Dear colleagues –

While the world’s attention is understandably focused on the Ebola outbreak affecting several countries of West Africa, we would also like to remind and update you about several emerging respiratory viruses (ERV) with ongoing global monitoring since our last bulletin of June 17, 2014, including:

1. **MERS-CoV**. Activity has declined substantially relative to the dramatic surge that occurred in April 2014. However, sporadic cases continue to be reported from affected regions in the Middle East, including an imported MERS-CoV case reported this week in Austria, the first from that country.

   This year, the Hajj – an annual pilgrimage to Mecca, Saudi Arabia – will take place during the first week of October. Due to the increase in travel to the affected region in the coming weeks, further importation of cases to countries outside of the Arabian Peninsula may be anticipated. Although no confirmed cases were detected in association with the 2013 Hajj, several travel-associated cases were reported in 2014 in pilgrims returning from Umrah, a religious pilgrimage that can occur at any time of year.

2. **Avian influenza A(H7N9)**. Activity remains at low levels, with only 4 cases reported since our last bulletin but with two of the most recent cases extending the geographic distribution of H7N9 to the furthest northwest region of China. As with other influenza viruses, A(H7N9) shows a winter seasonality; accordingly, ongoing monitoring for a third resurgent H7N9 epidemic wave is warranted as we enter the fall/winter period.

3. **Swine influenza A(H3N2)v**. Two cases were reported in children in Ohio this summer, with evidence in the viral genome of additional genetic reassortment with A(H1N1)pdm09.

4. **Enterovirus D68 (EV-D68)**. This virus has been detected in association with severe respiratory illness and possibly also neurologic manifestations among children in the United States and Canada, as communicated to you earlier on September 16 and October 1, 2014.

Below, we provide you with additional details on these four ERVs of public health interest, beginning with epidemiologic updates, followed by recommended action and advice.
A. EPIDEMIOLOGIC UPDATE

1. Middle East Respiratory Syndrome Coronavirus (MERS-CoV), Middle East
Since the dramatic surge in activity that occurred in April 2014, the number of reported MERS-CoV cases has declined substantially (see attached MERS-CoV Epidemic Curve). Only 14 cases were reported to the World Health Organization (WHO) in July and August from Saudi Arabia (11), the United Arab Emirates (UAE; 2), and Iran (1). Since September 1, 2014, 13 additional cases have been reported, each from Saudi Arabia.

On September 30, 2014, Austria reported its first confirmed case of MERS-CoV in a visitor from Saudi Arabia, becoming the thirteenth country outside of the Arabian Peninsula to be affected. Prior travel-associated cases have been reported from countries in Europe, North Africa, Southeast Asia, and the United States (see attached MERS-CoV Map). All cases that have been reported outside of the Arabian Peninsula either had recently traveled to the affected region during their exposure period or had an epidemiological link to an individual with such travel history.

As of October 3, 2014, the WHO has been informed of 855 lab-confirmed cases of MERS-CoV, including at least 302 related deaths (per case fatality of 35%). However, these numbers are likely an underestimate of the true burden of disease and do not reflect more recently reported cases in Saudi Arabia, including 19 retrospectively identified cases, all with onset dates prior to June 3, 2014, that were reported on September 18 by the Saudi Ministry of Health (MOH). Despite instances of close contact spread, notably nosocomial, there remains no evidence of sustained human-to-human community transmission.

On October 1, 2014, the WHO released a statement on its 7th Meeting of the International Health Regulations (IHR) Emergency Committee concerning MERS-CoV. As with prior meetings, the Committee unanimously concluded that the conditions for a Public Health Emergency of International Concern (PHEIC) have not yet been met. The Committee reiterated its previous advice regarding the Hajj, including improved awareness about MERS-CoV among pilgrims and ongoing surveillance for MERS-CoV during and after the Hajj. For more information: www.who.int/mediacentre/news/statements/2014/7th-mers-emergency-committee/en/.

While camels are now recognized as the animal reservoir for MERS-CoV, the exact route of direct or indirect transmission to humans remains unknown. However, a new study published last week in Emerging Infectious Diseases provides some clues as to how this virus may be spread from camels to humans. In this study, the authors inoculated 3 adult male camels with a human isolate of MERS-CoV. All 3 camels developed only mild upper respiratory tract illness (rhinorrhea) and had a slight elevation in body temperature for 2-3 days. Infectious virus was detected in nasal secretions up to 7 days post-infection and viral RNA up to 35 days post-infection. No viral RNA was detected in fecal, urine, whole blood or serum samples. These findings are consistent with surveillance observations of camels in close contact with human cases and suggest transmission to humans from camels likely occurs through close contact, large respiratory droplets and fomites. For the full-text article: wwwnc.cdc.gov/eid/article/20/12/14-1280_article.

In anticipation of the upcoming Hajj pilgrimage, clinicians are reminded that a history of travel or other possible epidemiological links to affected areas is paramount to elicit from patients presenting with severe acute respiratory illness (SARI). The median incubation period for MERS-CoV is estimated at 5-6 days, but could be up to 14 days.

WHO travel advice for pilgrimages: www.who.int/ith/updates/20140603/en/.
For more information on MERS-CoV: www.who.int/csr/disease/coronavirus_infections/en/.
2. Avian Influenza A(H7N9), China
Since our last bulletin on June 17, 2014, only 4 cases of human infection with avian influenza A(H7N9) have been reported from China. Two of these cases, however, with onset dates in July and August, were reported in the far northwest corner of China in the Xinjiang autonomous region (UAR), a newly affected region that is not adjacent to any provinces or municipalities, mostly along the eastern coast of China, that had previously reported cases (see attached H7N9 Epidemic Curve and Map). The cases are not considered epidemiologically linked. The 2 other cases, both with onset dates in June, were reported in Hunan and Zhejiang Provinces, two of the more-affected provinces during the second wave of the outbreak.

As of July 7, 2014, the WHO has been informed of 451 lab-confirmed cases of A(H7N9) and 171 deaths (per case fatality of 38%). These numbers do not include the 2 most recently reported cases from Xinjiang UAR. As shown in the attached epidemic curve, the second wave of H7N9 was earlier than the first wave (peaking in January 2014 vs. April 2013) and comprised more than double the number of cases. Given the fall-winter seasonality of avian influenza viruses generally, vigilance for cases associated with a possible third H7N9 wave through the 2014-15 season will be important.

3. Swine Influenza A(H3N2)v, United States
Two human cases of swine influenza A(H3N2)v were reported in children in Ohio in week 33 (ending August 16, 2014) and week 34 (ending August 23, 2014). Both children had close contact with swine in the week prior to illness onset. The cases are not considered epidemiologically linked. A(H3N2)v viruses isolated from the cases contained both the nucleoprotein (NP) and matrix (M) gene from the 2009 pandemic A(H1N1) virus. In previous years 2011-2013, A(H3N2)v viruses from human cases contained only the M gene from the 2009 pandemic A(H1N1) virus, suggesting these more recent A(H3N2)v detections contain a different combination of internal genes resulting from further reassortment.

These are the first 2 A(H3N2)v cases reported in 2014. A total of 342 cases have been reported since August 2011 in 13 US states, the majority from Indiana and Ohio and during the summer/fall months in association with agricultural fairs that bring children into contact with swine. Cases present as typical ILI. To date there have been 18 hospitalizations (one in 2014) and one death associated with H3N2v since July 2012. See the attached map for distribution of H3N2v detections in the United States since 2011.

4. Enterovirus D68 (EV-D68), United States and Canada
Beginning in mid-August 2014, children's hospitals in several US cities reported clusters of severe respiratory illness in hospitalized children due to EV-D68. Since then (as of October 3, 2014), a total of 538 cases in 43 US states and the District of Columbia have been confirmed to have respiratory illness caused by EV-D68. Although not nationally notifiable, cases of EV-D68 have also been identified in 5 Canadian provinces (BC, Alberta, Saskatchewan, Manitoba, and Ontario). More case reports are anticipated as diagnostic testing for EV-D68, which requires sequencing of the virus, is completed on suspect cases.

As of October 3, 2014, the BC provincial laboratory has confirmed 9 sporadic cases of EV-D68 in children (aged 0-19 years: 6 < 10 years of age and 3 aged 10-19 years). However, unlike the current situation in some areas of the United States, BC has not experienced clusters/outbreaks or increases in severe respiratory illness to date and overall rates of influenza-like illness (ILI) remain within or below expected ranges for this time of year. However, all public primary and secondary schools had been closed in BC due to a teacher's strike that recently ended with school only having resumed from summer recess on September 22, 2014. Ongoing monitoring for possible upswing in ILI activity is in place.
Emerging Respiratory Virus bulletin 2014-10-04

Investigations into the early US clusters suggest that children with a history of asthma or wheezing may be at higher risk for severe EV-D68 infection. Notably, fever has not been a common symptom. Some children have required ICU admission and mechanical ventilation. To date, 4 deaths have been reported among recently confirmed cases in the United States although a causal role for EV-D68 has not been established. We are not aware of any reported deaths in association with confirmed EV-D68 infection in Canada.

On September 26, 2014, the US CDC issued a Health Advisory to clinicians reporting a cluster of polio-like illness in 9 children (aged 1-18 years) in Colorado. Of the 8 tested specimens, 6 were positive for entero/rhinoviruses, of which 4 were confirmed as EV-D68, with 2 typing results pending at the time of report. As part of this advisory, the US CDC requested further information on patients ≤21 years of age presenting with acute onset of focal limb weakness occurring on or after August 1, 2014, and an MRI showing spinal cord lesion largely restricted to grey matter. In response to this request, the BC Centre for Disease Control in collaboration with Fraser and Interior Health Authorities issued a notice through ProMED-mail providing additional information on 2 BC cases with lab-confirmed EV-D68 infection and presenting with neurologic illness, as communicated to you in our bulletin on October 1, 2014. It remains unclear whether EV-D68 is causally or coincidentally associated with neurologic findings. For the full ProMED-mail posting see: www.promedmail.org/direct.php?id=2819618. Since then, clusters of polio-like illness have been cited in other provinces including Ontario and Alberta although information about whether these may have been associated with EV-D68 is still pending.

In the current outbreak, EV-D68 has more often been reported in association with severe respiratory illness but neurologic findings in association with EV-D68 have also been reported from an earlier cluster of EV-D68 cases in California described in February 2014 and in a 2008 fatal case of meningomyeloencephalitis in a child from New Hampshire in whom EV-D68 was detected in the CSF (Kreuter JD et al Arch Pathol Lab Med. 2011;135:793-96).

For a description of neurologic findings in the context of increased respiratory illness and/or EV-D68 detections in California and Colorado, please see the following early release MMWR bulletins, posted Friday October 3, 2014 by the US CDC: www.cdc.gov/mmwr/preview/mmwrhtml/mm63e1003a2.htm?s_cid=mm63e1003a2_w and www.cdc.gov/mmwr/preview/mmwrhtml/mm63e1003a1.htm?s_cid=mm63e1003a1_w

The US CDC also held a Clinician Outreach and Communication Activity (COCAs) on Friday October 3, 2014 to share recent findings related to clusters of neurologic illness in children and to provide guidance on investigation and reporting. Transcripts from this teleconference are anticipated to be posted next week and may be sought here: emergency.cdc.gov/coca/calls/2014/callinfo_100314.asp

For more information on EV-D68, see:
BCCDC: www.bccdc.ca/dis-cond/a-z/_e/EnterovirusD68/default.htm.
US CDC: www.cdc.gov/non-polio-enterovirus/about/EV-D68.html
B. RECOMMENDED ACTION AND ADVICE

MERS-CoV or Avian Influenza

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.

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. 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.

Enterovirus D68

Clinicians should consider EV-D68 infections in children presenting with severe respiratory illness and report any increase or unusual clusters/outbreaks of respiratory illness to their local health authority/Medical Health Officer. More severe respiratory presentations of EV-D68 may be anticipated in association with underlying comorbidity, notably a history of asthma. EV-D68 diagnosis and reporting should also be considered alongside other investigations in patients ≤ 21 years of age presenting with acute onset of focal limb weakness and an MRI showing spinal cord lesion largely restricted to grey matter. There is no specific treatment or vaccine for EV-D68. Clinical care is supportive. Healthcare providers should implement routine infection control practices, including droplet and contact precautions for patients with suspected EV-D68 infection. Surfaces should be cleaned with a hospital-grade disinfectant with a DIN and label claim for non-enveloped viruses.

Suspect EV-D68 investigations should be conducted in consultation with the local Medical Microbiologist and Medical Health Officer, with referral to the BC PHMRL as indicated for EV-D68 typing. Clinicians are requested to submit respiratory (nasopharyngeal/oropharyngeal) and other specimens as clinically indicated. Only certain laboratories in the Lower Mainland conduct enterovirus testing; however, the PCR-based screening assays generally used do not reliably identify the specific type of enterovirus. At present, sequencing of the virus which is performed by the BCPHMRL is required before cases can be considered confirmed.

Further Information

To review prior bulletins, and to obtain higher resolution images of epidemic curves and maps issued by the BCCDC Influenza & Emerging Respiratory Pathogens team, see: www.bccdc.ca/dis-cond/DiseaseStatsReports/EmergingRespiratoryVirusUpdates.htm

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BC Centre for Disease Control
MERS-CoV Epidemic Curve

* Cases are shown by country of exposure (or by reporting country if place of exposure unknown) and by symptom onset date (or by reporting date if onset date unavailable or case is asymptomatic).

Notes: In a retrospective report from Saudi Arabia on 2014-09-18, a duplicate case previously reported was retracted (but still shown here); 19 cases (16 of which from Jeddah) with onset prior to 2014-06-03 were identified, but are not displayed here, due to insufficient case details.

Prepared by BCCDC Influenza & Emerging Respiratory Pathogens Team 2014-10-03
MERS-CoV case activity as of October 3, 2014

Individual cases in light green-shaded countries are confirmed as either imported from the Arabian Peninsula or a close contact of an imported case indigenous to the indicated country.

Cases with unknown city location in Saudi Arabia:
For countries outside the Arabian Peninsula, non-indigenous cases imported from that region are duplicated on map. As such, only indigenous cases should be added to those shown within the Arabian Peninsula in deriving the total global case count. Cases with origin and history of travel restricted to Arabian Peninsula are shown once on map, according to reporting country. In a retrospective report from Saudi Arabia on 2014-09-18, two cases were retracted (one false positive, one duplicate) but are still displayed here; 19 cases (16 of which from Jeddah) with onset prior to 2014-06-03 were identified, but are not displayed here, due to insufficient details.

Maps produced by British Columbia Centre for Disease Control (BCCDC). Data compiled from Kingdom of Saudi Arabia Ministry of Health, WHO, and European Centre for Disease Prevention and Control (ECDC).
*Does not include: 1 Henan, 4 Jiangsu, and 1 Guizhou cases with unknown onset date; one asymptomatic case in Beijing.*
H7N9 avian influenza first and second wave cases by province of residence

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<th>Province</th>
<th>Cumulative # of cases</th>
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<tbody>
<tr>
<td>Anhui</td>
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<td>Hebei</td>
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<tr>
<td>Henan</td>
<td>4</td>
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<td>Hunan</td>
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<table>
<thead>
<tr>
<th>Province</th>
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<tr>
<td>Taiwan</td>
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**Total**: 454 cases

* Two cases with symptom onset in July 2013 (one in Hebei and one in Guangdong) are not represented on the map.
** Case was likely exposed in Zhejiang.
† Cases reported travel to mainland China during exposure period.
‡ One case residing (and apparently exposed) in Guangdong was identified during travel to Malaysia, where the case was reported and hospitalised. Four other cases who lived in and were likely exposed in Guangdong were hospitalised and diagnosed in Hong Kong.

Data compiled from ProMed, GPHIN alerts and other public reports. Map created October 3, 2014 by BCCDC.