Influenza 101: The Virus and its Epidemiology in Swine

Biosecurity Research Institute (BSL-3Ag), Kansas State University
Manhattan, KS

Jürgen A. Richt, DVM, PhD
Kansas State University, Manhattan, KS
Swine Influenza Viruses

Family Orthomyxoviridae

- Genera: Influenza A, B, C et al.
- Enveloped, negative-sense single-stranded RNA virus
- 8 gene segments, 10/11 gene products
- Typical zoonotic agents
Influenza A Surface Proteins

- HA, NA, and M2 embedded in the envelope
- HA & NA are the major surface glycoproteins
  - Virulence
  - Immunity
  - Diagnostics
- HA (Trimer) attaches to host receptors
  - Mediates fusion of virus to endosomal membrane
- NA (tetramer) involved in detachment & budding

**Influenza A Virus Replication Cycle**

- **Attachment**
- **Budding**
- **Endocytosis**
- **Fusion and Uncoating**
- **Import**
- **Packaging**
- **Posttranslational Processing**
- **Translation**
- **RNP-Export**
  - mRNA
  - vRNA (-)
  - cRNA (+)
Influenza A Viruses

- Antigenic serotypes (subtypes) based on surface glycoproteins HA & NA:
  - 16 HA
  - 9 NA
  - e.g. H1N1, H3N2, H5N1, etc.

- Swine influenza – 3 primary subtypes circulating in North America
  - H1N1
  - H1N2
  - H3N2
## Influenza A: 16 Hemagglutinin subtypes

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Human</th>
<th>Swine</th>
<th>Horse</th>
<th>Bird</th>
</tr>
</thead>
<tbody>
<tr>
<td>H1</td>
<td>🕰️</td>
<td>🐷</td>
<td>🐴</td>
<td>🐓</td>
</tr>
<tr>
<td>H2</td>
<td>🕰️</td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H3</td>
<td>🕰️</td>
<td>🐷</td>
<td>🐴</td>
<td>🐓</td>
</tr>
<tr>
<td>H4</td>
<td>🕰️</td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H5</td>
<td></td>
<td>🐷</td>
<td>🐴</td>
<td>🐓</td>
</tr>
<tr>
<td>H6</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H7</td>
<td></td>
<td>🐷</td>
<td>🐴</td>
<td>🐓</td>
</tr>
<tr>
<td>H8</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H9</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H10</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H11</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H12</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H13</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H14</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H15</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
<tr>
<td>H16</td>
<td></td>
<td>🐷</td>
<td></td>
<td>🐓</td>
</tr>
</tbody>
</table>
Host Specificity of Influenza A

• HA binds to sialic acid linked to galactose as its receptor
  - Human/mammalian viruses prefer $\alpha$-2,6 linkage on respiratory epithelium
  - Avian viruses prefer $\alpha$-2,3 linkage on G.I. epithelium
  - Pig tracheal epithelium express both receptor linkages on respiratory cells
    • “Mixing vessel” for avian-human reassortant viruses with pandemic potential
Type A influenza cannot be eradicated.

[Diagram showing various animals and their interactions with different glycosyltransferases: $\alpha2-3\text{Gal}$, $\alpha2-6\text{Gal}$, $\alpha2-3\text{Gal}$, and $\alpha2-6\text{Gal}$].
Mechanisms of molecular evolution

• A constantly evolving virus

• Rapid evolution result of two major properties
  1) infidelity of viral RNA polymerase
     - **Antigenic Drift**

  2) segmented nature of genome
     - **Antigenic Shift/Reassortment**
Swine as a host of Influenza Viruses

- Swine influenza is a worldwide endemic respiratory disease of pigs (except Australia?, Norway?)
- SIV first isolated in 1930 by Dr. R. Shope (Sw/IA/1930)
- Swine are uniquely susceptible to avian and mammalian viruses ("mixing vessel" for human/avian/swine influenza viruses)
- Influenza in swine similar to influenza in humans (good model - NHP?)
- Viruses sporadically pass between humans and swine
Epidemiology of North American SIVs

1918 Spanish Flu Pandemic

1930 H1N1 evolves

cH1N1

1997-98 Double Reassortant H3N2

Triple Reassortant H3N2

H4N6

H3N1

H2N3

2003-05 huH1N1 huH1N2

2006 rH2N3

Current H3N2 H1N2 rH1N1 cH1N1 huH1N1 huH1N2

static period
Reassortment Events in Swine Flu

huH3N2

swH1N1: >1918

~1998

H3N2

rH1N1

rH1N2
Reassortment Events in Swine Flu

swH1N1: >1918

huH3N2/H1N1

huH1N1

huH1N2

rH3N1

> 1998

Avian/human polymerase complex plus swine genes: TRIG cassette
Epidemiology of North American SIVs

1918 Spanish Flu Pandemic
1930 H1N1 evolves to cH1N1
1997-98 Double Reassortant H3N2
1997-98 Triple Reassortant H3N2
2003-05 huH1N1 huH1N2
2006 rH2N3
Current H3N2 H1N2 rH1N1 cH1N1 huH1N1 huH1N2
Epidemiology of North American SIVs

1918 Spanish Flu Pandemic
1930 H1N1 evolves

1997-98 Double Reassortant H3N2
Triple Reassortant H3N2

2003-05 huH1N1 huH1N2
2006 rH2N3
Current H3N2 H1N2 rH1N1 cH1N1 huH1N1 huH1N2
Circulating swine influenza viruses in the U.S.: mainly H1N1, H1N2 and H3N2

= triple reassortant viruses with avian/human polymerase genes
Swine Influenza in the U.S. in 2009

1918
Spanish Flu Pandemic

1997–98
Double reassortant H3N2

1998
Classic swine H1N1 evolves

2003/2005
HuH1N1

2006
rH2N3

Current
H3N2
H1N2
cH1N1

rH1N1
cH1N1
HuH1N1
HuH1N2

novel pandemic H1N1
Genetic composition of novel pandemic H1N1

Swine triple reassortant virus

Swine H1N2

Eurasian swine (H1N1/H3N2)

PB1, PB2, PA, NP, NS

HA

NA

PB1

PB2

PA

NP

M

NS

Avian-like gene segment
Human-like gene segment
Swine-like gene segment
Eurasian swine-like segment

H1N1

HA

NA

PB1

PB2

PA

NP

M

NS
Swine origin flu
As of October 11, 2009, there have been more than 399,000 laboratory confirmed cases of pandemic influenza H1N1 worldwide and over 4,735 deaths reported to WHO.
Pandemic H1N1 virus isolated from non-human species

Human-animal Transmissions:
Pigs: Canada, Argentina, Australia, Singapore, Ireland, Norway, USA, Japan
Turkeys: Chile, Canada
Ferrets: USA

Experimental Infections: Ferrets, Mice, Monkeys, Pigs, Turkeys

Pandemic H1N1 virus:
• is able to infect and transmit among pigs
• potential of introduction and maintenance in swine herds is high
Fact:

- ~60% of EID are zoonotic (majority wildlife origins)
- Effective surveillance and control requires integration of human and animal populations worldwide

Integration of human medicine and veterinary medicine improves the lives of all species - human and animal.

The veterinarian is the only health care professional likely to see both people and their animals.
Thank you!