**Bluetongue and related Orbiviruses – a global update**

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**Today’s Presentation**

- Orbiviruses – a very short update!
- Presentation will concentrate on Bluetongue
- Lessons learnt from the BTV-8 outbreak in Europe
- Recent global findings - should we be worried in the USA?
- Bluetongue and EHD in the Caribbean – recent studies
- My take on the international and regional trade debate

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**Family Reoviridae: Genus Orbiviruses**

There are currently 22 recognized virus species as well as 13 unassigned viruses in this genus:  
- African horse sickness virus  
- Bluetongue virus  
- Chuanz virus  
- Corriparte virus  
- Epizootic haemorrhagic disease virus  
- Equine encephalosis virus  
- Eubenengee virus  
- Ngoupe virus  
- Tilligerry virus  
- Great Island virus  
- Broadhaven virus  
- Great Island virus  
- Kemerovo virus  
- Lipovnik virus  
- Tribec viruses  
- Lake Clarendon virus  
- Palyam virus  
- CSIRO Village virus  
- Pala virus  
- European horse sickness virus  
- Elsey virus  
- St Croix fever virus  
- Umatilla virus  
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- Umatilla virus  
- St Croix fever virus  
- Waimak virus  
- Wongon virus  
- Yunnan virus  
- Middle Point virus

These viruses are known to be transmitted by midges (Culicoides), mosquitoes and ticks.

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**Bluetongue virus – 27 Serotypes (27 diseases)**

[Website link](http://www.iah.bbsrc.ac.uk/dsRNA_virus_proteins/bt_v-seg-2.htm) (Peter Mertens, Pirbright)
**Bluetongue – the disease**

BTV infects all species of ruminant - severe disease is usually seen only certain breeds of sheep (fine wool & mutton) & some species of deer (white-tailed).

Cattle - are usually are sub-clinically infected; reservoir

**Transmission of BTV**

- Bite of an infected *Culicoides* midge
- Spread of infected *Culicoides* on the wind

![Transmission of BTV](image)

**Bluetongue – Clinical disease**

![Bluetongue – Clinical disease](image)

**EIP dependent on temperature**

![EIP dependent on temperature](image)
Bluetongue virus global ecosystems - Evolving

Different species of Culicoides vector disseminate different serotypes of BTV in relatively distinct global ecosystems.

Thanks to Kiki Nomikou for this slide.
2. BTV-8 was affecting cattle

<table>
<thead>
<tr>
<th>BELGIUM</th>
<th>Cattle</th>
<th>Sheep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidity %</td>
<td>6.8%</td>
<td>27.3%</td>
</tr>
<tr>
<td>Mortality %</td>
<td>0.6%</td>
<td>11.2%</td>
</tr>
<tr>
<td>Case fatality %</td>
<td>17.7%</td>
<td>41.9%</td>
</tr>
</tbody>
</table>

3. BTV-8 was a reproductive disease

Fertility problems + abortions + foetal abnormalities in both cattle and sheep

4. BTV-8 was being transmitted both transplacentally and orally

Levels of transplacental transmission?

- 60 farmers with animals infected with BTV contacted
- 23/54 calves PCR positive (＞1/3 transplacentally infected)
- 1/23 Stillborn, 1/23 died 3 days old, 2/23 BTV +ve calves are “dummy calves”. All other calves healthy.
5. New BTV serotypes in goats

BTV-26 – adapted to goats?
No clinical signs
High viraemia
Happy Virus!
Happy Goats!
6. BTV-26 is being transmitted by direct contact (probably not by midges)

Culicoides midges were fed a BTV-26 spiked blood meal. Viral RNA measured at day 7 post infection. The declining levels of viral RNA observed revealed that the midges only have a sub-transmissible infection. Unlikely to be competent to transmit BTV-26.

Eva Veronesi, The Pirbright Institute

Other BTVs (BTV-27, BTV-28...... out there that can be transmitted by direct contact?)
DANGER: Reassortment of co-circulating BTV strains
Increase virulence in Cattle?
Gain ability to cross placenta?
Direct / oral transmission?

What have we discovered about BTV?
Big changes affecting international trade

- Rapidly moving and adapting to new ecosystems – climate change
- Some strains affect cattle as well as sheep / goats
- Can be a reproductive disease
- Can pass transplacentally – significance for over-wintering / trade?
- Can be passed orally – significance?
- Some strains can be transmitted directly (BTV-26)
- Circulating strains (field and vaccine strains) are reassorting in the field

Where are we now?

Successful vaccination
Outbreaks of BTV-8 in Europe, 2007-2009

End of 2012
Successful vaccination: BTV in Germany 2007

France – end of 2007

• France reported over 15,500 outbreaks in 2007 and 27,000 outbreaks in 2008.
• Limited (due to lack of vaccine) vaccination was carried out in 2008
• Compulsory vaccination was carried out in 2009 resulting in a high proportion of immune animals (estimates at between 50 and 90%)
• Voluntary vaccination in 2010 (no information on vaccine take-up)
• Final outbreak was in June 2010 therefore
• France was declared free of BTV-8 in 2012

Successful vaccination – BTV in Germany 2008

France – end of 2008


No cases of BTV-8 reported in Northern and Western Europe (Germany, Holland, Belgium, France, UK).
BTV circulation in Europe - 2014

- BTV-1 and 4 Spain, Portugal and Italy
- BTV-4 mainland Greece
- Potential novel serotype in Goats in Corsica
- BTV-4 outbreak in the Balkans

Romania 2015/16 – mass vaccination not implemented due to high cost

Variable vaccination strategies in BTV-4 affected countries
- Compulsory vaccination in Croatia and Bulgaria – good coverage achieved
- Hungary – plans to vaccinate but not initiated (May 2015)
- Greece and Slovenia – no vaccination

Evolution of cases from 23rd August, to 3rd of December 2014 (1)

<table>
<thead>
<tr>
<th>Data on animals</th>
<th>Bovine</th>
<th>Sheep</th>
<th>Goats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of animals</td>
<td>2,047,869</td>
<td>1,003,978</td>
<td>1,721,383</td>
</tr>
<tr>
<td>In infected counties</td>
<td>1,020</td>
<td>3,041</td>
<td>17</td>
</tr>
<tr>
<td>Total number of dead</td>
<td>38</td>
<td>878</td>
<td>4</td>
</tr>
<tr>
<td>% of dead from affected</td>
<td>3.7%</td>
<td>29%</td>
<td>30.8%</td>
</tr>
</tbody>
</table>

Thanks to Kiki Nomikou for this slide
France - Where did BTV-8 come from in 2015?

- BTV-8 vaccine strain circulating? No
- A new introduction? – BTV-8 came from the original 2006 source? Unlikely but possible
- Silent circulation for 5 years? – 2010-2015 probable
- Wildlife circulation? – deer or other wildlife possible
- Clinical signs not seen in vaccinated animals but virus circulating? possible
- Transplacental spread – immunotolerant carriers? possible

Lessons learned – European BTV-8 outbreak

Need for rapid response to future BT outbreaks

- Prompt vaccination – preferably before virus circulation
- High levels of coverage to eradicate (>80%)
- Vaccination over multiple years to eradicate (compulsory vs voluntary)
- Length of protection post vaccination may be longer than expected

Constant increasing risk - new BTV serotypes lining up.
Morocco: BTV-4, BTV-1, Algeria BTV-1, Mediterranean BTV-16
Israel: BTV-15, BTV-4, BTV-16, BTV-8, BTV-24, BTV-5

Risks of genetic exchange by reassortment – mixed viral phenotypes

Need for pan-bluetongue protective vaccines to protect livestock

Reverse Genetic approaches – promising results
- DISC (DISA) vaccines (disabled infectious single cycle vaccines) – NS-3 / VP-2
- Inactivated vaccines – universal vaccine platform
- Subunit vaccines
- VLP vaccines

Inactivated vaccines may give protection for at least 4 years in cattle and 2.5 years in sheep

Possible reason for rapid control and eradication of BTV from Northern Europe despite a reduced vaccine coverage after the first year.
Bluetongue virus (BTV) in the Americas

<table>
<thead>
<tr>
<th>18/24 serotypes present</th>
<th>Virus Isolation</th>
<th>Serotype Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trinidad and Tobago</td>
<td>3</td>
<td>1, 3, 4, 6, 8, 12, 17</td>
</tr>
<tr>
<td>Barbados</td>
<td>1, 3</td>
<td>1, 3, 4, 8, 12, 17</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>4, 6, 8</td>
<td>3, 4, 6, 8, 17</td>
</tr>
<tr>
<td>Martinique/Guadaloupe</td>
<td>1, 2, 3, 5, 9, 10, 11, 13, 14, 17, 18, 22, 24</td>
<td></td>
</tr>
<tr>
<td>French Guyana (South America)</td>
<td>1, 2, 6, 10, 12, 13, 17, 24</td>
<td></td>
</tr>
</tbody>
</table>

USA (1999-2012)
1, 2, 3, 5, 6, 9, 10, 11, 12, 13, 14, 17, 19, 22, 24

Fifty-nine naïve BTV antibody negative dairy cattle (Holstein and Jersey breeds) were imported into Trinidad from the USA
• All seroconverted in 3 months
• BTV-1, 2, 3, 5, 12 and 17
• Some cattle were co-infected, providing opportunities for reassortment.
• Gene sequencing in progress

Culicoides vectors present in Trinidad

Culicoides species identified to date:
C. furens
C. guerrai
C. guyanensis
C. insignis
C. maruim
C. occumarensis
C. pusillus
Unknown 1
Unknown 2
Unknown 3

The mtCOI sequences were analyzed phylogenetically against other known Culicoides mtCOI sequences from GenBank

Epizootic Haemorrhagic Disease virus (EHDV)

Seven Serotypes: EHDV-1-7

Eyal Klement, Koret School of Veterinary Medicine Hebrew University, Jerusalem
Epizootic Haemorrhagic disease (EHD) in the Caribbean

7 proposed serotypes of EHDV:
Very little information available on EHDV in the Caribbean
USA: EHDV-1, EHDV-2 and EHDV-6 (2006 ....)

Reassortment between a EHDV-6 (Australian origin?) and an endemic strain of EHDV-2 from the USA generated a reassortant virus able to cause severe outbreaks in deer.

- Guadaloupe and Martinique: EHDV-6
- French Guyana: EHDV-1 and EHDV-6
- Trinidad - All 59 cattle seroconverted to EHDV within 6 months of arrival in Trinidad. Serotyping in progress

Bluetongue in the Americas:

Very different to BTV-8 / BTV-4 in Northern Europe

Multiple serotypes circulating with very little or no clinical signs seen in susceptible ruminants

- Endemic stability
- Indigenous breeds may be resistant
- High levels of immunity likely to be present (cross-serotype)

How to trade animals safely from BTV-affected countries?

What to avoid:
- Importation of novel serotypes / strains into BTV free countries
- Introduction of nasty strains such as the European strain of BTV-8

What you need to know:
- Need to know BTV status of animals – antibody and virus (PCR)
- Need to know which serotypes are circulating where.
- Need to know BTV transmission-free season (winter months)

What you need to do:
- Monitoring and surveillance – check for new and existing serotypes. Ideally know serotypes circulating in exporting and importing country / state and carry out a risk assessment

Trade within the Americas between countries with circulation of multiple, similar serotypes and no clinical signs – very low risk.

Thanks very much

Any Questions?

Carrie Batten
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Karen Darpel
Lara Harup
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Peter Mertens