained human-to-human transmission in the community remains low.

In a recent epidemiological comparison of H7N9 and H5N1 viruses, researchers show that H7N9 may have a greater pandemic potential risk than H5N1, although both viruses had estimated reproductive numbers (R) below the epidemic threshold. Conversely, H5N1 was associated with a higher proportion of clusters and increased risk for infection in blood-related contacts than H7N9, suggesting that susceptibility to H5N1 is more likely limited and familial. Findings were published in *Clinical Infectious Diseases*: cid.oxfordjournals.org/content/early/2015/05/04/cid.civ345.short.

On April 7, the US Centers for Disease Control and Prevention (US CDC) released new antiviral treatment and chemoprophylaxis guidelines for human infections with novel influenza A viruses, including H7N9 and H5N1. This guidance recommends antiviral treatment as soon as possible for all hospitalized cases of human infection with novel influenza A viruses associated with severe human disease and for confirmed and probable outpatient cases or outpatient cases under investigation who have had recent close contact with a confirmed or probable case. In addition, recommendations for chemoprophylaxis have been adjusted. Specifically, treatment frequency dosing for oral oseltamivir or inhaled zanamivir at one dose *twice* daily is recommended instead of the typical antiviral chemoprophylaxis regimen (*once* daily). Related details are available from: www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm and www.cdc.gov/flu/avianflu/novel-av-chemoprophylaxis-guidance.htm.

2. Other Influenza

i. Swine-origin Influenza A(H1N1) variant (H1N1v)

On May 8, the US CDC reported a fatal human case of influenza A(H1N1) variant (H1N1v) of classical swine origin in Ohio. Subsequent partial genetic sequencing conducted at the US CDC indicated that this virus is similar to H1N1 viruses currently circulating in swine. The case worked at a livestock facility that housed swine but reported no direct contact with swine in the week prior to illness onset. No further human-to-human transmission was identified.

This latest case brings the total number of H1N1v cases reported in the United States since 2005 to 18 and is the second human case of H1N1v reported in 2015. In January, a non-fatal case was reported in Minnesota.

ii. H5 Avian Influenza Outbreaks (H5N1, H5N2, H5N3, H5N6, H5N8)

Multiple outbreaks of highly pathogenic avian influenza (HPAI) due to H5 subtype viruses continue to be reported in poultry around the globe.

In North America, outbreaks of HPAI H5 in wild and domestic birds have been reported in two Canadian provinces and 17 US states to date in 2015. These outbreaks are the first due to HPAI H5 reassortants of Eurasian origin in North America, resulting from a reassortment of Eurasian H5N8 viruses with endemic avian viruses. The current H5N1 virus detected in North American birds is a new reassortant virus of mixed origin which is considered genetically distinct from the avian-origin H5N1 virus causing human infections in Egypt and parts of Asia. To date, no human cases of avian influenza have been reported associated with these recent outbreaks in North America but ongoing monitoring is warranted.

In addition to human health implications with respect to pandemic potential with opportunities for adaptation, the geographic expansion of HPAI H5 viruses has serious implications for the poultry industry. As of May 19, 2015, 29 countries have reported HPAI H5 detections to the World Organization for Animal Health (OIE) so far in 2015, including in:

- **North America**
  - H5N1: Canada (British Columbia); United States (Washington)
  - H5N2: Canada (British Columbia, Ontario); United States (Arkansas, Idaho, Iowa, Kansas, Kentucky, Minnesota, Missouri, Montana, North Dakota, Oregon, South Dakota, Washington, Wisconsin, Wyoming)
  - H5N8: Canada (British Columbia); United States (California, Idaho, Nevada, Oregon, Utah, Washington)
- **Europe**
  - H5N1: Bulgaria; Romania; Russia; Turkey
  - H5N8: Germany; Hungary; Italy; Netherlands; Sweden
- **Asia**
  - H5N1: Bhutan; China; India; Indonesia; North Korea; Myanmar
  - H5N2: China; Chinese Taipei; Vietnam
  - H5N3: Chinese Taipei
  - H5N6: China; Hong Kong
  - H5N8: Chinese Taipei; Japan; South Korea

- **Middle East**
  - H5N1: Israel; Palestine
- **Africa**
  - H5N1: Burkina Faso; Egypt; Libya; Niger
  - Subtype not specified: Nigeria

For more information on outbreaks of HPAI due to H5 subtype viruses in North America, see: www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=29809&lang=en.

3. Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

Since our last bulletin to you on February 27, 2015, the WHO has reported 92 additional cases of MERS-CoV. Nearly all of these cases have been reported from Saudi Arabia (88/92, 96%), with over half (47/88, 53%) reported from the Riyadh region. On March 7, Germany reported a case in an adult male who had recently returned from travelling in the United Arab Emirates (UAE). This is the third imported MERS-CoV case in Germany since the start of the outbreak in March 2012. On March 9, Qatar reported its second case of 2015 in an adult male who reported frequent contact with camels and regular consumption of raw camel milk. This month, Iran reported a case, its first since July 2014, in an adult male who was epidemiologically linked to two pilgrims with influenza-like symptoms returning from Umrah. Most recently, on May 18, the UAE reported a case in an adult male who frequently transports camels from Oman to UAE.

Among these recent 92 cases, the epidemiologic profile is similar to previous summaries. Ages range from 20 to 93 years (median: 56 years) and over three-quarters (70/92, 76%) are male. Most cases (67/92, 73%) had at least one chronic comorbidity. Over 40% of cases had no known exposure to risk factors for MERS-CoV in the 14 days prior to symptom onset. Of the 54 cases with known exposure, 26 (48%) reported exposure to a healthcare setting (including 11 who were healthcare workers), 9 (17%) were household contacts of previously identified cases, and one (the Iranian case) was epidemiologically linked to two suspect cases. Only 17 (31%) reported direct or indirect contact with camels, including consumption of raw camel milk, and one reported direct contact with sheep but not camels.

The current epidemiological pattern is consistent with earlier periods of the outbreak characterized by exposure to a primary animal source (likely dromedary camels) followed by secondary amplification in healthcare settings. Despite a small upswing in case reports at the beginning of 2015, recent nosocomial outbreaks, mostly in the Riyadh region, remain smaller in scale than prior outbreaks, likely due to improvements in infection prevention and control practices.

In other developments, German and Saudi researchers recently published a nationwide MERS-CoV serosurvey, including samples from over 10,000 individuals in 13 provinces in Saudi Arabia. Anti-MERS-CoV antibodies were detected in 0.15% (95% CI: 0.09-0.24%) of patients, with higher antibody prevalence found in men and residents of central (versus coastal) provinces. Compared to the general population, seroprevalence was 15 to 23 times higher in camel-exposed individuals, providing further evidence that camels are the primary source of MERS-CoV infection. The authors postulate that subclinical infections in healthy, younger adults may be a source of infection (i.e. human-to-human transmission) in index cases with no known camel exposure. The findings were published in *Lancet Infectious Diseases*: www.thelancet.com/journals/laninf/article/PIIS1473-3099(15)70090-3/abstract.

As of May 18, 2015, the WHO has been informed of 1,118 laboratory-confirmed cases of MERS-CoV including at least 423 deaths (case fatality: 38%).

For an infographic of MERS-CoV activity (March 31), see:
www.emro.who.int/images/stories/csr/documents/MERS-CoV_March_2015.pdf?ua=1.

C. ACTION AND ADVICE

In the event of severe acute respiratory illness (SARI) in a patient with links to affected areas in the two weeks prior to symptom onset (i.e. residence, travel history or contact with someone with such history), clinicians should notify their local health authority/Medical Health Officer. Clinicians should obtain relevant travel, animal (direct or indirect), or other contact exposure history from patients presenting with severe acute respiratory illness (SARI).

Health care workers should implement respiratory precautions immediately, and cases should be managed in respiratory isolation with contact and droplet precautions. Airborne precautions are warranted in the event of aerosol-generating procedures or conditions. Given a spectrum of illness inclusive of milder or atypical presentations, clinicians are encouraged to use their judgement and/or consult infection control for guidance around enhanced measures where the index of suspicion (e.g. based on contact, comorbidity or clustering history) and exposure risk may be higher. Facilities should be mindful of the protection of other patients and visitors, in addition to healthcare workers, to minimize nosocomial transmission and risk.

Please discuss with your local health authority/Medical Health Officer and consult a virologist or microbiologist at the BC Public Health Microbiology & Reference Laboratory (PHMRL) to arrange advance notification and direct shipping of diagnostic specimens. For diagnostic testing for suspected MERS-CoV or avian influenza, lower respiratory specimens (e.g. sputum, endotracheal aspirate, or bronchoalveolar lavage) are recommended where possible and clinically indicated. Follow strict infection prevention and control guidelines when collecting respiratory specimens.

Sincerely,

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BC Centre for Disease Control