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Influenza Risk Assessment Tool (IRAT) - Virus Report

Prepared by the CDC Influenza Division

Influenza A(H9N2) virus

Virus Strain: A/Anhui-Lujiang/39/2018 A(H9N2) lineage Y280

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

Low pathogenicity avian influenza A(H9N2) viruses are enzootic in poultry in many countries in Africa, Asia, the Middle East, and Europe. Since the late 1990s when the first human cases of infection with influenza A(H9N2) virus were identified [1], detection of this virus has been reported infrequently in humans and in swine and other mammals [2]. Human cases of infection have consisted of two major poultry-adapted lineages based on the reference strains A/quail/Hong Kong/G1/1997 (G1) and A/chicken/Beijing/1/1994 (Y280/G9). In 2018, there were 7 reported human cases, most with known exposure to poultry and with the majority involving viruses of the Y280/G9 lineage.

In July 2019, the CDC assessed the pandemic potential of a representative strain of A(H9N2) virus, Y280/G9 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(H9N2) virus strain A/Anhui-Lujiang/39/2018 lineage Y280 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 [3].

The summary average risk score for influenza A/Anhui-Lujiang/39/2018 was 6.2 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 5.9 (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 Analysis and Antigenic Relatedness. The variation in the scores for these two elements spanned from a moderate 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 Analysis from SMEs resulted in an adjusted range of 6.1 – 6.3 for the overall emergence risk and 5.8 – 6.0 for potential impact, indicating that the categorization of A/Anhui-Lujiang/39/2018 as moderate risk is unchanged by varying the range of Genomic Analysis scores. Similarly, a sensitivity analysis using the lowest and highest scores received for Antigenic Relatedness from SMEs resulted in an adjusted range of 6.1 – 6.3 for the overall emergence risk and 5.7 – 6.1 for potential impact indicating that the variability seen with this element does not have undue influence on the overall risk categorization of the virus.

Table 1: Estimated Risk of Emergence

Risk Element	Weight (W)	Risk Score (RS)	W X RS
Human Infections	0.2929	4.8	1.4
Transmission in Lab Animals	0.1929	8.0	1.5
Receptor Binding	0.1429	6.0	0.9
Population Immunity	0.1096	7.0	0.8
Infections in Animals	0.0846	6.0	0.5
Genomic Analysis	0.0646	6.0	0.4
Antigenic Relatedness	0.0479	6.7	0.3
Global Distribution in Animals	0.0336	7.5	0.3
Disease Severity & Pathogenesis	0.0211	5.5	0.1
Antiviral/Treatment Options	0.0100	4.8	0.0
Total			6.2

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	7.0	1.4
Human Infections	0.1429	4.8	0.7
Antiviral/Treatment Options	0.1096	4.8	0.5
Antigenic Relatedness	0.0846	6.7	0.6
Receptor Binding	0.0646	6.0	0.4
Genomic Analysis	0.0479	6.0	0.3
Transmission in Lab Animals	0.0336	8.0	0.3
Global Distribution in Animals	0.0211	7.5	0.2
Infections in Animals	0.0100	6.0	0.1
Total			5.9

Individual Risk Element Summaries

Human Infections: Sporadic human cases were reported. Limited information exists, but no confirmed reports of spread between humans. Information meets the definition of moderate risk for this element.

Transmission in Laboratory Animals: In ferret studies, this virus transmitted well by direct contact between animals, and consistently by respiratory droplets, suggesting a high risk for this element.

Receptor Binding: The predicted amino acid sequence of HA protein indicates that this virus possesses residues that may promote binding to human receptors. Only weak binding to α2,3 and α2,6 glycans has been observed in glycan array studies with recombinant HA.

Population Immunity: Limited data are available, but the expectation of cross-reactive antibodies in humans to this virus is low. However, some level of cross-reactive antibodies may be possible in individuals with past exposure to seasonal viruses.

Infections in Animals: Endemicity is established in poultry, mainly chickens, in affected countries. Sporadic detections occur in swine and other mammals.

Genomic Analysis: The virus is a reassortant, but all segments are of avian lineage. A/Anhui-Lujiang/39/2018 internal genes cluster within genomes of low pathogenicity avian influenza A(H7N9) virus sequences.

Antigenic Relatedness: This virus showed a lack of antigenic relatedness to seasonal human vaccines and reacts poorly with currently available pre-pandemic Candidate Vaccine Viruses (CVV), although CVV development is underway.

Global Distribution in Animals: The Y280 lineage is widespread in wild birds and poultry populations in southeast and southcentral Asian countries.

Disease Severity & Pathogenesis: Generally mild uncomplicated disease observed with H9N2 infections. In an experimental animal model, a moderate level of weight loss was observed.

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.

Comparison to other Viruses Scored with IRAT

The scores for the emergence risk and potential public health impact for the A/Anhui-Lujiang/39/2018 virus were plotted along with a selection of other influenza viruses scored using the IRAT (Figure 1). The A/Anhui-Lujiang/39/2018 virus falls in the moderate risk range for both risk of emergence and potential impact.

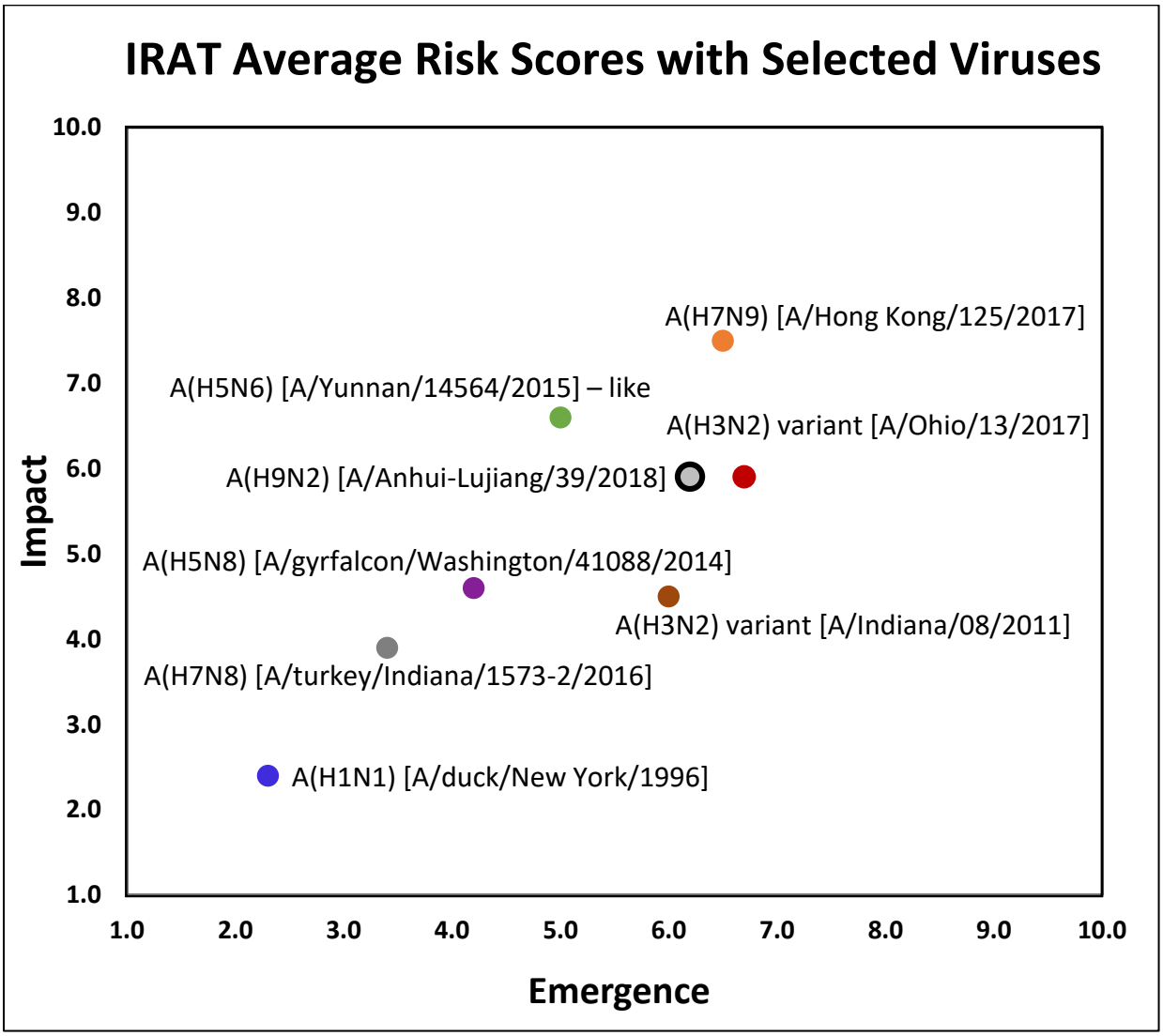

Figure 1: Average IRAT scores for A/Anhui-Lujiang/39/2018 plotted by emergence score and impact score. Additional viruses scored using IRAT are displayed for comparison.

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

1. Peiris, M., Yuen, KY., Leung, CW., Chan, KH., Ip, PLS., Lai, RWM., Orr, WK., Shortridge, KF. Human infection with influenza H9N2. Lancet 1999; 354 (9182): 916-7.
2. Peacock, TP., James, J., Sealy, JE., Iqbal, M. A Global Perspective on H9N2 Avian Influenza Virus. Viruses 2019; 11(7): 620.
3. Trock SC, Burke SA, Cox NJ. Development of a framework for assessing influenza virus pandemic risk. Emerg Infect Dis. 2015;21:1372–8.