Influenza Risk Assessment Tool (IRAT) - Virus Report

Prepared by the CDC Influenza Division

Asian Lineage Low Pathogenic Avian Influenza A(H7N9) virus

Virus Strain: A/Hong Kong/125/2017

Date of Evaluation: May 2017

Introduction

Human infections with novel influenza A viruses that originate in animals are rare and the overall risk of such infections in humans is generally low. Sporadic infections with novel influenza A viruses do occur, but typically in situations where individuals are exposed to infected animals through direct or close contact. The IRAT is used to examine multiple attributes of novel influenza A viruses that have not gained the ability to spread human-to-human to assess their potential to acquire this ability and the consequent potential public health impact.

Situation

Human infections of avian influenza A(H7N9) virus were first detected in China in 2013 (1) and over one hundred cases were identified in the ensuing outbreak. In the subsequent four years, an epidemic wave occurred every year with the fifth wave beginning in October 2016. A significant increase in the number of cases was reported during the fifth wave compared to the previous year's epidemics. Although it was observed that clinical and epidemiological factors had not changed, genetic sequence analyses indicated that A(H7N9) viruses diverged into two distinct lineages (2). The pandemic potential of a representative strain of Asian lineage low pathogenic avian influenza A(H7N9) virus was first evaluated using the Influenza Risk Assessment Tool (IRAT) in 2013, and with each epidemic wave a reassessment was performed (3). In May 2017, the IRAT was used to evaluate a representative virus of the newly identified fifth wave Yangtze River Delta lineage.

IRAT Evaluation

Influenza subject matter experts (SMEs) from the CDC, USDA, and FDA were asked to evaluate A/Hong Kong/125/2017 using ten risk elements defined in the IRAT. Each SME scored 1 to 3 elements based on their particular areas of expertise. SMEs can provide scores based on a scale between 1 and 10. 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 was 6.5 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 impact public health if it were to achieve sustained human-to-human transmission was 7.5 (Table 2) and was between the moderate and high-risk range. Overall, the virus is categorized in the moderate-high risk range and is similar to scores determined for Asian lineage A(H7N9) viruses in previous evaluations.

Some variability was observed among SME point estimate scores in the risk elements of Genomic Variation, Global Distribution in Animals, and Infections in Animals likely reflecting knowledge gaps and lower confidence in the data available to generate point scores for these elements.

Table 1-Estimated Risk of Emergence

Risk Element	Weight (W)	Risk Score (RS)	W x RS
Human Infections	0.2929	6.50	1.90
Transmission in Lab Animals	0.1929	5.30	1.02
Receptor Binding	0.1429	6.50	0.93
Population Immunity	0.1096	8.75	0.96
Infections in Animals	0.0846	6.40	0.54
Genomic Variation	0.0646	7.70	0.50
Antigenic Relatedness	0.0479	5.25	0.25
Global Distribution in Animals	0.0336	5.40	0.18
Disease Severity & Pathogenesis	0.0211	8.75	0.18
Antiviral/Treatment Options	0.0100	6.50	0.07
Total			6.54

Table 2-Estimated Potential Public Health Impact

Risk Element	Weight (W)	Risk Score (RS)	W x RS
Disease Severity & Pathogenesis	0.2929	8.75	2.56
Population Immunity	0.1929	8.75	1.69
Human Infections	0.1429	6.50	0.93
Antiviral/Treatment Options	0.1096	6.50	0.71
Antigenic Relatedness	0.0846	5.25	0.44
Receptor Binding	0.0646	6.50	0.42
Genomic Variation	0.0479	7.70	0.37
Transmission in Lab Animals	0.0336	5.30	0.18
Global Distribution in Animals	0.0211	5.40	0.11
Infections in Animals	0.0100	6.40	0.06
Total			7.48

A moderate emergence score was influenced by the top three weighted risk elements that all fell in the moderate range. Humans are not expected to have immunity to this virus, which results in a high individual score for population immunity risk, but this factor alone is not sufficient to raise the aggregate emergence risk score out of the moderate risk category. When answering the IRAT question of risk of potential public health impact, the top two weighted risk elements scored relatively high while the next four highest weighted elements were all in the moderate range resulting in a final score at the high end of the moderate range.

Individual Risk Element Summaries

Human Infections: Despite increased numbers of human infections with the fifth epidemic wave, cases are still associated with exposure to infected poultry/birds. There were no changes in the characteristics of case clusters.

Transmission in Laboratory Animals: In multiple ferret studies, the A(H7N9) viruses have consistently shown efficient direct contact transmission, but inefficient respiratory droplet transmission. Results suggest moderate risk to humans.

Receptor Binding: Sequence analysis reveals no hemagglutinin substitutions that suggest changes in binding preference compared to previously characterized viruses. Receptor studies with recombinant hemagglutinin revealed a weak binding pattern to α2,6 receptors similar to A/Shanghai/2/2013.

Population Immunity: The overall population immunity to this virus is expected to be very low, raising the risk score to a high level for this element.

Infections in Animals: The virus is detected in domestic poultry and likely endemic in several provinces in China. There is no evidence currently of sustained transmission in any species other than domestic poultry.

Genomic variation: A high level of diversity is observed in circulating genotypes. The hemagglutinin, neuraminidase (NA), and internal genes possess several genetic markers predictive of mammalian adaptation, as well as signatures in gene segments that impact disease.

Antigenic relatedness: Ferret antisera raised to a newly recommended candidate vaccine virus (CVV) showed hemagglutination inhibition of the majority of low pathogenic avian influenza A(H7N9) viruses tested.

Global Distribution in Animals: Asian lineage low pathogenic avian influenza A(H7N9) viruses have been detected in poultry and environmental samples in many regions of China, but not outside China. Spread is likely via transport and commerce in live bird markets.

Disease Severity & Pathogenesis: There is a high case fatality proportion among hospitalized patients of approximately 40%. Severity appears similar compared to previous epidemic waves.

Antivirals and Treatment Options: Similar to other avian influenza A(H7N9) viruses, A/Hong Kong/125/2017 is resistant to M2 blockers. The NA gene does not contain known or suspected markers of resistance to NA inhibitors; however, a high percentage of viruses collected from patients receiving antiviral therapy contained known markers of oseltamivir resistance suggesting a high propensity for mutation following drug treatment.

Comparison to other Viruses Scored with IRAT

The scores for the risk of emergence and potential public health impact for A/Hong Kong/125/2017 were plotted along with a selection of other viruses previously scored using the IRAT (Figure 1). The Yangtze River Delta lineage A(H7N9) virus aligns with the previously scored Asian lineage A(H7N9) virus in a category of moderate-high risk. Among the viruses evaluated with the IRAT, these Asian lineage A(H7N9) viruses score the highest.

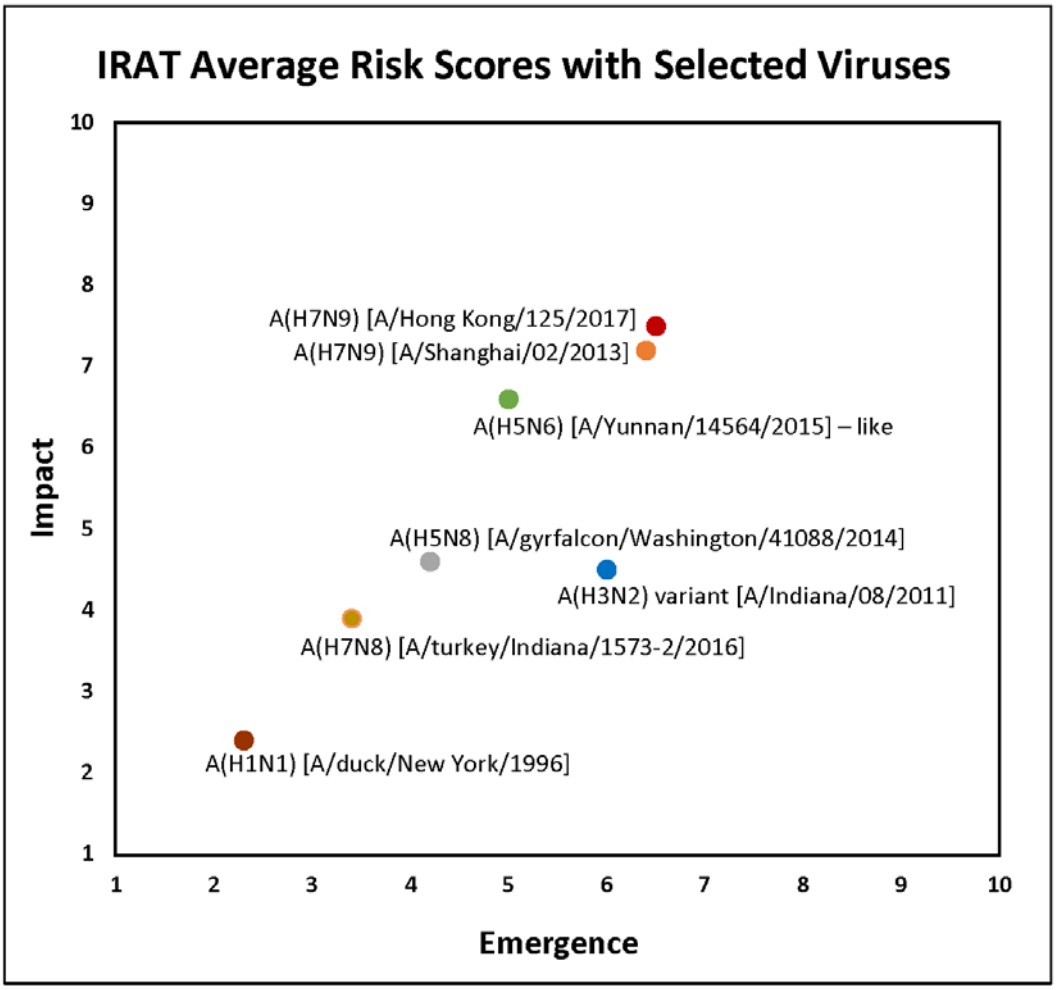

Figure 1: Average IRAT scores for A/Hong Kong/125/2017 plotted by emergence score and impact score. Additional viruses scored using IRAT are displayed for comparison.

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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