Influenza Updates

The newsletter of the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne

@WHOCCFluMelb

Volume 7, Issue 3, December 2018

Reflection on 2018: thank you and happy holidays

As 2018 draws to a close we would like express our sincere thanks to all the laboratories who sent us influenza samples during the past year. While it was somewhat quieter compared with recent years, we still received more than 3400 samples during 2018. We were also pleased to be involved in several training activities both at the Centre and in regional laboratories this year. We wish you all the best for the holiday season and look forward to working with you again in 2019.

WHO Shipping Fund Project reminder

In anticipation of the WHO Consultation on the Composition of Influenza Vaccines for the Northern Hemisphere 2019-2020, which will be held in February 2019, this is a reminder that the WHO Shipping Fund Project (SFP) is available to assist National Influenza Centres in shipping samples to WHO Collaborating Centres up to four times per year. The recommended timing of these shipments is: one between the end of December to mid-January and one between the end of June and mid-August, to support the WHO vaccine composition recommendation-making for each hemisphere; the third and fourth shipments can be used at your own judgement, which may depend on the seasonality, intensity of the season, the finding of unusual or untypable viruses, or notable outbreaks.

We encourage you to send samples in a timely manner as soon as possible after collection. Please avoid sending your samples in large batches collected over long periods, as up-to-date data for the current season are the most useful for WHO GISRS surveillance and vaccine formulation. If you have any questions about shipping samples or would like information about accessing the WHO Shipping Fund, please contact us at *whoflu@influenzacentre.org*.

Baloxavir marboxil approved for treatment of influenza in Japan and USA

The novel antiviral drug baloxavir marboxil (Xofluza®) has now received regulatory approval for use in the treatment of influenza in two countries - Japan and the USA. The recent approval in October 2018 by the U.S. Food and Drug Administration (FDA) follows approval which was granted by the Japanese Ministry of Health, Labour and Welfare in February 2018.

Baloxavir acts by inhibiting the PA endonuclease of influenza A and B viruses, thereby preventing viral replication in host cells. This is the first time in almost 20 years that the FDA has approved an antiviral drug with a novel mechanism for combatting influenza. During clinical trials, viruses with reduced susceptibility to baloxavir were detected in treated patients, but the potential for these viruses to spread from treated individuals to others in the community is currently unknown. Therefore, as part of our antiviral drug resistance surveillance program, our Centre has now developed an assay to detect and monitor circulating influenza viruses with reduced baloxavir sensitivity, and will commence testing of selected viruses in 2019.

Recent meetings attended by Centre staff

Asian-Pacific Centenary Spanish 1918-Flu Symposium, Shenzhen, China

The Centre's Deputy Director Prof Ian Barr attended and spoke at this two day meeting on 1–2 November 2018. The meeting bought together approximately 200 scientists from around the world to discuss the Spanish Influenza Pandemic of 1918–9 and the events and control measures that have eventuated since this event.

The meeting also saw the launch of World Flu Day which will be recognised on 1 November each year. This initiative was endorsed by the meeting attendees and also by the current Director General of WHO Dr Tedros Adhanom Ghebreyesus.

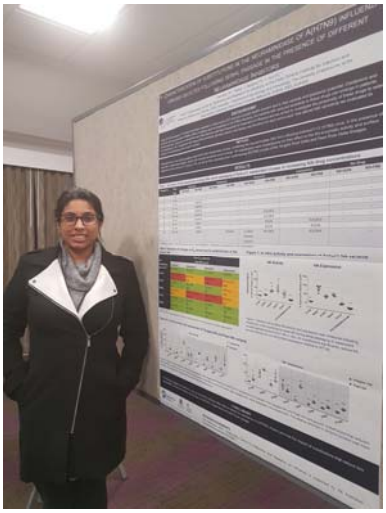
Third Regional Forum of WHO Collaborating Centres in the Western Pacific, Ho Chi Minh City, Vietnam

Prof Ian Barr attended the Forum which was held on 22–23 November 2018 and attended by 240 people from 149 of the 192 Collaborating Centres in the WHO Western Pacific Region (WPR). There is rich diversity of WHO Collaborating Centres in the WPR with 14% of them focussed on Communicable Diseases. The two-day day meeting focussed on improving the contributions that WHO Collaborating Centres can make at the country level.

For more details see
http://www.wpro.who.int/whocc_forum/highlights/

6th ISIRV-Antiviral Group Conference: Advances in Respiratory Virus Therapeutics, Washington DC, USA

A/Prof Aeron Hurt and Ms Rubaiyea Farukee from the Centre attended and presented talks and a poster at this conference, held 13–15 November 2018. The conference, which was attended by approximately 200 registrants, addressed both pre-clinical and clinical advances in therapeutic and prophylactic agents for influenza, RSV and other respiratory viruses and regulatory issues central to advancing such agents to clinical practice.



Recent activity at the Centre (1 October — 30 November 2018)

Below is a summary of surveillance activities at the Centre from 1 October to 30 November. With the end of the Southern Hemisphere influenza season overall we have received relatively fewer samples in recent months.

Samples received

The Centre received 813 influenza samples from the laboratories and institutions listed below:

AUSTRALIA: Westmead Hospital, John Hunter Hospital, The Children's Hospital at Westmead, Royal Darwin Hospital, Queensland Health Forensic and Scientific Services, SA Pathology, Australian Clinical Labs, Royal Children's Hospital, Alfred Hospital, Dorevitch Pathology, Monash Medical Centre, Hobart Pathology, Royal Hobart Hospital, Royal Melbourne Hospital, VIDRL, Pathwest QE II Medical Centre

BRUNEI: RIPAS Hospital

NEW ZEALAND: Canterbury Health Laboratories

Isolation of viruses in eggs

The Centre undertakes primary isolation of selected viruses in eggs to obtain potential vaccine strains. From 1 October to 30 November 2018, 4 A(H1N1)pdm09 viruses were successfully isolated in eggs at the Centre.

	Antigenic analysis: A total of 459 influenza isolates were analysed by HI assay.					**Genetic analysis:** Sequencing was performed on 54 HA, 52 NA, 41 MP and 5 NS genes from 54 viruses by Sanger sequencing or Next Generation Sequencing (NGS) techniques.				**Neuraminidase inhibitor susceptibility:** A total of 1032 influenza isolates were tested by neuraminidase inhibition (NAI) assay for susceptibility to oseltamivir, zanamivir, peramivir and laninamivr.					
Country of submitting laboratory	**No. of viruses analysed by HI assay***					**No. of viruses sequenced by NGS or Sanger sequencing**				**No. of viruses tested by NAI assay***					
	A(H1N1) pdm09	A(H3N2)	A (mixed subtype)	B/Victoria	B/Yamagata	A(H1N1) pdm09	A(H3N2)	B/Victoria	B/Yamagata	A(H1N1)pdm09	A(H3N2)	A (mixed subtype)	A (unsubtyped)	B/Victoria	B/Yamagata
Australia	258	72		1	32	23	15	1	5	402	160	1	2	3	88
Brunei		1								7	1				
Fiji											4				12
Malaysia	16	8			5	1	1			33	53	1		1	9
New Caledonia								1		8	2			5	20
New Zealand	15	3			3					36	5				27
Philippines		1								5	30				
Singapore										4	8				
South Africa										7					
Sri Lanka										7	7			2	2
Thailand										5	16				13
Timor-Leste	5	2	1	32	4	1		6		5	3	2		32	4
TOTAL	**294**	**87**	**1**	**33**	**44**	**25**	**16**	**8**	**5**	**519**	**289**	**4**	**2**	**43**	**175**

* *Subtypes and lineages are based on analysis of HA and in some cases confirmed by genetic analysis of NA.*

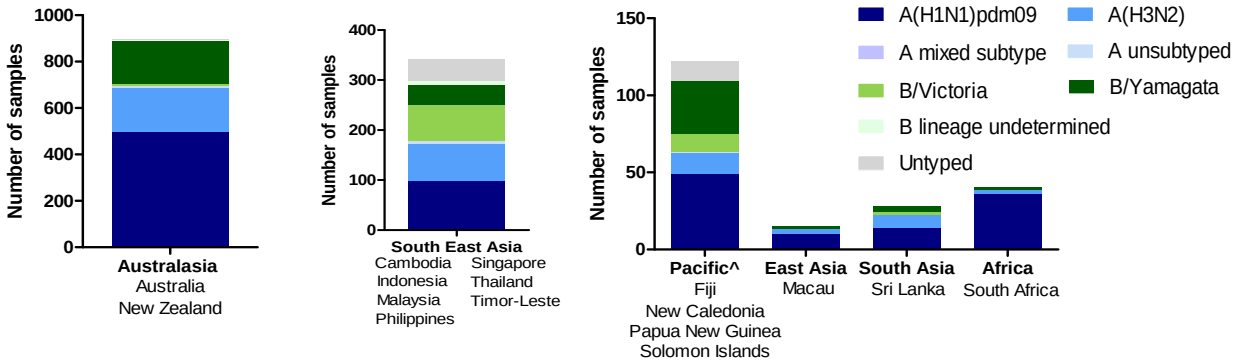
Surveillance update: Virus activity 1 January—30 November 2018

The data below are results for viruses collected between 1 January and 30 November 2018 that have been analysed at the Centre as of 4 December 2018.

Virus types/subtypes*

The type and subtype/lineage of 2154 viruses have been determined. Of viruses analysed to date, the largest proportion have been A(H1N1)pdm09 (52.9%), followed by A(H3N2) (19.4%) and B/Yamagata viruses (14.3%).

Samples collected 1 January—30 November 2018 and analysed at the Centre, by geographical region of submitting laboratory:



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Neuraminidase inhibitor susceptibility

Viral isolates are routinely tested for their susceptibility to the antiviral drugs oseltamivir (Tamiflu), zanamivir (Relenza), peramivir and laninamivir using the neuraminidase inhibition (NAI) assay. Viruses with reduced inhibition by antiviral drugs in the NAI assay undergo genetic analysis of the neuraminidase gene to detect mutations associated with the functional change.

Of 1530 viruses tested, two A(H1N1)pdm09 viruses from Singapore showed highly reduced inhibition to oseltamivir and peramivr. Genetic analysis of both viruses showed that they contained the H275Y mutation which reduces inhibition of these viruses by oseltamivir and peramivir. The relationship between reduced inhibition and the clinical effectiveness of a neuraminidase inhibitor is not well understood. Further studies would be required to determine whether a virus with reduced inhibition in the NAI assay is clinically resistant.

		Oseltamivir		Peramivir		Laninamivir		Zanamivir	
Type/Subtype*	No. tested	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition	Reduced inhibition	Highly reduced inhibition
A(H1N1)pdm09	851	-	2 (0.2%)	-	2 (0.2%)	-	-	-	-
A(H3N2)	338	2 (0.6%)	-	1 (0.3%)	-	1 (0.3%)	-	2 (0.6%)	-
A (mixed subtype)	3	-	-	-	-	-	-	-	-
B/Victoria	69	-	-	-	-	-	-	-	-
B/Yamagata	269	1 (0.4%)	-	1 (0.4%)	-	-	-	-	-
TOTAL	**1530**	**3 (0.2%)**	**2 (0.13%)**	**2 (0.13%)**	**2 (0.13%)**	**1 (0.07%)**	**0**	**2 (0.13%)**	**0**

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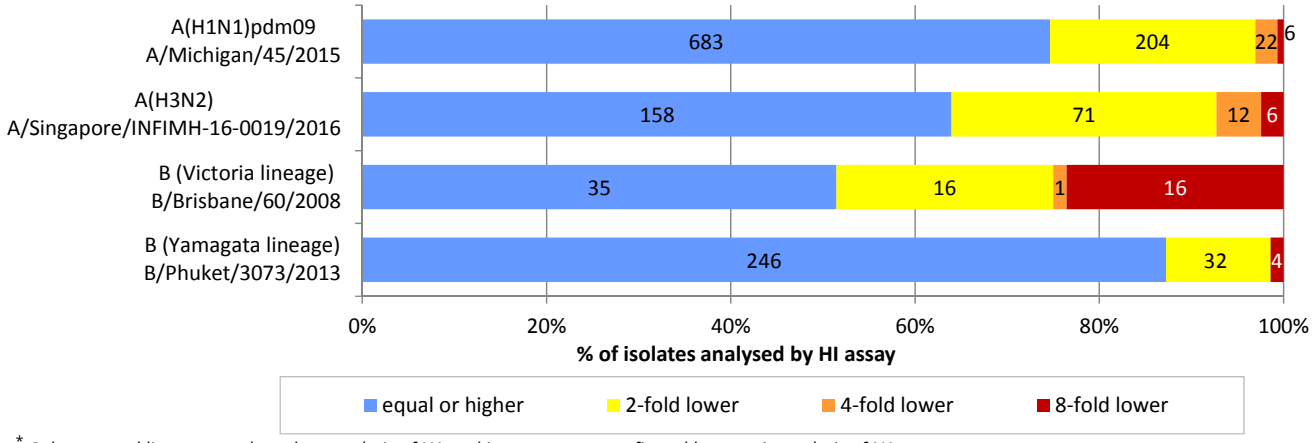
Antigenic analysis*

Haemagglutination inhibition (HI) assays indicate that the vast majority of A(H1N1)pdm09, A(H3N2) and B/Yamagata isolates tested were antigenically similar to the 2018 Southern Hemisphere vaccine strains. Approximately 23% of A/Victoria isolates had a titre 8-fold lower compared to the cell-propagated reference virus A/Brisbane/60/2008.



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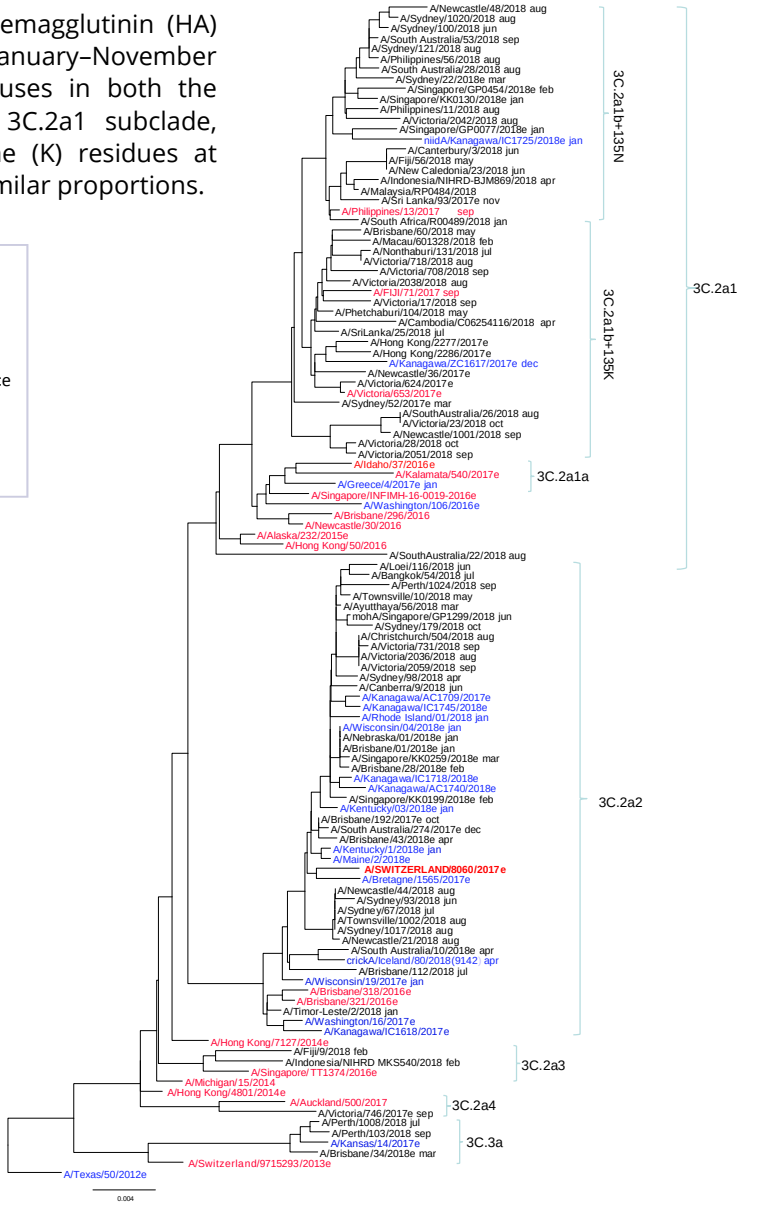
Genetic Analysis: Focus on A(H3N2)

Sequencing and phylogenetic analysis of haemagglutinin (HA) genes from A(H3N2) viruses collected during January–November 2018 shows continued co-circulation of viruses in both the 3C.2a1 and 3C.2a2 subclades. Within the 3C.2a1 subclade, viruses containing asparagine (N) and lysine (K) residues at position 135 have been detected in roughly similar proportions.

Legend
2019 SOUTHERN HEMISPHERE VACCINE STRAIN
Reference virus
Viruses received by other WHO Collaborating Centres
e: egg isolate
Scale bar represents 0.4% nucleotide sequence difference between viruses.
| Vertical lines indicate clades



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