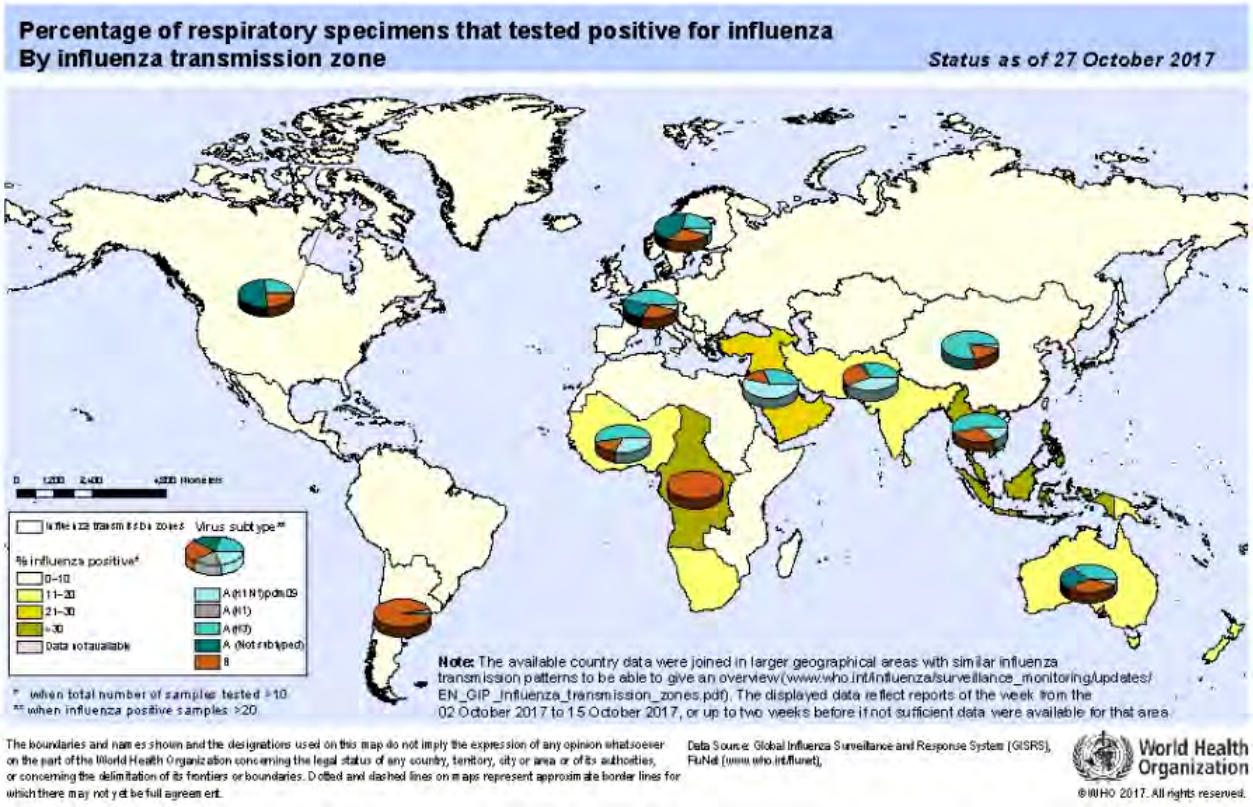
SANOFI PASTEUR

Influenza Global Epidemiologic Update

November 10th, 2017

1. GLOBAL WHO SUMMARY – based on data up to 15 October 2017



North America: Overall influenza virus activity remained low, with detections of predominantly influenza A(H3N2) and B viruses in the past few weeks. Respiratory illness indicators were below seasonal thresholds except in Mexico where ARI remained just above the alert threshold.

Europe: In Europe, influenza activity remained low, with detections of predominantly influenza A(H3N2) and B viruses in the past weeks.

Northern Africa: Little to no influenza virus detections was reported.

Western Asia: Influenza activity continued to increase in Oman, with influenza A(H1N1)pdm09 virus predominantly detected followed by a small proportion of A(H3N2) and B viruses.

Central Asia: In Central Asia, ILI and SARI indicators appeared to increase in Kazakhstan, Tajikistan and Uzbekistan, with few influenza detections.

Eastern Asia: In East Asia, influenza activity remained low.

2. VIROLOGICAL SURVEILLANCE AND STRAIN CHARACTERIZATION

WHO GISRS laboratories: from 02 October 2017 to 15 October 2017
The WHO GISRS laboratories tested more than 84217 specimens of which 4193 (4,9%) were positive for influenza viruses. 3269 (78%) were typed as influenza A and 924 (22%) as influenza B. Of the sub-typed influenza A viruses, 524 (20.6%) were influenza A(H1N1)pdm09 and 2022 (79.4%) were influenza A(H3N2). Of the characterized B viruses, 234 (71.8%) belonged to the B-Yamagata lineage and 92 (28.2%) to the B-Victoria lineage.

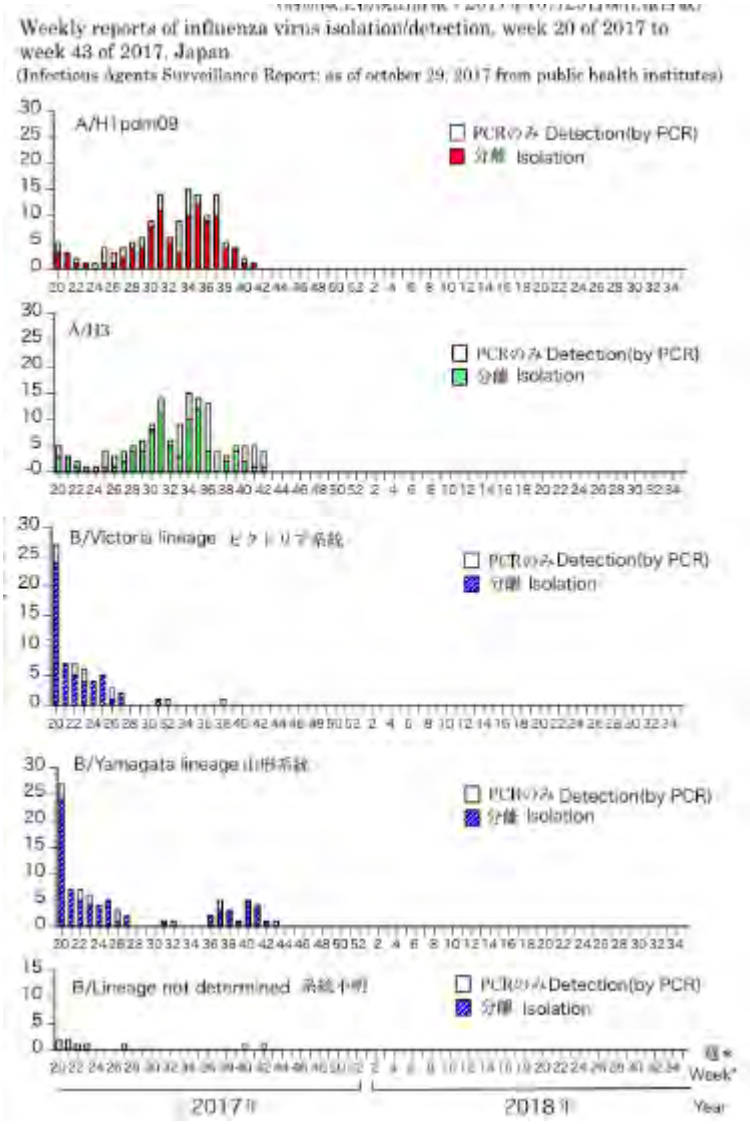
NB: The recommended components for the 2017-2018 Northern hemisphere Influenza vaccine includes:
an A/Michigan/45/2015 (H1N1)pdm09-like virus; an A/Hong Kong/4801/2014 (H3N2)-like virus; a B/Brisbane/60/2008-like virus (Vic Lineage). and a B/Phuket/3073/2013-like virus (Yam Lineage) in QIV vaccine.

EUROPE weeks: Week 40 to 44/2017
Since week 40/2017, few influenza viruses have been detected in sentinel and non-sentinel specimens.
Of the viruses subtyped or assigned to a lineage, for detections in both sentinel or non-sentinel surveillance systems, most were identified as A(H3N2) or B/Yamagata viruses.
For week 44/2017, no genetic characterizations were reported. The latest characterization data are summarised in the ECDC summary report for September.

US-CDC- Until Nov 4th,2017
Nationally, the percentage of respiratory specimens testing positive for influenza viruses in clinical laboratories during the week ending November 4 was 3.4%.
Regionally, the three week average percent of specimens testing positive for influenza in clinical laboratories ranged from 0.5% to 6.1%.
During the week ending November 4, of the 529 (3.4%) influenza-positive tests reported to CDC by clinical laboratories, 381 (72.0%) were influenza A viruses and 148 (28.0%) were influenza B viruses.
The most frequently identified influenza virus type reported by public health laboratories was influenza A virus.
During the week ending November 4, 108 (80.6%) of the 134 influenza-positive tests reported to CDC by public health laboratories were influenza A viruses and 26 (19.4%) were influenza B viruses. Of the 101 influenza A viruses that were subtyped, 91 (90.1%) were H3N2 viruses and 10 (9.9%) were (H1N1)pdm09 viruses.
The majority of the influenza viruses collected from the United States during May 21 through October 28, 2017 were characterized antigenically and genetically as being similar to the cell-grown reference viruses representing the 2017–18 Northern Hemisphere influenza vaccine viruses.

HPA-London until Week 44
35 influenza viruses have been detected since late summer. Of the 7 A(H1N1)pdm09 influenza viruses that have been characterised, all belong in the genetic subgroup 6B.1, which was the predominant genetic subgroup in the 2016/17 season. The two viruses antigenically analysed are similar to the A/Michigan/45/2015 Northern Hemisphere 2017/18 (H1N1)pdm09 vaccine strain.
Genetic characterisation of 20 A(H3N2) influenza viruses detected since late summer, showed that they all belong to genetic subclade 3C.2a, with 12 belonging to a cluster within this genetic subclade designated as 3C.2a1. (vaccine strain A/HongKong/4801/2014 belongs in genetic subclade 3C.2a).
Eight influenza B viruses have been analysed; 6 characterised as belonging to the B/Yamagata/16/88-lineage and 2 belonging to the B/Victoria/2/1987-lineage. Of 6 influenza B viruses antigenically characterised, two B/Victoria/2/87-lineage viruses were antigenically similar to B/Brisbane/60/2008, the influenza B/Victoria-lineage component of 2017/18 Northern Hemisphere TIV and QIV. 4 B/Yamagata/16/88-lineage viruses were antigenically similar to B/Phuket/3073/2013, the influenza B/Yamagata-lineage component of 2016/17 Northern Hemisphere QIV.

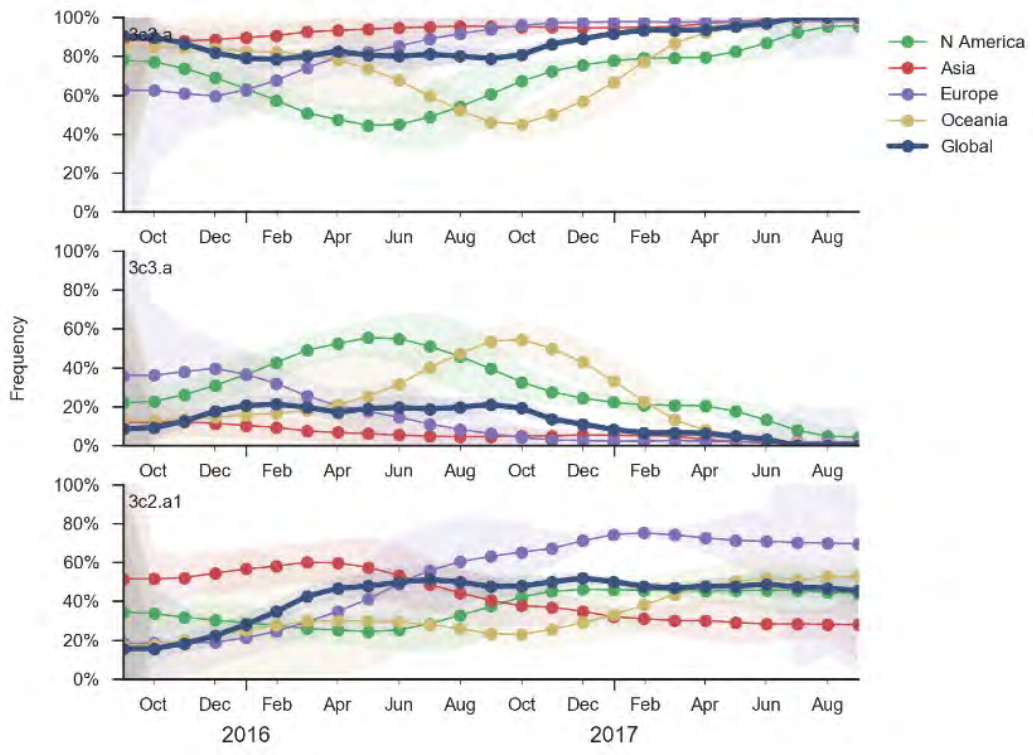
JAPAN National infectious dieseases- Week 43



3. Real-time tracking of influenza virus evolution

Next-Flu (Sept 19th 2017 report) Neher RA, Bedford T. 2015. nextflu: real-time tracking of seasonal influenza virus evolution in humans. Bioinformatics DOI: 10.1093/bioinformatics/btv381.

H3N2 continues to diversify with many coexisting clades, all of which carry several amino acid mutations at previously characterized epitopes sites. The majority of viruses fall into the 3c2.a clade which has been dominating globally for >3 years, but 3c3.a viruses continue to persist. The common ancestor of circulating H3N2 viruses is now more than 5 years old, which is rare for H3N2. Despite extensive genetic diversity, serological assays suggest limited, but non-zero, antigenic evolution. We expect multiple competing clades within 3c2.a to persist into the future with no clear immediate winner.



A/H1N1pdm: A clade comprising mutations S74R and I295V has risen to >60% global frequency. Although it shows no antigenic distinction by ferret HI data, the rapidity of its rise suggests a selective origin.

B/Vic

A clade with a two amino acid deletion 162-/163- has altered serological properties and is increasing in frequency, albeit slowly. Two other clades (carrying mutations K209N and V87A/I175V) have increased in frequency moderately.

B/Yam

A clade comprising M251V within clade 3 viruses continues to dominate. This is little genetic differentiation within this clade and no evidence of antigenic evolution.

4. MORE DATA FROM REGIONAL OR COUNTRIES SURVEILLANCE

Canada Government, FluWatch Report http://healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/flu-grippe/surveillance/fluwatch-reports-rapports-surveillance-influenza-eng.php

China Chinese National Influenza Center – Influenza Weekly Report- Week http://www.cnic.org.cn/

Europe ECDC/ WHO Europe Weekly Influenza update – http://flunewseurope.org/

Hong Kong Centre for Health Protection- Flux Express Surveillance Report http://www.chp.gov.hk/en/guideline1_year/134/441/304.html

PAHO Regional Update: http://www.paho.org/hq/index.php?option=com_content&view=article&id=3352&Itemid=2469&to=2246&lang=es

Russian Federation WHO NIC at Research Institute of Influenza and D.I Ivanovsky Institute of Virology, Integrated data of influenza morbidity and diagnosis http://www.influenza.spb.ru/en/influenza_surveillance_system_in_russia/epidemic_situation/

Singapore Ministry of Health – weekly infectious disease bulletin https://www.moh.gov.sg/content/moh_web/home/statistics/infectiousDiseasesStatistics/weekly_infectiousdiseasesbulletin.html

Unites States Of America Centers for Disease Control and Prevention, Weekly U.S. Influenza Surveillance Report http://www.cdc.gov/flu/weekly/