Ruminant arbovirus infections in Japan

Tohru Yanase

Subtropical Disease Control Unit, Division of Transboundary Animal Disease
Kyushu Research Station, National Institute of Animal Health, NARO, Japan
Kyushu Research Station
(Subtropical Disease Control Unit)
Today’s topics

1. General introduction
2. Ruminant arbovirus infections in Japan
3. Vector: *Culicoides* biting midges
4. Epidemiology and surveillance
5. Recent topics on arbovirus infections
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What is arbovirus?

◆ The word *arbovirus* is an acronym (*Arthropod-Borne* virus).

◆ The virus is transmitted by arthropod vectors (e.g. mosquitoes, tick, sand-flies, biting midges) via blood sucking process.

◆ The virus replicates in both arthropod vectors and vertebrate hosts.

◆ The word arbovirus has no taxonomic significance, but describes the mode of transmission of viruses of many families.

Arbovirus contains the families *Togaviridae, Flaviviridae, Reoviridae, Bunyaviridae, Rhabdoviridae* and *Asfaviridae*.
Life cycle of Arboviruses

Vertebrate host → Biting → Vector → Vertical transmission → Vertebrate host

Mosquitoes, Ticks
Biting midges, Sand flies etc.

Vertebrate host → Biting → Vector → Vertical transmission → Vertebrate host

Vertebrate host → Biting → Vector → Vertical transmission → Vertebrate host
Arbovirus infections listed by OIE

- Bluetongue
- Crimean Congo hemorrhagic fever
- Epizootic hemorrhagic disease
- Infection with Rift Valley fever virus
- Japanese encephalitis
- West Nile fever
- Nairobi sheep disease
- African swine fever
- Equine encephalomyelitis (Western)
- Infection with African horse sickness virus
- Venezuelan equine encephalomyelitis

Eleven arbovirus infections are currently listed
Arbovirus infections listed by OIE

- **Bluetongue**
  - Crimean Congo hemorrhagic fever
- **Epizootic hemorrhagic disease**
  - Infection with Rift Valley fever virus
- **Japanese encephalitis**
  - West Nile fever
  - Nairobi sheep disease
  - African swine fever
  - Equine encephalomyelitis (Western)
  - Infection with African horse sickness virus
  - Venezuelan equine encephalomyelitis

Three arbovirus infections have been recorded in Japan
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**Official diseases cause by arboviruses**

designated by the domestic animal infectious disease control law in Japan

<table>
<thead>
<tr>
<th>Disease</th>
<th>Species of animals</th>
<th>Occurrence in Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzootic encephalitis*</td>
<td>Cattle, Buffalo, Deer, Horses, Sheep, Goats, Swine, Boar</td>
<td>Occasional</td>
</tr>
<tr>
<td>Vesicular stomatitis</td>
<td>Cattle, Buffalo, Deer, Horses, Swine, Boar</td>
<td>No</td>
</tr>
<tr>
<td>Rift Valley fever</td>
<td>Cattle, Buffalo, Deer, Sheep, Goats</td>
<td>No</td>
</tr>
<tr>
<td>African horse sickness</td>
<td>Horses</td>
<td>No</td>
</tr>
<tr>
<td>African swine fever</td>
<td>Swine, Boar</td>
<td>No</td>
</tr>
</tbody>
</table>

*Enzootic encephalitis caused by Japanese encephalitis virus in horses and cattle have been reported occasionally.*
### Notifiable diseases cause by arboviruses in the regulations supplementing the law in Japan

<table>
<thead>
<tr>
<th>Disease</th>
<th>Species of animals</th>
<th>Occurrence in Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bluetongue</td>
<td>Cattle, Buffalo, Deer, Sheep, Goats</td>
<td>Occasional</td>
</tr>
<tr>
<td>Akabane disease</td>
<td>Cattle, Buffalo, Sheep, Goats</td>
<td>Frequent</td>
</tr>
<tr>
<td>Chuzan disease</td>
<td>Cattle, Buffalo, Goats</td>
<td>Occasional</td>
</tr>
<tr>
<td>Aino virus infection</td>
<td>Cattle, Buffalo</td>
<td>Frequent</td>
</tr>
<tr>
<td>Ibaraki disease</td>
<td>Cattle, Buffalo</td>
<td>Occasional</td>
</tr>
<tr>
<td>Bovine ephemeral fever</td>
<td>Cattle, Buffalo</td>
<td>Occasional</td>
</tr>
<tr>
<td>Nairobi sheep disease</td>
<td>Sheep</td>
<td>No</td>
</tr>
</tbody>
</table>

- Seven arboviruses are associated with the notifiable diseases.
- Epidemics of Akabane disease and Aino virus infection have frequently occurred.
- Occurrence of other diseases is occasional or has been never observed.
Bluetongue

Etiological agent:
Bluetongue virus (BTV) (at least 26 serotypes)
Genus: *Orbivirus*, Family: *Reoviridae*
* Six serotypes (2, 3, 9, 12, 16 and 21) were identified in Japan

Occurrence of bluetongue in Japan

<table>
<thead>
<tr>
<th>year</th>
<th>Cattle</th>
<th>Sheep</th>
<th>Etiological agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>23</td>
<td>32</td>
<td>BTV-21</td>
</tr>
<tr>
<td>2001</td>
<td>45</td>
<td></td>
<td>BTV-21</td>
</tr>
<tr>
<td>2005</td>
<td>2 (suspected)</td>
<td></td>
<td>BTV-21?</td>
</tr>
</tbody>
</table>

◆ Seroconversion in cattle has been observed through Japan, except Hokkaido.
◆ A few cases associated with BTV-21 have been recorded.

Economic impact of bluetongue is limited in Japan.
Ibaraki disease

Etiological agent:
Ibaraki virus
(strain of epizootic hemorrhagic disease virus (EHDV) serotype 2)
Genus: *Orbivirus*
Family: *Reoviridae*

Clinical Symptoms:
Fever, stop feeding, foamy salivation,
Swallowing difficulty*
* Causing aspiration pneumonia

Affected hosts:
Cattle, water buffalo

Distribution:
East Asia

Foamy salivation
Occurrence of Ibaraki disease in Japan

Over 4,000 deaths!
with 1,200 abortions/still births
Akabane disease

Etiological agent:
Akabane virus
  Genus: *Orthobunyavirus*
  Family: *Bunyaviridae*

Symptoms:
Abortion, premature birth, still birth, congenital abnormalities (arthrogryposis, hydranencephaly), Encephalomyelitis (in young cattle)

Affected hosts
Cattle, water buffalo, sheep, goat

Distribution:
East Asia, Southeast Asia, Middle East, Africa, Australia
Bovine epizootic encephalomyelitis caused by Akabane virus

Affected host: Young cattle*
Symptoms: neurological disorders (astasia, ataxia, hyper sensitivity)
Pathology: encephalomyelitis
Etiological agent: Akabane virus (Iriki type variant)
Occurrence: Japan, Taiwan, South Korea

*The affect cattle were not recovered and finally culled.
Confirmed cases of Akabane disease in Japan between 1998 and 2013
Aino virus infection

Etiological agent:
Aino virus
   Genus: *Orthobunyavirus*
   Family: *Bunyaviridae*

Symptoms:
Abortion, premature birth, still birth, congenital abnormalities
(arthrogryposis, hydranencephaly, cerebellar hypoplasia*)
* cerebellum is smaller than usual

Affected hosts
Cattle, water buffalo, sheep, goat

Distribution:
East Asia, Australia
Chuzan disease

Etiological agent:
Chuzan (Kasuba) virus
Genus: Orbivirus
Family: Reoviridae

Symptoms:
Congenital abnormalities (hydranencephaly, cerebellar hypoplasia), impairment of moving, blindness

Affected hosts
Cattle

Distribution:
East Asia
Bovine ephemeral fever

Etiological agent:
Bovine ephemeral fever virus (BEFV)
  Genus: Ephemerovirus
  Family: Rhabdoviridae

Clinical Symptoms:
High fever, recumbency, disability, respiratory problems, reduction of milk etc. ......

Affected hosts:
Cattle, water buffalo

Distribution:
Asia, Middle East, Africa, Australia

Astasia   (inability to stand)
Bovine ephemeral fever

◆ In 1949-1951 epidemic, a total of 770,000 cases and over 10,000 deaths were reported in Japan.
◆ Between 1993 and 2014, no occurrence of bovine ephemeral fever was recorded in mainland Japan. But it reemerged in 2015.
◆ Periodic epizootics have been identified in subtropical islands in the western bordering region.

Outbreaks of bovine ephemeral fever have been often reported in Mainland China and Taiwan in recent years.
Phylogenetic tree based on BEFV G gene

1996-2013
Japan (Okinawa),
Taiwan, China

1984-1989
Japan, Taiwan

Turkey 2012
China 2011, 2012
Taiwan 2013, 2014
Japan 2015

New lineage

Turkey 2008, 2012
Australia 1968
Prevention and control of arbovirus infections

◆ Vaccination is the most effective measure to minimize livestock loss.

Commercial vaccines against Akabane, Aino, Chuzan, Ibaraki and bovine ephemeral fever viruses are available in Japan

◆ Vaccinations have likely inhibited spreading of the above-mentioned arbovirus infections.

◆ There are still some difficulties to promote vaccinations. (due to large financial costs, and lack of knowledge and precise warning systems)

◆ Vaccines are not suitable for emergency use. (it takes over month to induce enough immunity)
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## Important arboviruses affecting ruminants

<table>
<thead>
<tr>
<th>Virus</th>
<th>Vector</th>
<th>Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Akabane</td>
<td><em>Culicoides</em> biting midge</td>
<td>Asia, Africa, Australia</td>
</tr>
<tr>
<td>Aino</td>
<td><em>Culicoides</em> biting midge</td>
<td>Asia, Australia</td>
</tr>
<tr>
<td>Chuzan</td>
<td><em>Culicoides</em> biting midge</td>
<td>Asia, Australia</td>
</tr>
<tr>
<td>Epizootic hemorrhagic disease (Ibaraki)</td>
<td><em>Culicoides</em> biting midge</td>
<td>Asia, Africa, North and South America, Australia</td>
</tr>
<tr>
<td>Bluetongue</td>
<td><em>Culicoides</em> biting midge</td>
<td>Asia, Africa, Europe, North and South America, Australia</td>
</tr>
<tr>
<td>Bovine ephemeral fever</td>
<td>mosquito, <em>Culicoides</em> biting midge</td>
<td>Asia, Africa, Australia</td>
</tr>
<tr>
<td>Vesicular stomatitis</td>
<td>mosquito, <em>Culicoides</em> biting midge etc.</td>
<td>North and South America</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>mosquito</td>
<td></td>
</tr>
<tr>
<td>Nairobi sheep</td>
<td>tick</td>
<td>Africa</td>
</tr>
</tbody>
</table>
What are *Culicoides* biting midges?

- They belong to the genus *Culicoides* of the family Ceratopogonidae.
- Their body is from 1 to 3 mm in length.
- Many species in the genus prefer to feed blood from mammals and avian.
- Several species of them play an important role on transmitting human and animal pathogens.

Suspected to transmit:
- 27 nematodes
- 66 arboviruses
- 16 protozoa
Culicoides biting midge

Mosquito

糠蚊
蚊
The mouthpart has sharp teeth
Life cycle of *Culicoides* biting midges

1. **Egg**
2. **Larva**
3. **Pupa**
4. **Emergence**
5. **Mating**

**Habitats of:**
- Rice paddy field
- Dung pats
- Rotting plant stems
- and so on

**Biting** *(Pathogen transmission)*
Entomological surveillance

- Virus isolation with established hamster cells
- Identification of isolated viruses
### Isolation of arboviruses from *Culicoides* biting midges in southern Japan between 1985-2013

<table>
<thead>
<tr>
<th></th>
<th><em>C. oxystoma</em></th>
<th><em>C. punctatus</em></th>
<th><em>C. jacobsoni</em></th>
<th><em>C. tainanus</em></th>
<th><em>C. lungchiensis</em></th>
<th><em>C. sumatrace</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Akabane</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aino</td>
<td>8</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peaton</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sathuperi</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chuzan</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D’Aguilar</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Bunyip Creek</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EHDV 1</td>
<td></td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ibaraki</td>
<td>24</td>
<td>1</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>EHDV 7</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BTV 16</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>91</strong></td>
<td><strong>4</strong></td>
<td><strong>1</strong></td>
<td><strong>1</strong></td>
<td><strong>2</strong></td>
<td><strong>1</strong></td>
</tr>
</tbody>
</table>

*Culicoides oxystoma* potentially has vector capacity!!
Knowledge gaps for vectors

◆ Vector competence of almost *Culicoides* species remains unclear.

◆ There is little information for biology (life cycle, distribution, active period…) of *Culicoides* biting midges.

◆ Taxonomy of the genus *Culicoides* is still changeable.

◆ There is no effective measure to control the biting midges at present. (insecticides and repellents are not enough to prevent the virus transmission)
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Epidemiology of arbovirus infections in Japan

- In most cases, arboviruses can not overwinter in Japan. Discontinuing of vector activity during winter and lack of transovarial transmission in vectors are possibly involved.

- The infected vectors are probably brought by seasonal winds from overseas in summer. The long-distance transport (up to several hundreds km) of insects by wind were considered in past outbreaks.

- Periodical outbreaks of arbovirus infections have occurred. The cycles may depend on decline of seroprevalence in cattle population.
Nationwide monitoring system of arboviruses in Japan

Sentinel cattle
◆ Calves, not experience previous summer
◆ At least 50 animals per each of 47 prefectures (approx. 3,000 animals)
◆ 2 to 3 animals in each farm

Materials and Tests
◆ Blood sampling in June, Aug. ,Sep. and Nov. (4 times each year)
◆ Serum neutralization test for Akabane, Aino, Chuzan, bovine ephemeral fever and Ibaraki viruses

Watching sero-conversion

Location of sentinel cattle
Sero-conversion to Akabane virus in Japan

- August
- September
- November

2008

2009

2010

2011

2012

2013
Backward trajectory analysis showed that the source of air stream reaching the outbreak area were lower latitude regions during the incursion risk period.
Mitochondrial phylogeography of *Culicoides oxystoma* in East and Southeast Asia, and Australia

- Long distance dispersal events of arbovirus vectors between the temperate and tropical locations in Asia and the Pacific
- The genetic separation of the Australian/Indonesian populations from the other Asian populations
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Incursions of three orthobunyaviruses to Japan

Peaton virus

Sathuperi virus

Shamonda virus

Arthrogryposis caused by Peaton virus
What is Schmallenberg virus/

◆ Schmallenberg virus was first identified in Germany in 2011.

◆ Fever, diarrhea, reduction in milk yield in the infected dairy cattle were observed in summer and autumn of that year.

◆ Abortion and congenital abnormalities in the infected cattle, sheep and goats occurred in the following winters and springs.

◆ Over 10,000 farms have been affected by Schmallenberg virus infection in European countries.
Bluetongue, Akabane, Aino, Chuzan, Ibaraki, Bovine ephemeral fever, etc.

Seasonal winds bring the infected *Culicoides* biting midges to temperate regions.
Neutralization antibodies against ruminant arboviruses in Indonesian cattle

<table>
<thead>
<tr>
<th>Virus (strain)</th>
<th>No. tested</th>
<th>Positive</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td><strong>Orthobunyavirus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Akabane</td>
<td>90</td>
<td>72</td>
<td>80.0</td>
</tr>
<tr>
<td>Aino</td>
<td>90</td>
<td>89</td>
<td>98.7</td>
</tr>
<tr>
<td>Tinaroo</td>
<td>83</td>
<td>56</td>
<td>67.5</td>
</tr>
<tr>
<td>Peaton</td>
<td>90</td>
<td>52</td>
<td>57.8</td>
</tr>
<tr>
<td>Douglas</td>
<td>59</td>
<td>7</td>
<td>11.9</td>
</tr>
<tr>
<td><strong>Orbivirus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EHDV 1</td>
<td>75</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>EHDV 2 (Ibaraki)</td>
<td>90</td>
<td>65</td>
<td>72.2</td>
</tr>
<tr>
<td>EHDV 2 (Alberta)</td>
<td>75</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>BTV 1</td>
<td>82</td>
<td>44</td>
<td>53.7</td>
</tr>
<tr>
<td>BTV 12</td>
<td>77</td>
<td>3</td>
<td>3.9</td>
</tr>
<tr>
<td>BTV 20</td>
<td>72</td>
<td>47</td>
<td>65.3</td>
</tr>
<tr>
<td><strong>Rhabdovirus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bovine ephemeral fever</td>
<td>99</td>
<td>71</td>
<td>78.9</td>
</tr>
</tbody>
</table>

Miura et al. (1982)
Occurrence of orthbunyaviruses related with congenital abnormalities in ruminants

- Akabane virus
- Aino (Shuni) virus
- Sathuperi (Douglas, Schmallenberg) virus
Confirmed cases

Neglected cases

Lack of:
- knowledge
diagnostic system
human resource
financial support
reporting system
etc......

Development of sensitive monitoring and diagnostic systems should be essential!!
Predicted risk factors for arbovirus spread

**Human economic activities:**
- increase susceptible live-stock animals
- provide ideal habitats for vector arthropods

**Global transportations:**
- accidentally introduce infected vectors and animals, and contaminated foods and biological products

**Global warming:**
- changes in the weather conditions (temperature, precipitation, air stream......)
- affects ecosystem (vector distribution, behavior, abundance, migration......)

- increase occurrence of arbovirus infections and expand their range to previously unaffected region
◆ Arbovirus infections are transboundary diseases!

◆ International collaboration is essential!!

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