Current surveillance knowledge from Europe – focus UK

Ian Brown
Director of OIE Reference Laboratory for Swine Influenza
Coordinator of ESNIP3

Animal and Plant Health Agency-Weybridge
ESNIP 3 PARTNER RESULTS FROM 2014-15

Hungary, Belgium, France, Poland, UK

ESNIP3
Coordinator Ian Brown, AHVLA, UK
2010-2013
Figure 1: SIV genotypes isolated from European swine between 2009 and 2013. The 23 distinct genotypes are labelled A to M, with the lineage of origin for each segment indicated by a colored block.

ESNIP3 NOVEL INSIGHTS
Regional variation in the epidemiology of SIV in Europe (ESNIP3) ~ 23 variants detected

- **H1avN1** (53%)
- **H3N2** (9%)
- **H1huN2** (16%)
- **rH1huN1 and rH1avN2** (8%)
- **H1N1pdm and reass.** (14%)

Enzootic lineages

Epizootic lineages (occasional detections)
Data courtesy of Kristien Van Reeth, UGent

• 2014
  – av-like H1N1 9/22 (41%)
  – H1N2 5/22 (23%)
  – H3N2 8/22 (36%)

• 2015
  – av-like H1N1 3/3

No pdm09!?
Farm system data captured
Vaccination historically used
Data courtesy of Adam Dan, Veterinary Diagnostic Directorate Laboratory for Molecular Biology, Budapest

- 2014-15
  - av-like H1N1 3/4 (75%)
  - pdmH1N1 1/4 (25%)

Vaccination??
Data courtesy of Iwona Markowska-Daniels, NVRI, Pulawy

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of herds</th>
<th>Number of Influenza A positive cases</th>
<th>Frequency of positive cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poland</td>
<td>42</td>
<td>7</td>
<td>16.28</td>
</tr>
<tr>
<td>Slovakia</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

- av-like H1N1 2/7 (29%)
- pdm09 5/7 (71%)

Farm system data captured
Vaccination?
Surveillance criteria – to detect virus

- Acute respiratory disease
- Necropsy
  - Viral aetiology suspected
  - Lungs with specified gross lesions
  - Lungs with any gross lesions if clinical presentation is suggestive of influenza infection
- Carcasses
  - from animals which have died within 24 hours
  - presented moribund
  - up to 3 carcases/case submission
- Nasal swabs of up to 20 pigs acutely affected (pooled for PCR)
Schematic overview of diagnostic steps for confirmation of SI

1. Detection of influenza A virus
   - Negative
   - Positive
     - Step 2
       - Specific identification of influenza virus subtype
2. Classical pathway
   - Virus isolation (embryonated fowl eggs or cells)
3. Molecular pathway
   - M-gene PCR
   - HA-gene PCR (H1, H3)
   - Serological Characterisation HI/NI
   - Genotyping Sequencing of full genome

Animal & Plant Health Agency
## UK SI SURVEILLANCE RESULTS 2014

<table>
<thead>
<tr>
<th>Month</th>
<th>No. of submissions</th>
<th>No. of samples submitted</th>
<th>No. (+ve) submissions (samples)</th>
<th>AVH1N1</th>
<th>H1N2</th>
<th>H3N2</th>
<th>PH1N1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-14</td>
<td>23</td>
<td>151</td>
<td>7(23)</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feb-14</td>
<td>18</td>
<td>95</td>
<td>2(14)</td>
<td></td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar-14</td>
<td>21</td>
<td>104</td>
<td>4(8)</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr-14</td>
<td>17</td>
<td>66</td>
<td>4(10)</td>
<td>1</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>May-14</td>
<td>8</td>
<td>45</td>
<td>4(7)</td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Jun-14</td>
<td>15</td>
<td>65</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jul-14</td>
<td>12</td>
<td>37</td>
<td>4(6)</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Aug-14</td>
<td>20</td>
<td>70</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sep-14</td>
<td>20</td>
<td>89</td>
<td>3(3)</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Oct-14</td>
<td>13</td>
<td>35</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov-14</td>
<td>10</td>
<td>19</td>
<td>1 (1)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dec-14</td>
<td>8</td>
<td>27</td>
<td>1 (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>185</strong></td>
<td><strong>27</strong></td>
<td><strong>1 (1)</strong></td>
<td><strong>1</strong></td>
<td><strong>7</strong></td>
<td><strong>11</strong></td>
<td></td>
</tr>
</tbody>
</table>
## UK SI SURVEILLANCE RESULTS 2015

<table>
<thead>
<tr>
<th>Month</th>
<th>No. of submissions</th>
<th>No. of samples submitted</th>
<th>No. (+ve) submissions (samples)</th>
<th>AVH1N1</th>
<th>H1N2</th>
<th>H3N2</th>
<th>PH1N1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan-15</td>
<td>15</td>
<td>50</td>
<td>2 (3)</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Feb-15</td>
<td>21</td>
<td>62</td>
<td>3 (5)</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mar-15</td>
<td>25</td>
<td>99</td>
<td>4 (5)</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apr-15</td>
<td>15</td>
<td>42</td>
<td>1 (2)</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>May-15</td>
<td>15</td>
<td>47</td>
<td>3 (6)</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Jun-15</td>
<td>14</td>
<td>50</td>
<td>3 (3)</td>
<td></td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Jul-15</td>
<td>11</td>
<td>34</td>
<td>2 (2)</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Aug-15</td>
<td>14</td>
<td>37</td>
<td>1 (4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sep-15</td>
<td>11</td>
<td>56</td>
<td>3 (6)</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>141</strong></td>
<td><strong>477</strong></td>
<td><strong>22</strong></td>
<td><strong>4</strong></td>
<td></td>
<td></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>
SwIV pdmH1N1 surveillance across the EU

- **ESNIP 3 - 14 countries, November 2010 to October 2013**
  - pdm 194/1885 ~10% conventionally typed submissions,
  - Seq. Genotyping 12% total, European av. 8%.
  - at least 32 separate introductions from humans into swine have occurred 2009-2013 (Wats
  - ? Swine to humans.

- **UK 2009-14, pdm 60/187, 32%**
  - Nov. 2009 first detection
  - Differences in disease presentation, spread and duration,
  - mild or clinically inapparent disease in breeders
    typical respiratory disease in progeny.
  - mortality was low where disease was uncomplicated
    by environmental stresses or concurrent infections.
  - Where deaths occurred in pigs infected with A(H1N1)pdm09
    influenza, they were mainly due to other infections,
    including Strep. suis.

<table>
<thead>
<tr>
<th>Year</th>
<th>pH1N1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>4</td>
</tr>
<tr>
<td>2010</td>
<td>19</td>
</tr>
<tr>
<td>2011</td>
<td>15</td>
</tr>
<tr>
<td>2012</td>
<td>8</td>
</tr>
<tr>
<td>2013</td>
<td>14</td>
</tr>
<tr>
<td>2014</td>
<td>11</td>
</tr>
<tr>
<td>2015(m6)</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>64</strong></td>
</tr>
</tbody>
</table>

Williamson SM et al., Vet Rec. 2012 [**Combating Swine Influenza (COSI) UK collaboration**]
Genetic analyses for HA of UK pdm H1N1 viruses

Clinical Samples:
2011-15
ESNIP3 A/H1N1pdm09 viruses - HA
Antigenic sites : HA

A/Cal07/09 – vaccine
A/Eng195/09 – APHA typing Ag.
A/sw/Eng1353/09 – swine field isolate

All three isolates identical at all 5 Ag sites, except 1 aa in the swine field isolate.

UK 33 swine isolates (clinical/egg grown, 18/15) most had 1-2 aa changes per Ag site, one isolate* had 1-5 aa changes / site

<table>
<thead>
<tr>
<th>Ag Site</th>
<th># with AA variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca2</td>
<td>17/33 (51%) – D225X</td>
</tr>
<tr>
<td>Sb</td>
<td>11/33 (33%) – D190</td>
</tr>
<tr>
<td>Ca1</td>
<td>6/33 (18%)</td>
</tr>
<tr>
<td>Sa</td>
<td>6/33 (18%)</td>
</tr>
<tr>
<td>Cb</td>
<td>3/33 (9%)</td>
</tr>
</tbody>
</table>
Epizootic in humans in India with pdm09 raised concerns in swine industry
Emergent ‘India’ human pdm virus / pigs

• K166Q    T200A    D225N

? Swine pdm viruses
➤ Worldwide the consensus in pigs is KAD

Consensus n=89
Variants n=84

K/Q  ↓vacc ab sensitive
T/A  ↑hu/mammalian lung
D/G/N  2,6 (URT) – 2,3 (LRT)

Variant classes – World (non clinical)

<table>
<thead>
<tr>
<th></th>
<th>K</th>
<th>A</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>(2)</td>
<td>T(14)</td>
<td>N(10)</td>
</tr>
<tr>
<td>T</td>
<td>(2)</td>
<td>S(1)</td>
<td>V(1)</td>
</tr>
<tr>
<td>I</td>
<td>(1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q</td>
<td>(32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>E(8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Y(1)</td>
<td></td>
</tr>
</tbody>
</table>
European and UK pig pdm H1N1

- Europe 15 pdm isolates sequenced (ESNIP3),
  - 14 were KAD, 1 (Poland) KAG
  - 225G variants have also been ‘isolated’ from European pigs (Belgium, France, Hungary).

- UK – 31 pdm viruses sequenced
  - 94% K (1Q, 1R),
  - 97% A (1T),
  - 75% D, 4 G (egg), 4 E (3 EP/2 clinical), 1N (clinical)

- UK clinical material n=17 2011-15,
  - 13 KAD, 1 RAD, 1 KAN, 2 KAE, 1 QAD

- The motif K166;T200;D225N was not selected for in European viruses analysed

- UK classical and avian-like H1N1 HA have 225G
Molecular Epidemiology and Evolution of Influenza Viruses Circulating within European Swine between 2009 and 2013.


Figure 1. SIV genotypes isolated from European swine between 2009 and 2013. The 23 distinct genetic constellations are labeled A to W, with the lineage-of-origin for each segment indicated by a colored block.
UK submissions

pdmH1N1/09 UK
(Brookes et al., Vet Rec 2009; PlosOne 2010)

swH1N2r (pdm internals)
(Howard W et al., EID. 2011)
Perspectives from UK surveillance

- Dynamic stable since 2012
  - Pdm09
  - Hu1n2 (pdm09 cassette)
  - Avian-like virus low level; replacement after 20 years as dominant UK strain
- Viruses with pdm09 cassette of internal genes have selection advantage
- Little independent evolution to date in pdm09 HA
- Vaccination being applied increasingly

- Risks to ongoing surveillance flow!
  - Commercial vaccine manufacturers offering free testing
Acknowledgements

ESNIP network
Kristien Van Reeth
Iwona Markowska-Daniel
Adam Dan
Gaelle Simon
Simon Watson
Nicola Lewis

Defra for funding through project SV3041

APHA flu group
Sharon Brookes

ESNIP3
European Surveillance Network for Influenza in Pigs
3 project #259949
Project website address:
Thank you for your attention

http://flu-lab-net.eu/