To:	BC MHOs, PHNLs, ICPs, ERDOCs, IDSPEC, MEDMICRO, AMBULANCE, BCCDC Internal Groups, National Partners
Subject:	**April 30, 2014** – Emerging Respiratory Virus (ERV) Update
Purpose:	Heightened clinician awareness in light of recent surge in MERS-CoV cases and nosocomial transmission in the Arabian Peninsula
Action required:	Yes
Recommendations:	Enhanced vigilance, notification and infection control by clinicians in response to cases of severe acute respiratory illness (SARI) with links to affected areas in the two weeks prior to symptom onset.

In this bulletin:

***** Please share with your workplace colleagues as appropriate. *****

Dear Colleagues –

There has been a staggering surge in the number of MERS-CoV cases reported among individuals with links to the Arabian Peninsula in the past few weeks.

This is well-illustrated in the attached **Epidemic Curve** in which it is evident that more cases of MERS-CoV have been reported for the month of April 2014 alone than had previously been reported in total since the beginning of the outbreak (from April 2012 - March 2014).

The majority of these recent cases have occurred within nosocomial settings, reminiscent of the SARS-CoV transmission pattern of 2003. For this reason, clinicians are reminded to be aware of possible MERS-CoV importations, to take travel history among patients presenting with severe acute respiratory illness (SARI) and to implement infection control precautions while investigating and managing such patients.

Below we provide you with an updated epidemiological summary in support of that response.

1. MERS-CoV UPDATE [Total: 453 cases; Deaths: 126+], Middle East

a. Sudden surge in cases, April 2014

As of 30 April 2014, 453 human cases of MERS-CoV have been reported in total since the beginning of the outbreak.

In the month of April 2014 alone, more than 200 MERS-CoV cases were reported worldwide, including >80% from Saudi Arabia and ~15% from the United Arab Emirates (UAE), as well as two from Jordan and one each from Egypt, Greece, Malaysia and the Philippines (see attached **MERS Epidemic Curve** and **Map**).

Many (at least 80%) of the cases from Saudi Arabia have yet to be officially reported by the WHO, which may account for some discrepancy in tallies across various sources. For instance, just this morning, 16 new cases were reported by the Saudi Ministry of Health (MOH), which currently reports a total of 361 confirmed cases and 107 deaths, more than half of these having been accrued this month alone. Globally, from September 2012 to 26 April 2014, the WHO reports 261 laboratory-confirmed cases and 93 deaths in total.

As with previously reported cases, these latest cases have been predominantly middle-aged and older adult men with a 2:1 male-to-female ratio and a mean/median age of about 50 years. Almost all cases (~95%) have been identified in adults ≥20 years old. The case fatality remains high at about 30%. Up to 75% of the latest cases represent secondary transmission. This week, a case was reported in a 9-month-old infant, the youngest documented case to date, who likely acquired infection while in hospital following admission for a kidney condition. The infant died in hospital. Secondary cases, often identified through active case finding and contact tracing, more often present with mild or asymptomatic illness, and asymptomatic cases are on average younger (median age: 24 vs. 55 years among recent cases) than symptomatic cases. People with chronic comorbidities (e.g. diabetes, chronic lung or renal disease, immunodeficiency) remain at higher risk of severe infection.

b. SARS-like nosocomial amplification

The recent upswing in cases, with increase in healthcare worker reports, is largely driven by two large nosocomial outbreaks in Jeddah, Saudi Arabia, and Abu Dhabi, UAE, involving multiple health care facilities. Smaller nosocomial clusters have also been observed in other parts of Saudi Arabia, including Riyadh, Mecca, and Tabuk. However, ongoing reports of sporadic community-acquired index cases, mostly in people with underlying comorbidity, have also increased in certain regions, notably Riyadh, Saudi Arabia, since mid-March 2014.

More cases of MERS-CoV in healthcare workers (HCWs) have been reported during the month of April 2014 than previously reported since the start of the outbreak in April 2012. Among the ~100 healthcare workers affected to date, nearly two-thirds were reported in April 2014 alone.

While most nosocomial infections have been identified in HCWs, patients and visitors have also been affected. Despite the size of these nosocomial outbreaks and the large proportion of secondary cases, no sustained human-to-human transmission has yet been observed. This epidemiologic pattern is highly reminiscent of the SARS-CoV experience back in the spring of 2003, driven by amplification in some nosocomial settings but without sustained community spread.

c. Recent travel-related importations

Since our last update, a number of countries outside of the Arabian Peninsula have received imported cases, including Malaysia (1 case), the Philippines (1 case), Greece (1 case), and Egypt (1 case). So far, no human-to-human transmission or subsequent outbreaks have been reported in association with these latest importations, as was previously observed in a limited way among earlier affected countries receiving cases (e.g. France, United Kingdom, and Tunisia). Of note, at least two of these more recent travel-related cases (Jordan and Malaysia) were identified in persons following pilgrimage to Saudi Arabia.

Further export of cases to countries outside of the Arabian Peninsula may be anticipated. As a reminder, unrecognized importations, super-spreading events and transmission facilitated by aerosol-generating procedures in some hospital settings amplified SARS-CoV, culminating in large-scale nosocomial outbreaks in some areas in 2003. Although not yet reported, this remains a possibility also in association with MERS-CoV importation. Although travel between British Columbia and the Arabian Peninsula is less common than links to eastern China, clinicians should be aware of possible importations, take history for links to MERS-CoV affected areas from patients presenting with severe acute respiratory illness (SARI) and implement infection control precautions to protect themselves, other patients and their facilities from the risk of an outbreak (see below, **Action and Advice**).

d. Possible reasons for the sudden surge

There are a number of possible explanations for the recent upswing in cases in the Arabian Peninsula including, but not limited to, changes in screening protocols and enhanced surveillance with increased detection of mild or asymptomatic cases; infection prevention and control issues in heath care settings; and seasonality, possibly related to increased transmission in the animal reservoir (i.e. camels) at this time of year (see below).

The possibility of changes in the virus that promote more effective human-to-human transmission has also been raised. However, so far genetic sequencing of recent MERS-CoV isolates has revealed no significant mutations.

In a recent ProMED post, Dr. Christian Drosten of the University of Bonn in Germany, in partnership with the Saudi MOH, provides evidence that the virus has not substantially changed based on isolates collected in Jeddah, the site of ongoing nosocomial outbreaks this month. Full genome sequence results from three viral isolates obtained from two separate health care facilities were highly similar (albeit not identical), to each other and to a large number of published human MERS-CoV sequences, suggesting that the virus has not acquired genetic changes to explain the recent increase in cases. Partial sequences of spike protein genes from an additional 25 viruses were 100% identical to known sequences. For the full ProMED post, see: http://www.promedmail.org/direct.php?id=20140426.2432140. The analysis of additional sequences to corroborate these findings is awaited.

e. The camel connection

There is now a growing body of evidence to suggest that dromedary (single-humped) camels are the primary source of MERS-CoV infection and that they play an important role in the transmission to humans; however, in the absence of case-control studies to identify exposure risks, the route of direct or indirect transmission between camels and humans currently remains unknown.

The first evidence of dromedary camels being part of the transmission chain was the detection of high levels of antibodies against MERS-CoV in dromedary camels in Oman and the Canary Islands (Spain) [1]. Since that initial report, subsequent serological studies have provided evidence of MERS-CoV infection in camels across the Arabian Peninsula and in parts of Africa [2-9], with greater sero-prevalence identified in adult than juvenile camels [9]. Antibody cross-reactive to MERS-CoV has been detected in archived sera collected from dromedary camels in Saudi Arabia as far back as 1992 [9], suggesting that MERS-CoV or a closely-related virus has been circulating in camels for at least two decades. The reasons that MERS-CoV emerged in people in April 2012, but not prior, remain unknown. More recently, viral RNA has been detected in different specimens collected from camels with links to outbreaks of MERS-CoV in humans [10-11]. Phylogenetic analysis shows that camel viruses are highly similar to MERS-CoV sequences obtained from humans [7, 9-14], supporting the hypothesis that camels serve as a primary source of MERS-CoV infection in humans.

The detection of MERS-CoV in dromedary camels imported from Sudan and Ethiopia for slaughter in Egypt [7], as well as serologic evidence of previous MERS-CoV infection in dromedaries in Nigeria, Ethiopia and Tunisia [8], suggest that the virus could be geographically widespread in the dromedary camel population on the African continent, and that transmission to humans may occur outside of the Arabian Peninsula.

Per above, one possible explanation for the recent surge in cases is an increase in zoonotic transmission from this animal reservoir into human populations, corresponding to calving season and an increased pool of susceptible camels shedding virus in early spring. Coronaviruses are known to have a winter/spring seasonality and previous nosocomial outbreaks have been identified in spring months, including the first known case of the virus associated with a hospital cluster in Jordan in April 2012 and the largest prior nosocomial outbreak involving 23 confirmed cases in Al Hasa, Saudi Arabia, in April 2013.

For the latest WHO Risk Assessment (24 April 2014), see:
http://www.who.int/csr/disease/coronavirus_infections/MERS_CoV_RA_20140424.pdf.

For the latest ECDC Epidemiological Update on MERS-CoV (30 April 2014), see:
http://www.ecdc.europa.eu/en/press/news/_layouts/forms/News_DispForm.aspx?List=8db7286c-fe2d-476c-9133-18ff4cb1b568&ID=994

For the latest ECDC Rapid Risk Assessment on MERS-CoV (24 April 2014), see:
http://www.ecdc.europa.eu/en/publications/Publications/Middle-East-respiratory-syndrome-coronavirus-risk-assessment-25-April-2014.pdf.

For ongoing WHO MERS-CoV updates, see:
www.who.int/csr/disease/coronavirus_infections/en/index.html.

2. H7N9 UPDATE [Total: 432 cases; Deaths: 146+], China

Although the second wave H7N9 peak appears to have considerably subsided since January, ongoing avian influenza A(H7N9) activity continues in affected regions of China, with 19 additional cases and 25 deaths reported since our last bulletin to you on 7 April 2014. Further travel-related cases have been reported from Hong Kong and Taiwan (see attached **H7N9 Epidemic Curve**). To date, a total of 432 cases have been reported, including at least 146 deaths.

To stay current with ongoing developments, please consult the WHO avian influenza A(H7N9) page: www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html.

3. ACTION AND ADVICE [abbreviated]

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.

For diagnostic testing for suspected MERS-CoV or novel influenza viruses, 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. 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.

To review prior bulletins issued by the BCCDC Influenza & Emerging Respiratory Pathogens team, see: http://www.bccdc.ca/dis-cond/DiseaseStatsReports/EmergingRespiratoryVirusUpdates.htm.

Influenza & Emerging Respiratory Pathogens
BC Centre for Disease Control

4. REFERENCES [Camel Connection]:

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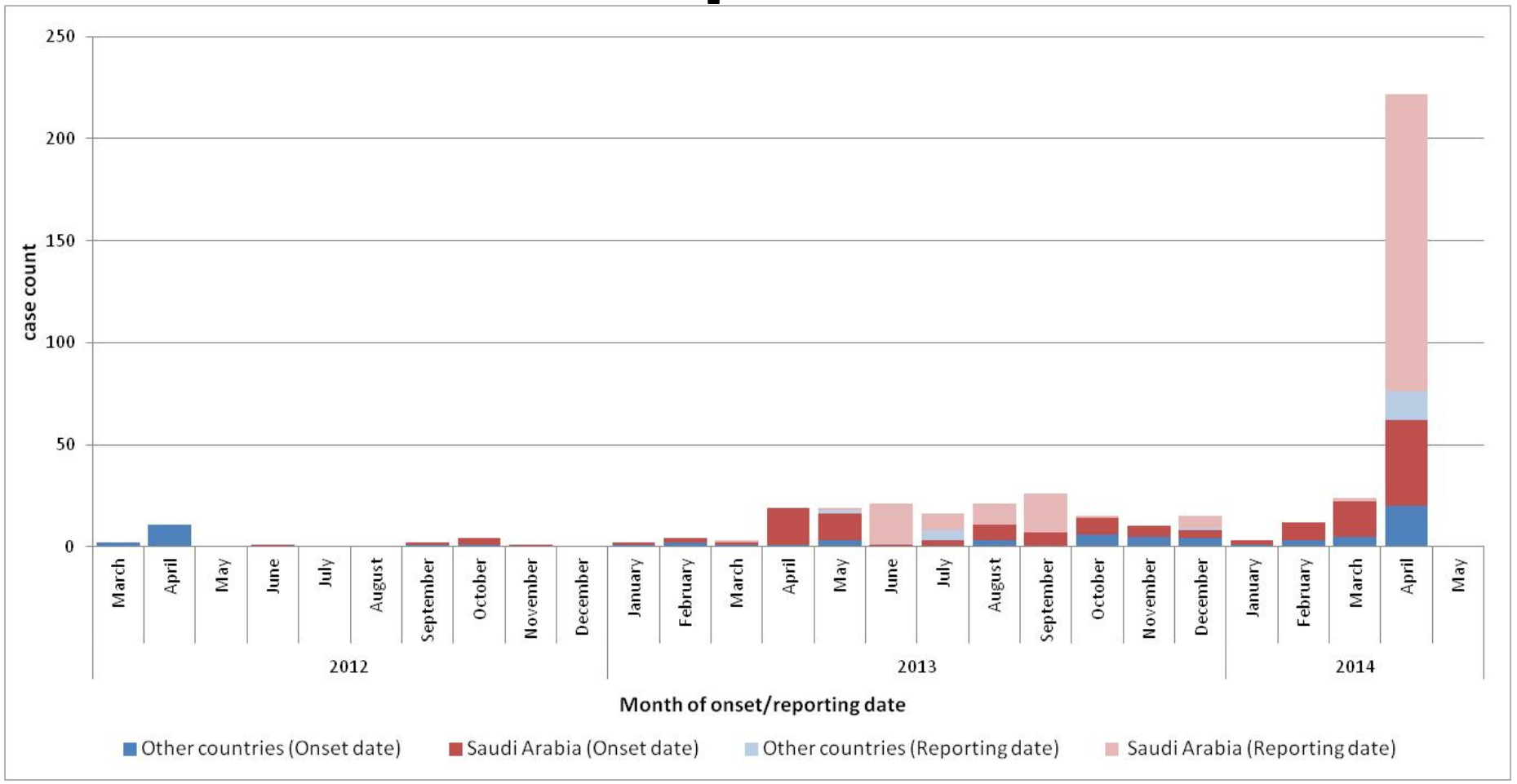
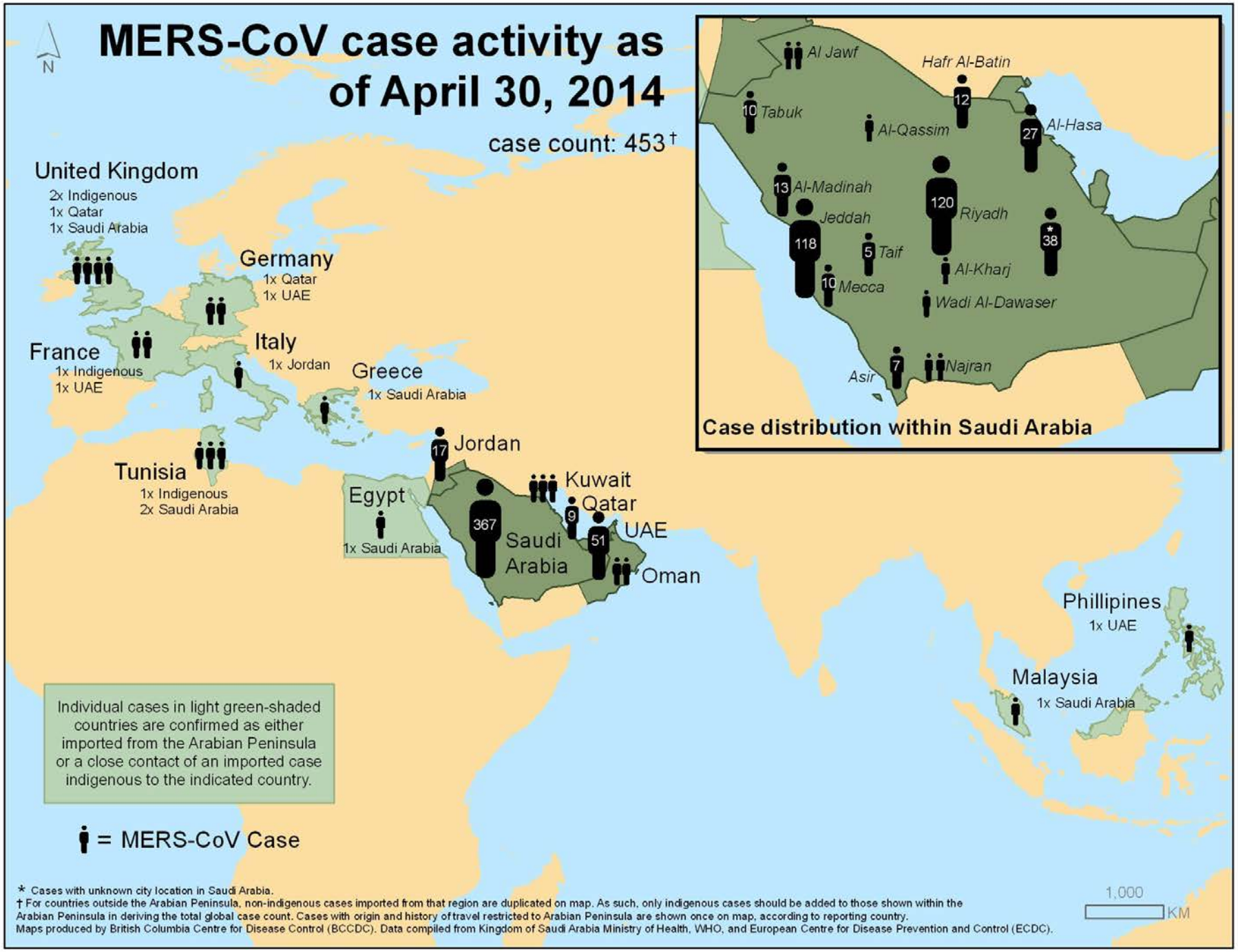
To review prior bulletins issued by the BCCDC Influenza & Emerging Respiratory Pathogens team, see: http://www.bccdc.ca/dis-cond/DiseaseStatsReports/EmergingRespiratoryVirusUpdates.htm.

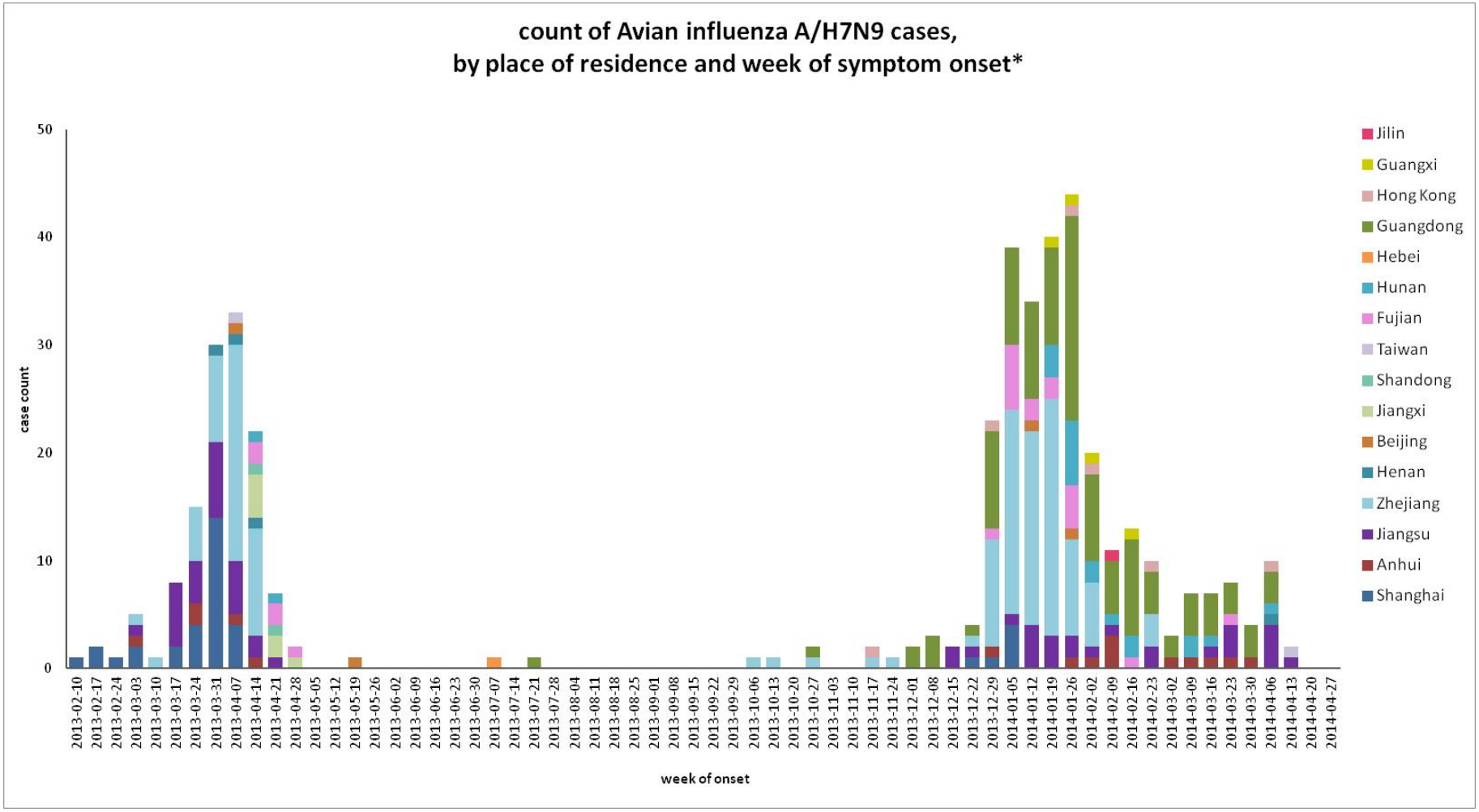
MERS-CoV Epidemic Curve*



*MERS-CoV cases plotted by most likely 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. Of the 236 cases shown by reporting date, 87 (37%) were asymptomatic.


MERS-CoV case activity as of April 30, 2014
case count: 453†
N
United Kingdom
2x Indigenous
1x Qatar
1x Saudi Arabia
Germany
1x Qatar
1x UAE
France
1x Indigenous
1x UAE
Italy
1x Jordan
Greece
1x Saudi Arabia
Tunisia
1x Indigenous
2x Saudi Arabia
Egypt
1x Saudi Arabia
17 Jordan
Kuwait
9 Qatar
51 UAE
367 Saudi Arabia
Oman
Phillipines
1x UAE
Malaysia
1x Saudi Arabia
Al Jawf
Hafr Al-Batin
12
10 Tabuk
Al-Qassim
27 Al-Hasa
13 Al-Madinah
120 Riyadh
Jeddah
118
5 Taif
38*
Al-Kharj
10 Mecca
Wadi Al-Dawaser
Asir
7
Najran
Case distribution within Saudi Arabia
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.
= MERS-CoV Case
* 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.
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).
1,000
KM

H7N9 Epidemic Curve



*Does not include: 1 Henan, 5 Jiangsu, 1 Guizhou and 1 Anhui cases with unknown onset date; one asymptomatic case in Beijing.