In this bulletin:

Dear colleagues –

In the context of recent detection of laboratory-confirmed avian influenza A(H7N9) in two British Columbia (BC) residents with relevant travel history, we would like to provide you with the following event description and situation report since our last Emerging Respiratory Virus (ERV) bulletin to you on November 5, 2014.

A. EVENT DESCRIPTION

The index case who had recently returned to Canada after travelling abroad was presumptively diagnosed with laboratory-confirmed influenza A(H7N9) infection at the BC Public Health Microbiology and Reference Laboratory (PHMRL) on January 23, 2015, confirmed by Canada's National Microbiology Laboratory (NML) on January 26. A second individual who travelled with the confirmed index case and resides in the same household has also been diagnosed with A(H7N9) infection, confirmed by the NML on January 29. These are the first documented cases of human infection with A(H7N9) imported to North America.

Both individuals are adults 50-60 years of age. Both cases developed influenza-like illness (ILI) after returning to Canada, but have now fully recovered. Neither case required hospitalization, and both were managed as outpatients. Due to common exposure histories abroad, the source of infection is likely the same for both (see details below).

These individuals traveled abroad on December 29, 2014 and returned to BC on January 12, 2015. During this period they traveled to Hong Kong, Taiwan and China. While in China, they recall seeing free-running chickens and droppings on one particular day, within one week prior to symptom onset, but did not have direct contact with poultry.

ILI onset was January 14 for the index patient who presented to a physician on January 15. A nasopharyngeal specimen was collected on January 15 and confirmed by PCR at the BC PHMRL on January 16 to be positive for influenza A. The patient was notified of this diagnosis on January 19 and prescribed a five-day course of oseltamivir.

Despite the low ct value (high virus titre), the influenza A virus collected from the index patient was non-subtypeable for human H1 or H3 at the BC PHMRL. Further sub-typing by PCR-based probes revealed H7 and subsequent sequencing of the matrix gene showed 99% homology with A(H7N9) and A(H9N2). Given that the subtyping probe targeted the haemagglutinin (H) gene, and given recent A(H7N9) detections in China that bear internal genes of A(H9N2), it was assumed likely to be A(H7N9). On that basis, the BC PHMRL reported a presumptive diagnosis of A(H7N9) in the index case on January 23, subsequently confirmed by Canada's NML on January 26.

The second case had ILI symptoms that started on January 13, one day earlier than the index case. This individual was seen at the physician's office on January 13 and an antibiotic was prescribed but no swab

was collected at that time. However, on January 19, this individual was treated speculatively with a five-day course of oseltamivir. No specimen was collected for diagnostic testing at that time either, but respiratory specimens were collected in follow-up investigation and have since also been confirmed positive for influenza A(H7N9) by Canada's NML on January 29. Paired sera are being collected from both the index and the second case.

Approximately 20 close contacts of these two individuals, including a health care worker, were identified and placed under ten-day surveillance by the local health authority. One contact felt unwell during the monitoring period but did not develop ILI and respiratory specimens collected from that individual, earlier treated with oseltamivir, have tested negative for influenza. Paired sera will also be assessed from the symptomatic contact.

B. GLOBAL SITUATION UPDATE

To date more than 500 cases of avian influenza A(H7N9) have been reported globally since first emergence of that virus in the human population in February 2013.

Since our last bulletin on November 5, 2014 and as of January 23, 2015, a third wave of at least 48 new human cases of avian influenza A(H7N9) has been evident in China, including:

- 18 in Guangdong,
- 6 in Fujian,
- 6 in Jiangsu
- 6 in Zhejiang provinces,
- 6 in Xinjiang Uyghur Autonomous Region (UAR) (the furthest northwest region of China),
- 3 in Shanghai,
- 1 in Jianxi
- 1 in Shandong, and
- 1 in Hong Kong (considered likely acquired in Shenzhen, Guangdong province)

See the attached A(H7N9) Epidemic Curve and Geographic Map of cases by wave, created by our team on January 23. This does not include at least another 16 cases identified over the past week alone, mostly from Guangdong, nor does it include the two Canadian cases.

The overall pattern of older male predominance among reported H7N9 cases has prevailed among recent reports (see attached Age/Sex Distribution overall). Among the 48 new cases since our last bulletin, ages range from 1.5 to 83 years (median age 54 years). Where details were given, most of the recent cases were listed in severe-to-critical condition in hospital; three middle-aged cases and four cases under the age of 10 were reported to be in mild-to-stable condition. Nine of the 48 cases were reported as fatal to date; of these, two were middle-aged and seven were over 65 years of age.

In its official tallies, the WHO has reported a total of 485 laboratory-confirmed cases of H7N9 and 185 deaths (case fatality of 38%) but this does not include recently reported cases. Based on information gathered from multiple reliable sources, we assess the current global tally to be at least 522 cases including 134 during the first wave spanning February to May 2013; two summer 2013 cases; 320 cases during last year's more substantial epidemic spanning October 2013 to September 2014 (peaking in January 2014); and a third wave we are categorizing from October 2014 that now includes at least 66 cases. Note that the WHO has not yet officially declared a third wave. We can anticipate further cases through the late winter and spring period as observed each year since 2013, although it is not yet evident whether the very large number of cases seen last winter will be repeated in the coming months of 2015.

To date overall, most cases have been identified in association with poultry contact, although multiple (at least 14) clusters of limited but likely human-to-human transmission in close contact settings (e.g. household/family members) have also been reported. Similarly, among the more recent case reports (where information was available), most were known to have had contact with live poultry.

C. SUMMARY AND ADVICE

Recently confirmed cases of A(H7N9) serve as important reminders that this avian influenza virus (and others) are still present in poultry in China. A(H7N9) is considered a low pathogenic avian influenza (LPAI) virus, meaning that clinical illness or outbreaks in poultry may not be apparent, making recognition in birds and control efforts through "stamping out" initiatives more difficult.

Avian influenza viruses show distinct winter-spring seasonality. Their circulation may increase in the coming weeks or months and may rarely be associated with illness in returning travelers. To further minimize this risk, travelers to China should be reminded to avoid high-risk areas such as poultry farms and live animal markets, or contact with birds including chickens, ducks and wild birds, their droppings or secretions. As always, poultry dishes, including eggs, should be well cooked before eating. Returning travelers seeking medical care for ILI within two weeks of their return from an affected area should notify the clinician upfront of their relevant travel and/or exposure history.

The finding of A(H7N9) in the two recently reported travelers returning from China to Canada with relatively mild ILI compared to other A(H7N9) cases underscores the spectrum of illness with which this virus may be associated, not only in children, as previously highlighted, but also in adults.

While a spectrum of illness is recognized for most infectious diseases, emerging zoonotic pathogens, newly adapting to the human host, are frequently associated with more severe clinical presentation and are more likely to be detected on that basis. A(H7N9) infection in people remains rare and the vast majority of ILI in returning travelers will be due to other causes. It is not possible to test, isolate and/or quarantine all individuals with mild ILI and links to affected areas. Surveillance protocols therefore continue to focus primarily on severe acute respiratory illness (SARI), while still allowing for clinician and public health judgment in assessing patients with milder presentations.

Accordingly, the following advice is provided but will be updated as needed based on evolving information and understanding:

In the event of 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 may also discuss with their local health authority/Medical Health Officer and consult a microbiologist at the BC PHMRL for guidance on diagnostic testing in patients with non-SARI presentations where the index of suspicion or exposure likelihood may be raised. Follow strict infection prevention and control guidelines when collecting respiratory specimens. In consultation with infection control, 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.

D. FURTHER INFORMATION

Public Health Agency of Canada, National interim case definition, avian influenza A(H7N9): http://www.phac-aspc.gc.ca/eri-ire/h7n9/case-definition-cas-eng.php

Government of Canada, travel health notice: http://travel.gc.ca/travelling/health-safety/travel-health-notices/h7n9-china

US Centers for Disease Control and Prevention, avian influenza A(H7N9) virus: http://www.cdc.gov/flu/avianflu/h7n9-virus.htm

For the latest WHO risk assessment on avian influenza A(H7N9) (October 2, 2014), see: www.who.int/influenza/human_animal_interface/influenza_h7n9/Risk_Assessment/en/.

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

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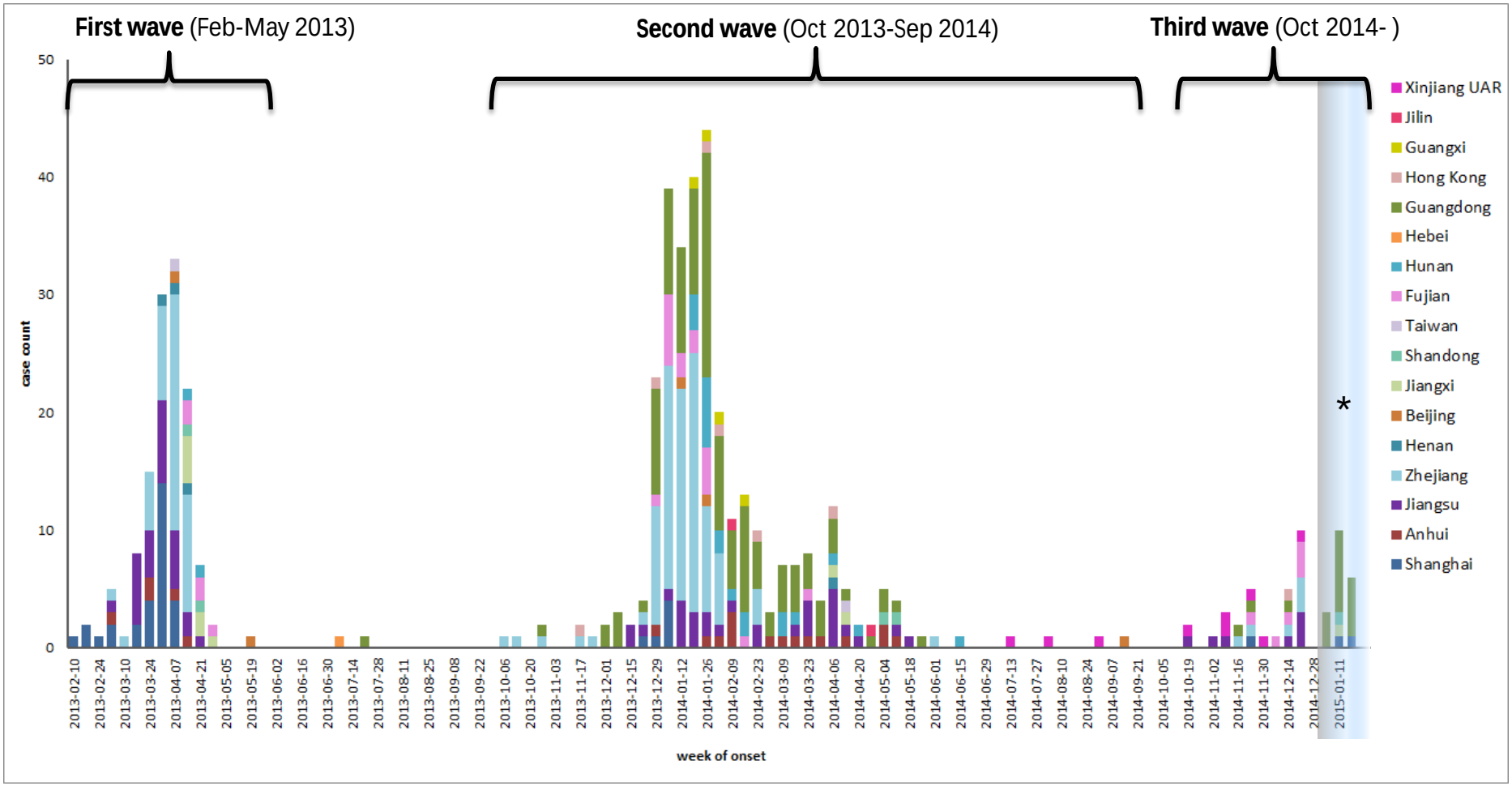
H7N9 Epidemic Curve

by place of residence and week of illness onset*



*Cases shown in January 2015 plotted by reporting date pending availability of onset date.
Does not include: 1 Henan, 4 Jiangsu, and 1 Guizhou cases with unknown onset date; one asymptomatic case in Beijing.

H7N9 avian influenza first, second and third wave cases by province of residence

Province	Cumulative # of cases
Anhui	20
Beijing	6
Fujian	28
Guangdong	*132
Guangxi	4
Guizhou	1
Hebei	*1
Henan	4
Hunan	23

Province	Cumulative # of cases
Jiangsu	67
Jiangxi	10
Jilin	2
Shandong	5
Shanghai	39
Xinjiang	9
Zhejiang	145
Hong Kong	7
Taiwan	2
Total	505

* Two cases with symptom onset in July 2013 (one in Hebei and one in Guangdong) are not assigned to a wave.

** Case was likely exposed in Zhejiang.

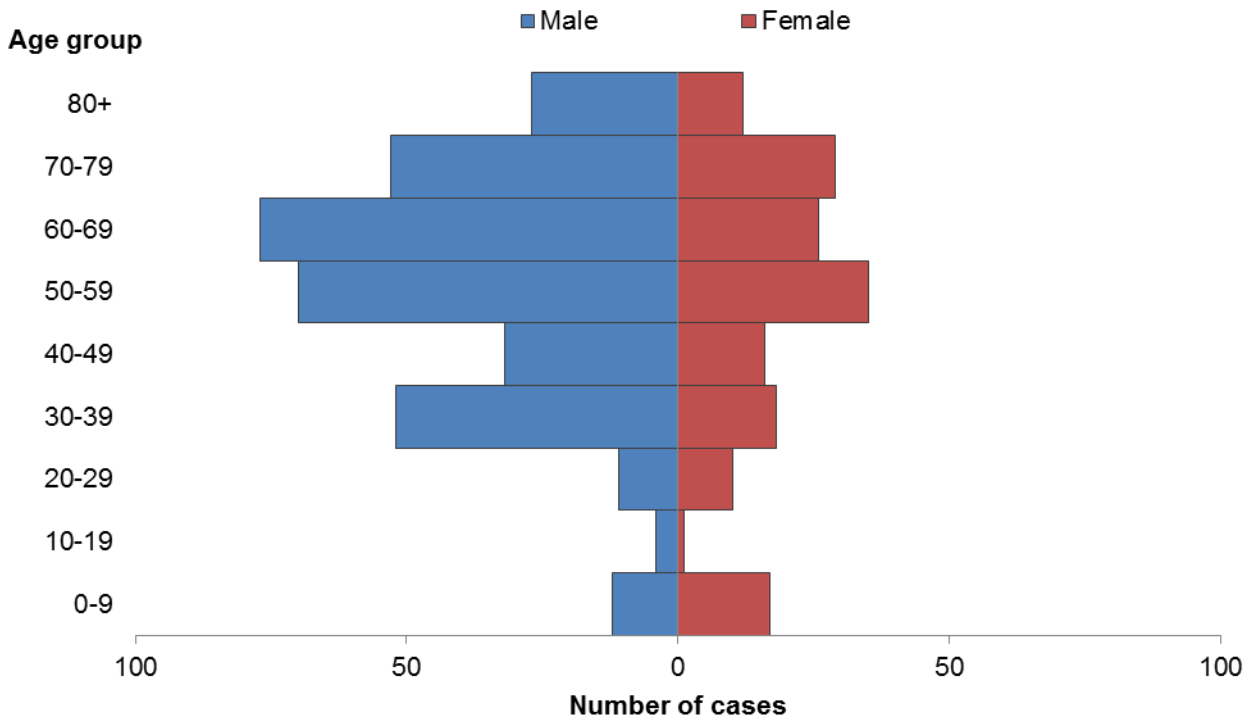
† Cases reported travel to mainland China during exposure period.

‡ 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 January 26th, 2015 by BCCDC.

Overall Age and Sex Distribution, H7N9

(N=502)*



* Three cases for whom age and/or sex are unknown are not shown.