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Influenza Risk Assessment Tool (IRAT) - Virus Report

Prepared by the CDC Influenza Division

North American Influenza A(H3N2) variant virus

Virus Strain: A/Ohio/13/2017 A(H3N2)v lineage 2010.1

Date of Evaluation: July 2019

Introduction

Novel human infections with influenza A viruses that commonly circulate in animals are rare and the risk of such infections overall to humans is generally low. Sporadic novel human infections with animal influenza A viruses do occur, but typically in situations where individuals are exposed to infected animals through direct or close contact or exposed to their virus contaminated environment. The Influenza Risk Assessment Tool (IRAT) is used to examine multiple attributes of influenza A viruses that have emerged yet have not gained the ability to spread among humans, and to assess the potential of these viruses to acquire this ability and the consequent potential public health impact.

Situation

In July and August 2016, 18 human infections of influenza A(H3N2) variant [A(H3N2)v] virus were identified in the U.S. in Michigan and Ohio. All 18 cases involved exposure to swine at agricultural fairs prior to onset of illness and swine at these fairs were found infected with swine influenza A(H3N2) virus [1]. Full genome sequence analysis of the viruses from these cases revealed that all possessed a human-like hemagglutinin (HA) likely derived from seasonal human A(H3N2) influenza virus from 2010. In 2017, sixty-two human infections with influenza A(H3N2)v virus were reported from nine different states and were closely related to the viruses detected in human infections in 2016 [2, 3].

In July 2019, the CDC assessed the pandemic potential of a representative strain of A(H3N2)v virus, 2010.1 lineage using the IRAT.

IRAT Evaluation

Influenza subject matter experts (SMEs) from the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Animal and Plant Health Inspection Service (APHIS), and Agricultural Research Service (ARS) were asked to evaluate influenza A(H3N2) virus strain A/Ohio/13/2017 lineage 2010.1 using ten risk elements defined in the IRAT. Each SME scored 1 to 3 elements based on their particular areas of expertise. The point estimate scores for each risk element were averaged, multiplied by predetermined weights, and summed to give an aggregate score for each of the two IRAT risk questions related to potential risk for emergence in humans and potential public health impact if the virus gained the ability to spread efficiently human to human [4].

The summary average risk score for influenza A/Ohio/13/2017 was 6.6 for the virus to achieve sustained human-to-human transmission (Table 1), placing the virus in the moderate risk category. The average risk score for the virus to significantly impact public health if it were to achieve sustained human-to-human transmission was 5.8 (Table 2) also in the moderate risk range. Overall, the virus is categorized in the moderate risk range.

Variability was seen among SME point estimate scores in the risk elements of Genomic Variation and Global Distribution in Animals. The greatest variation was seen in the scores for Genomic Variation where the range of scores spanned from a low to high risk range indicating some differences in interpretation of the available data. A sensitivity analysis using the lowest and highest scores received for Genomic Variation from SMEs resulted in an adjusted range of 6.3 - 6.6 for the overall emergence risk and 5.7 – 5.9 for potential impact, indicating that the categorization of A/Ohio/13/2017 as moderate risk is unchanged by the range of Genomic Variation scores. Similarly, a sensitivity analysis using the lowest and highest scores received for Global Distribution from SMEs resulted in an adjusted range of 6.5 - 6.6 for the overall emergence risk and 5.8 – 5.9 for potential impact, indicating that the categorization of A/Ohio/13/2017 as moderate risk is unchanged by the range of Global Distribution scores.

Table 1: Estimated Risk of Emergence

Risk Element	Weight (W)	Risk Score (RS)	W X RS
Human Infections	0.2929	5.0	1.5
Transmission in Lab Animals	0.1929	7.0	1.4
Receptor Binding	0.1429	9.3	1.3
Population Immunity	0.1096	6.0	0.7
Infections in Animals	0.0846	7.8	0.7
Genomic Analysis	0.0646	7.0	0.5
Antigenic Relatedness	0.0479	5.3	0.3
Global Distribution in Animals	0.0336	6.7	0.2
Disease Severity & Pathogenesis	0.0211	5.5	0.1
Antiviral/Treatment Options	0.0100	4.8	0.0
Total			6.6

Table 2: Estimated Potential Public Health Impact Risk

Risk Element	Weight (W)	Risk Score (RS)	W X RS
Disease Severity & Pathogenesis	0.2929	5.5	1.6
Population Immunity	0.1929	6.0	1.2
Human Infections	0.1429	5.0	0.7
Antiviral/Treatment Options	0.1096	4.8	0.5
Antigenic Relatedness	0.0846	5.3	0.5
Receptor Binding	0.0646	9.3	0.6
Genomic Analysis	0.0479	7.0	0.3
Transmission in Lab Animals	0.0336	7.0	0.2
Global Distribution in Animals	0.0211	6.7	0.1
Infections in Animals	0.0100	7.8	0.1
Total			5.8

Individual Risk Element Summaries

Human Infections: Sporadic human cases and presumed limited, non-sustained human-to-human transmission met the definition of moderate risk for this element.

Transmission in Laboratory Animals: In ferret studies, the virus transmitted well by direct contact between animals, but did not transmit consistently by respiratory droplets, suggesting moderate risk to humans for this element.

Receptor Binding: The HA is originally derived from human virus and glycan microarray data with recombinant HA illustrates strong α2-6 binding profile, characteristic of viruses that transmit in humans.

Population Immunity: Some data with adult and pediatric sera post vaccination suggests some cross-reactivity to this virus in adults, but very little in children.

Infections in Animals: Endemicity of influenza A(H3N2) virus is established in domestic swine which is a species in close contact with humans. Sustained transmission is not known in other species. This virus meets the criteria for high risk for this element.

Genomic Analysis: High divergence in gene segments, especially HA, from known host-adapted animal viruses of low risk. The virus is a reassortant containing viral RNA derived from swine, human, and avian sources. The HA is derived from previous human seasonal viruses, but also has diverged considerably.

Antigenic Relatedness: This virus showed a lack of antigenic relatedness to seasonal human vaccines but was well inhibited in hemagglutination inhibition testing with candidate vaccine viruses.

Global Distribution in Animals: Influenza A(H3N2) virus is endemic in swine in the U.S. Full extent of the 2010.1 lineage in swine is not known, but the proportion of A(H3N2) viruses with human-like H3 HA increased within U.S. commercial swine herds in 2016 to 46% [5].

Disease Severity & Pathogenesis: Generally uncomplicated disease, few hospitalizations, and no deaths reported. Moderate illness observed in a ferret study.

Antivirals and Treatment Options: The matrix protein 2 (M2) has a S31N substitution, a marker of M2 blocker resistance. The neuraminidase (NA) and polymerase acidic (PA) protein sequences do not have known or suspected markers of resistance to NA inhibitors and baloxavir PA endonuclease inhibitor. The virus was qualified as sensitive using the high-content imaging neutralization (HINT) assay [6].

Comparison to other Viruses Scored with IRAT

The scores for the emergence risk and potential public health impact for the A/Ohio/13/2017 virus were plotted along with a selection of other influenza viruses scored using the IRAT (Figure 1). The A/Ohio/13/2017 virus falls in the moderate risk range for both risk of emergence and potential impact. The risk of emergence score is essentially equivalent to the highest ranked virus evaluated to date with the IRAT, Asian lineage influenza A(H7N9) virus, but has a lower score for potential impact.

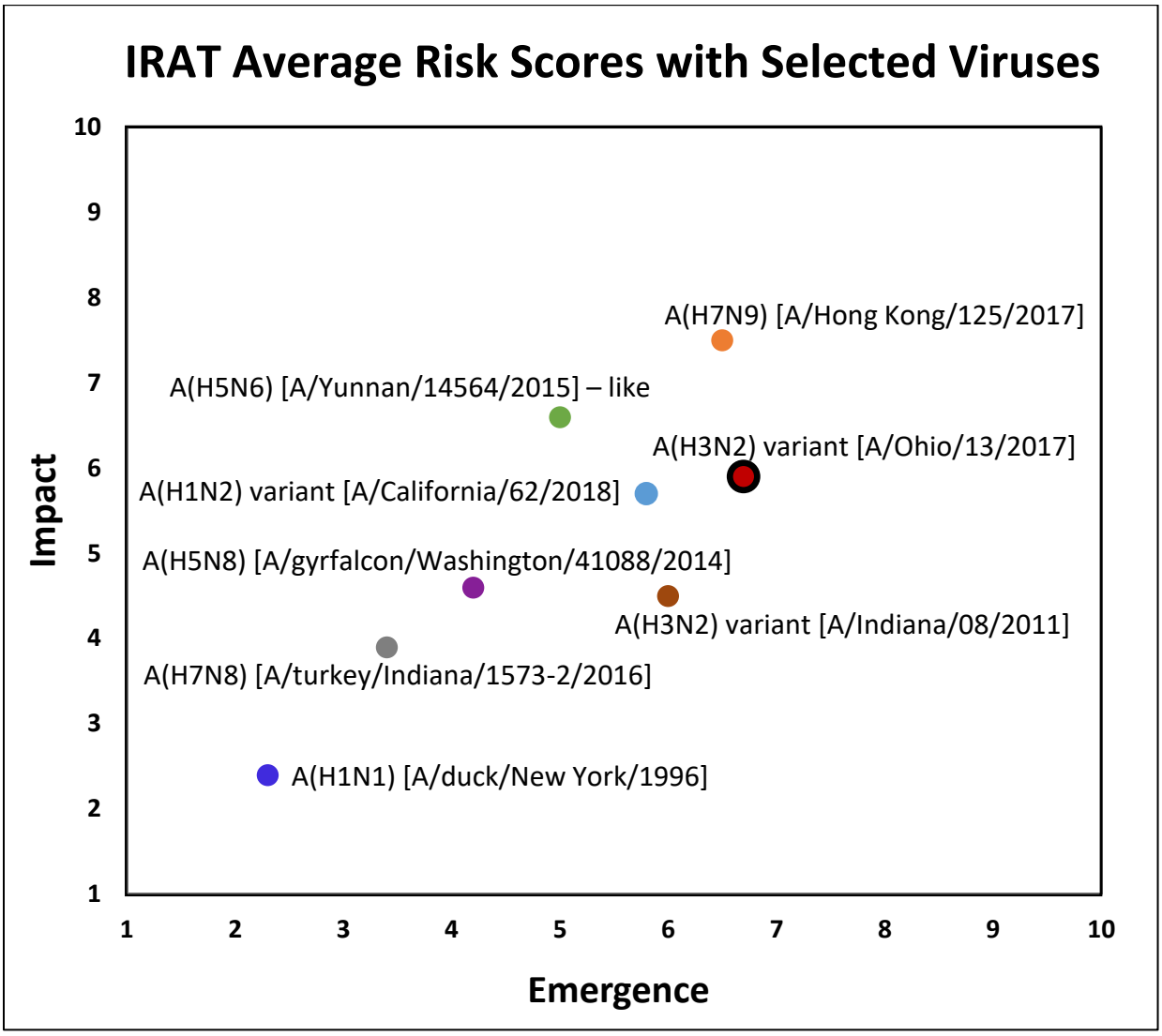

Figure 1: Average IRAT scores for A/Ohio/13/2017 plotted by emergence score and impact score. Additional viruses scored using IRAT are displayed for comparison.

Note: IRAT results were generated using information and data known to influenza subject matter experts at the time of the evaluation. Subsequent findings may raise or lower the overall risk scores associated with the virus.

References

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