Lumpy skin disease: an emerging disease?

Andy Haegeman, Ilse De Leeuw, Annebel De Vleeschauwer, Laurent Mostin, Willem Van Campe, Maria Vastag, Claude Saegerman, Eeva Tuppurainen, Kris De Clercq

ECVPH 3th October 2017
Lumpy skin disease
General information Virus

- Capripox
  - Classification

Poxviridae

Entomopoxvirinae
  - (insects)
    - Alpha
    - Beta
    - Gamma

Chordopoxvirinae

Avipoxvirus
- Cervidpoxvirus
- Leporipoxvirus
- Orthopoxvirus
- Suipoxvirus
- Yatapoxvirus
- Parapoxvirus
- Capripoxvirus

Sheeppox virus SPPV
Goatpox virus GTV
Lumpy skin disease virus LSDV

EM Photo courtesy Dr Jan Mast
Lumpy skin disease
Introduction

- High-impact transboundary cattle pox disease
- Notifiable disease by the World Organization for Animal Health (OIE)
- Stable virus, survives well in the environment
- Difficult to eradicate without vaccination
- Only 30-70% of the infected animals get sick (natural resistance ?)
- High fever, sharp drop in milk yield and secondary mastitis, reduced weight gain, infertility, sterility in breeding bulls, abortions and permanently damaged skins and hides
- Long recovery period and animals may not regain the same level of production
- Outbreak or vaccination inflicts heavy restrictions to the global trade of live cattle and their products
Lumpy skin disease

Clinical signs
Lumpy skin disease – Clinical signs
Lumpy skin disease – Clinical signs
Lumpy skin disease – Clinical signs

© Kris De Clercq, CODA-CERVA
Mechanical transmission has been demonstrated to occur by blood-feeding insects and some African tick species – no data available on vector potential European ticks - restriction zones need to cover the flying distance of vectors (50km)

Indirect contact via shared water and feed troughs and contaminated environment?

Iatrogenic intra-herd transmission may occur by injectable veterinary treatments and vaccinations

Seminal transmission – importance in the field setting needs to be confirmed

Infected pregnant cows are known to deliver calves with skin lesions

Direct contact = ?

Transmission of LSDV requires further research

NB Players in Israel
Lumpy skin disease

Epidemiology
Spread of Lumpy skin disease (LSD) 2013-2015 Middle-East, Turkey, Cyprus, Caucasus, Russia

<table>
<thead>
<tr>
<th>Country</th>
<th>Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>2012 (July)</td>
</tr>
<tr>
<td>Lebanon</td>
<td>2012 (Nov)</td>
</tr>
<tr>
<td>Jordan</td>
<td>2013 (April)</td>
</tr>
<tr>
<td>Irak</td>
<td>2013 (August)</td>
</tr>
<tr>
<td>Turkey</td>
<td>2013 (August)</td>
</tr>
<tr>
<td>Egypt</td>
<td>2013 (Decem)</td>
</tr>
<tr>
<td>Iran</td>
<td>2014 (May)</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>2014 (July)</td>
</tr>
<tr>
<td>Cyprus</td>
<td>2014 (Nov)</td>
</tr>
<tr>
<td>Kuwait</td>
<td>2014 (Nov)</td>
</tr>
<tr>
<td>Russia</td>
<td>2015 (Nov)</td>
</tr>
<tr>
<td>Greece</td>
<td>2015 (August)</td>
</tr>
</tbody>
</table>

Table from Dr Alessandro Rippani (OIE)

Lumpy Skin Disease epidemiological situation in recent years (Global)

Lumpy skin disease
Greece 2015

Greece 18 August 2015

Greece 7 September 2015

Slides from Dr Sotiria Eleni Antoniou, Greece
EFSA Opinion (Jan 2015)
Control measures

- No preventive vaccination
- Full stamping out of affected herds
- Protection zone (3km), surveillance zone (10km), restriction zone (20km) (minimal)
- Movement restrictions of animals and animal products
- If needed vaccination in the restricted zone (20 km minimal)
Lumpy skin disease
Worrying aspect of spread: jumps

Slides from Dr Sotiria Eleni Antoniou, Greece
Last outbreaks Greece 15/12/2015 Rodopi
14/12/Chalkidiki

Slide from Dr Sotiria Eleni Antoniou, Greece
Outbreaks Bulgaria April - May 2016

Slide from Dr Georgi Chobanov, Bulgaria
Lumpy skin disease
Greece – Bulgaria – FYROM May 2016
April – July 2016
Outbreaks Greece, Bulgaria, FYROM, Serbia, Kosovo, Montenegro, Albania

Several cases in vac herds < 2-3w after vac

Source OIE WAHIS
April - September 2016
Russian Federation: Kovalevo, Liskinsky, Voronezh administrative region, next to Ukraine

Source: OIE WAHIS
Lumpy skin disease

Vaccines and Vaccination
‘No vaccination’ is the least effective option in reducing LSDV spread.

If the objective is to minimise the number of outbreaks of LSD in regions at risk for LSDV introduction it is recommended to implement vaccination.

To increase the likelihood of extinction of outbreaks, high within- and between-farm vaccination coverage should be achieved.

The implementation of vaccination could be accompanied with partial stamping out instead of total stamping out if a small increase in the number of affected farms and/or a reduction in the probability of extinction of the outbreaks are considered acceptable.

ISRAEL LSD CONTROL POLICY:
1989- total Stamping-Out
2006/2007- Partial SO
2012- No SO
Current Control measures

Introducing:
- Free zone without vaccination
- Free zone with vaccination
- Infected zone (with vaccination)

Movement restrictions:
- Live bovine animals
- Semen, ova, embryo’s
- Milk and milk prod. for animals
- Unprocessed animal products
- Untreated hides and skins

AND

Derogations: movement of animals between zones with the same status or with different status
- Depending on specific conditions
- Vaccination and waiting period
- With or without risk analysis
- Without vaccination always with risk analysis
- Channeling procedure

Movements possible within the country, to other Member States and to Non-EU countries
LSD vaccination in South East Europe in 2016– Situation as at Jan 2017

Vaccination completed in:
• Bulgaria
• Greece (Northern part)
• Serbia
• FYROM
• Montenegro
• Kosovo
• Croatia
• Albania

Vaccination in progress in:
• Southern part of continental Greece

Vaccination Completed
Vaccination in progress
LSD outbreaks as at
1 Jan - 30 Nov 2016 (ADNS)
LSD vaccination in South East Europe – Situation as at May 2017

- Vaccination completed since 2016 in:
  - Bulgaria
  - Greece (Northern part)
  - Serbia
  - FYROM
  - Montenegro
  - Kosovo
  - Croatia
  - Albania

- Vaccination in progress in:
  - Southern part of continental Greece & islands
  - Bosnia & Herzegovina

- Single LSD outbreaks reported in 2017 (ADNS)
Live attenuated LSDV vaccines provide good protection in cattle and is superior to sheeppox virus (SPPV) vaccines (Ben-Gera et al 2015)

No DIVA (Differentiation of Infected from Vaccinated Animals) vaccine available

Vaccines should be produced according to Good Manufacturing Process (GMP), vaccine virus needs to be molecularly characterized, contain sufficient virus titre and be free of extraneous agents

Where distribution of SPP and GTP overlaps with LSD

- SPPV vaccines may be used for cattle against LSDV if sufficient vaccination coverage and other appropriate control measures are in place

- GTPV containing vaccines are not yet used against LSD but has been demonstrated to provide good protection against LSDV
Lumpy skin disease: Data collection and analysis
European Food Safety Authority (EFSA)

APPROVED: 27 March 2017
Figure 14: Number of outbreaks per month, temperatures and percentage of vaccinated animals in Bulgaria in 2016

Figure 19: Number of outbreaks per month, temperatures and percentage of vaccinated animals in Albania in 2016
EURL for diseases caused by capripox viruses

In vivo evaluation of Lumpy Skin Disease vaccine efficacy in controlled environment
LSDV: Infection Model

- **Infection route:**
  - Intravenously
  - Intra-dermal: 4 sites, 2 on each side of the neck

- **Infection dose:**
  - $10^{5.4-6}$ TCID$_{50}$/100 µl

- **Number of animals per group:** N = 8

- **Clinical scoring (21 days) includes:**
  - Body temperature, lymph swelling, nodule development (number and size), feed uptake, conjunctivitis, general behaviour, local reaction (vaccination and challenge sites)

- **Sampling**
  - EDTA blood, buccal swabs: PCR, Virus isolation
  - Biopsies, tissues and organs: PCR, Virus isolation
  - Serum: IPMA and virus neutralisation test
  - Heparinized blood: IFN release
**LSDV: Infection Model**
with LSDV field isolate from Israel

- **Clinical signs after challenge** Number of nodules /
generalisation / clinical scores

- **Body temperatures:** fever peak around 7/8 dpi
- **Seroconversion:** Onset: 4 to 13 dpi
- **Virus detection in blood:** detection as early as 2/3 dpi
- **IFNg release release upon stimulation in vitro**
**LSDV: Vaccine trials**

- **Commercial available → Live attenuated vaccines (LAV)**
  - LSDV-based
    - OBP (Onderste Poort; South-Africa)
    - LumpyVax (MSD; South-Africa)
    - HerbiVac (Deltamune, South-Africa)
  - Sheeppox based (RM-65)
    - JoviVac (Jordan Bio-Industries Center (JOVAC); Jordan)
    - Abic (Abic Biological Laboratories Ltd (Phibro); Israel)
    - Penpox (Pendink Institute; Turkey)
  - Goatpox based
    - CapriVac (Jordan Bio-Industries Center (JOVAC); Jordan)
  - Sheep and goatpox based or LSDV? (Cfr Tuppurainen et al., 2014)
    - KSGP 0240/0180 (Jordan Bio-Industries Center (JOVAC); Jordan)

- **New Inactivated Vaccine (MCI, Morocco)**
  - Sheeppox-based
  - LSDV-based
Results of Trial A : LAV 5-8

- **Number of animals:**
  - 7 animals per vaccine group
  - 5 control animals (not vaccinated)

- **Challenge:** 21 days after vaccination

**LAV6 & 7 = best efficacy**
Results of Trial B:
LAV1; INAC1-2

Trend of the mean clinical score by group of animals (Trial 1)

Acclimatisation period

Post vaccination period

Post challenge period

LAV1 = best efficacy
LSDV Vaccine trials: Viremia

- **Viremia** following challenge:
  - Completely blocked $\rightarrow$ Strong Vaccine effect
  - Almost completely blocked $\rightarrow$ Vaccine effect
  - No blocking $\rightarrow$ No Vaccine effect (LAV4)

**LAV3 group**
1 positive sampling in 1 animal

**LAV4 group**
LSDV Vaccine trials:
Serological response

Serological response:
• **Strong**
  ✓ Early detection
  ✓ At moment of challenge:
    - 100% seroconverted
    - Some moderate to strong positive

Serological response:
• **Weak**
  ✓ Starts later
  ✓ At moment of challenge:
    - Minority was seroconverted
    - Only weak positive
LSDV Vaccine trials: interferon gamma response

- **IFNgamma release** upon stimulation:
  - **Strong**
  - **Weak**
LSDV Vaccine trials:
Virus distribution

- Virus distribution in organs/tissues
  - **None or very limited** and with very low viral load (LAV2 and 3)
  - **Broad** distribution pattern (LAV4)
LSDV Vaccine trials: First conclusions

The LSD challenge model allows the identification of:

- Vaccines with very good potential
  - No viremia, elicits high Abs response and good IFNg release, almost no traces of viral DNA found in organs
  - Although very slight side effects after vaccination (fever)

- Vaccines with (moderate) potential
  - Almost no viremia, elicits good Abs and IFNg response, almost no traces of viral DNA found in organs

- Vaccines (partially) failing to protect the animals
  - Strong viremia, Low Abs and IFNg response, virus widely spread in the organs. Animals in this groups also secreted the virus as detected by buccal swabs.

- None of the LAV vaccines protected against the initial fever spike!

- Inactivated vaccines: booster vaccination needed; promising results.
Thank you for your attention!