North American Canine Influenza A(H3N2)


Date of Evaluation: March 2016

Introduction
Human infections with novel influenza A viruses that originate in animals are rare and the risk of such infections overall to 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 among humans to assess their potential to acquire this ability and the consequent potential public health impact.

Situation
In March 2015, a virus closely related to Asian lineage A(H3N2) canine influenza virus (CIV) was isolated during an outbreak among dogs in Chicago, Illinois. Since the initial discovery, the virus has spread to multiple states. There have been no reports of human infection. The first detection of A(H3N2) CIV occurred in South Korea in 2007 and has since been identified in China and Thailand [1-3]. Genetic analysis of the Asian lineage A(H3N2) CIV indicates that the virus is entirely of avian origin.

In March 2016, the CDC assessed the pandemic potential of a representative strain of influenza A(H3N2) CIV using the Influenza Risk Assessment Tool (IRAT).

IRAT Evaluation
Influenza subject matter experts (SMEs) from the CDC and USDA were asked to evaluate CIV A/canine/Illinois/12191/2015 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 was 3.7 for the virus to achieve sustained human-to-human transmission (Table 1), placing the virus in the low 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 3.8 (Table 2) also placing it in the lower risk range. Overall, the virus is categorized in the low risk range.

Little variation was observed in the SME point estimate scores for each risk element, with the exception of Global Distribution in Animals where lack of surveillance data and reporting contributed to a wider spread in the scores.
**Table 1-Estimated Risk of Emergence**

<table>
<thead>
<tr>
<th>Risk Element</th>
<th>Weight (W)</th>
<th>Risk Score (RS)</th>
<th>W x RS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Infections</td>
<td>0.2929</td>
<td>1.58</td>
<td>0.46</td>
</tr>
<tr>
<td>Transmission in Lab Animals</td>
<td>0.1929</td>
<td>4.20</td>
<td>0.81</td>
</tr>
<tr>
<td>Receptor Binding</td>
<td>0.1429</td>
<td>2.67</td>
<td>0.38</td>
</tr>
<tr>
<td>Population Immunity</td>
<td>0.1096</td>
<td>7.50</td>
<td>0.82</td>
</tr>
<tr>
<td>Infections in Animals</td>
<td>0.0846</td>
<td>6.40</td>
<td>0.54</td>
</tr>
<tr>
<td>Genomic Variation</td>
<td>0.0646</td>
<td>3.40</td>
<td>0.22</td>
</tr>
<tr>
<td>Antigenic Relatedness</td>
<td>0.0479</td>
<td>4.67</td>
<td>0.22</td>
</tr>
<tr>
<td>Global Distribution in Animals</td>
<td>0.0336</td>
<td>6.00</td>
<td>0.20</td>
</tr>
<tr>
<td>Disease Severity &amp; Pathogenesis</td>
<td>0.0211</td>
<td>2.79</td>
<td>0.06</td>
</tr>
<tr>
<td>Antiviral/Treatment Options</td>
<td>0.0100</td>
<td>2.00</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>3.74</strong></td>
</tr>
</tbody>
</table>

A low risk of emergence score was influenced by low scores in the top weighted risk elements. Specifically, there were no human infections, inefficient transmission in laboratory animal model testing, and an avian receptor binding preference for this virus. 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 low risk category. Similarly, when answering the IRAT question of risk of potential public health impact, the top weighted risk elements scored relatively low, although the population immunity score, because of its higher relative importance kept the score at the high end of the low risk range.

**Individual Risk Element Summaries**

**Human Infections:** Although likely that there have been many opportunities, there are no reports of human infection with this virus, resulting in a risk score in the lower range.
Transmission in Laboratory Animals: In ferret studies, this virus did not transmit efficiently between animals in the direct contact model. Another study has shown some evidence that reassortants of the H3N2 CIV and pdmH1N1 can be generated with increased transmission in ferrets.

Receptor Binding: Laboratory studies [5] show mostly avian-like receptor binding specificity. Hemagglutinin sequence analysis reveals signature amino acids in and around the receptor-binding site suggesting preferential binding to alpha 2,3-linked (avian-like) sialic acid receptors.

Population Immunity: Human seroprevalence data are lacking, but the overall population immunity to this virus is expected to be low, raising the risk score to a high level for this element.

Infections in Animals: The virus transmits readily among immunologically naïve dogs; it has also infected some cats. Sustained transmission in a species with close association to humans places this virus in a moderate risk category for this element.

Genomic variation: The virus has limited molecular markers of importance for human infection and disease. Very little variation has been observed among canine A(H3N2) viruses.

Antigenic relatedness: This virus is antigenically distinct from A(H3N8) viruses previously isolated from dogs in the U.S. and from contemporary human seasonal A(H3N2) viruses.

Global Distribution in Animals: Lack of targeted surveillance for canine influenza virus confounds a true determination of distribution, but A(H3N2) CIV has spread rapidly in the U.S. Distribution is easily explained by movement of animals. Beyond the U.S., the virus has been detected in South Korea, China, and Thailand.

Disease Severity & Pathogenesis: No human illness was observed. Experimental animal models showed mild-to-moderate disease in infected mice and ferrets [5].

Antivirals and Treatment Options: No known markers of adamantane drug resistance detected; no known or suspected markers of resistance to neuraminidase inhibitors.

Comparison to Other Viruses Scored with IRAT
The scores for the emergence risk and potential public health impact for the CIV A/canine/Illinois/12191/2015 were plotted with a selection of other viruses previously scored using the IRAT (Figure 1). Viruses with higher IRAT risk scores are included for comparison.
Figure 1: Average IRAT scores for A/canine/Illinois/12191/2015 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 necessitate a new assessment and raise or lower the overall risk scores associated with the virus.

References