HOMOLOGOUS VS HETEROLOGOUS LSD VACCINES
PRO’s and CON’S

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CVO, ISRAEL
(LSD3)
Istanbul, Turkey, 12-13 December 2016
Existing vaccines against LSDV

- SPPV: RM-65
- Bakirkoy
- Romanian

- GTPV: Gorgon, Kedong, Isiolo

- LSDV: Neethling
- KSGP O-240, KSGP O-180

- LSDV field strain

E. Klement
The real questions are...

- Effective or not-effective vaccine
  - No perfect vaccine - Effectiveness is Relative

- Confounders
  - Epidemiology
  - Entomology
  - Culling
  - Believes vs facts

- Differentiate Vaccine and vaccination
What makes a vaccine good?

- Effective
- Safe

Field efficacy studies
Field experience
Challenge studies
GMP
Reversion to virulence
Adverse effects

GOOD VACCINATION
Previous LSD outbreaks in Israel
Control methods used in Israel during past outbreaks

<table>
<thead>
<tr>
<th>Year</th>
<th>Region</th>
<th># of epi units</th>
<th>Vaccine used</th>
<th>Stamping out</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>South</td>
<td>1 village</td>
<td>SPPV around</td>
<td>total</td>
</tr>
<tr>
<td>2006</td>
<td>South</td>
<td>1 village</td>
<td>SPPV After incursion</td>
<td>clinical cases</td>
</tr>
<tr>
<td>2007</td>
<td>South</td>
<td>8 villages</td>
<td>SPPV Before outbreak</td>
<td>Clinical cases</td>
</tr>
<tr>
<td>2012-2013</td>
<td>North</td>
<td>293 herds</td>
<td>SPPV-1 SPPV-10 Neethling</td>
<td>few Salvage</td>
</tr>
</tbody>
</table>
1989 PEDUYIM

Map 1: Peduyim, ~25 km from Gaza Strip
Israel 1992
KSGP 0240 vaccine adverse reaction in dairy cows near GS

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number vaccinated</th>
<th>Number reactive</th>
<th>% reactive</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 years</td>
<td>3,638</td>
<td>360</td>
<td>9.89</td>
</tr>
<tr>
<td>Primiparae</td>
<td>1,536</td>
<td>222</td>
<td>14.4</td>
</tr>
<tr>
<td>Pregnant heifers</td>
<td>1,134</td>
<td>11</td>
<td>0.97</td>
</tr>
<tr>
<td>Female calves</td>
<td>2,959</td>
<td>12</td>
<td>0.40</td>
</tr>
<tr>
<td>Male calves</td>
<td>518</td>
<td>2</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9,785</strong></td>
<td><strong>607</strong></td>
<td><strong>6.2</strong></td>
</tr>
</tbody>
</table>

Delegate from Pirbright

An expert was delegated from Pirbright to visit the farms and discuss the issue. Infected material from Gaza (sampled from the mentioned calf, 18 Nov 1992) and from PV-reactive Israeli cows were submitted to Pirbright. Eventually, the material from Gaza was confirmed there to include a field strain of the LSD virus.

Following the event, Pirbright's user-instructions for the KSGP 0240 vaccine were revised to include a warning "not for the vaccination of Bos Taurus cattle". This falls in line with the findings that the said vaccine strain is, in fact, LSDV (Ref 4).

“not for Bos Taurus”- Breed differences ?

Cellular immunity to SP-RM65 in cows

"RM65 did not induce good cellular immunity against LSD. RM65 does not give good protection against LSD"

Klement 2007, unpublished
2006 EIN-ZURIM dairy farm
SPPV

Single farm (~600)
20 km from GS
Many farms near by
Late detection
Vaccinated at detection
Check & cull
3X / week

33% culled
LSD Morbidity in SPPV RM65
8 vaccinated herds near GAZA S. 2007

Klement
LSD in 8 SPPV- RM65 vaccinated herds 2007 – check & cull

**SHIKMIM- Beef**

**OR HANER - Beef**

**ALUMIM- Dairy**
morbidity in vaccinated herds

1989-2006-2007 J. Brenner (KVI)
Brenner et al Vaccine 2009

• The Romanian strain was used in Egypt during 1989 epidemic – No clear data on efficacy

• 2007- significant morbidity was observed in vaccinated herds.

• RM-65 vaccine (sheep dosage) was used in Israel in 2006 and 2007. ~50% effectiveness

• The outbreak ended and the disease disappeared
2012-2013 LSD
Cumulative # of infected Herds

- POX 1
- POX 10
- Neethling
- Spring Vectors

Herds cumulative:
- Jul-12
- Aug-12
- Sep-12
- Oct-12
- Nov-12
- Dec-12
- Jan-13
- Feb-13
- Mar-13
- Apr-13
- May-13
- Jun-13
- Jul-13
- Aug-13
Kibbutz GENOSAR – dairy farm 2012
Sea of Galilee, mild winter, 300 milking cows

36 culled (12%)

Pox 1
04/12/12

Pox 10
08-18/02/13

Neethling
18/03/13 ~
COMPARISON OF THE EFFICACY OF NEETHLING LUMPY SKIN DISEASE VIRUS AND X10RM65 SHEEP-POX LIVE ATTENUATED VACCINES FOR THE PREVENTION OF LUMPY SKIN DISEASE – THE RESULTS OF A RANDOMIZED CONTROLLED FIELD STUDY

controlled randomized field trial
Natural trial- Comparative efficiency
Neethling vs Pox-10 (10^4 2ml)

- After lab tests and field Safety trial
- March – July 2013
- 15 dairy herds >250 milking cows
- Unaffected herds near-by outbreak zone
- Each farm: ½ Neethling ½ Pox-10
- Clinical monitoring - VS and Vet School
- 8 farms infected
### Neethling vs. Pox-10
#### controled field trial results

<table>
<thead>
<tr>
<th></th>
<th>Neethling OBP</th>
<th>Pox-10 Jovac</th>
</tr>
</thead>
<tbody>
<tr>
<td># vaccinated</td>
<td>4,222</td>
<td>4,279</td>
</tr>
<tr>
<td># Non clinical</td>
<td>4,192</td>
<td>4,178</td>
</tr>
<tr>
<td>% non clinical</td>
<td>99.3%</td>
<td>98.8%</td>
</tr>
<tr>
<td>% Clinical cases</td>
<td>30 (0.7%)</td>
<td>51 (1.2%)</td>
</tr>
<tr>
<td>mild</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>severe</td>
<td>23</td>
<td>29</td>
</tr>
</tbody>
</table>

J. Ben Gera et al Vaccine (33) 2015
Results

significantly higher morbidity in the 10XRM65 group

Severe cases

Ben-Gera et al. *Vaccine*. 2015
Neethling vaccine adverse reactions

- 9 confirmed cases in vaccinated cows (incidence= 0.4%).
  1 severe case
- All within 14 days post vaccination
- No isolation of Neethling strain from a non-Neethling vaccinated cow

Ben-Gera et al. *Vaccine*. 2015
## Country LSD vaccine comparison

<table>
<thead>
<tr>
<th>Countries</th>
<th>Vaccine used</th>
<th>LSD cases</th>
<th>Vaccination- last case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel</td>
<td>Neethling (Pox 10)</td>
<td>none</td>
<td>5 months</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>Neethling</td>
<td>none</td>
<td>4 months</td>
</tr>
<tr>
<td>Serbia</td>
<td>Neethling</td>
<td>none</td>
<td>Several months</td>
</tr>
<tr>
<td>Balkan</td>
<td>Neethling</td>
<td>some</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>Neethling</td>
<td>some</td>
<td></td>
</tr>
<tr>
<td>Turkey</td>
<td>SPPV (Pox 3)</td>
<td>some</td>
<td></td>
</tr>
<tr>
<td>Russia</td>
<td>SPPV</td>
<td>some</td>
<td></td>
</tr>
</tbody>
</table>

Other countries: middle-east, Africa, Eurasia - unclear
LSD Vaccines History (Evolution) “from LARNACA 2013 to ISTANBUL 2016”

- **B.N - Before Neethling**
  - Southern Africa
  - Limited EBM
  - Field experience, sales

- **A.N - After Neethling**
  - EBM - efficiency, safety
  - Field experience
Conclusions

• To date most EBM favor Neethling vaccine
• Neethling is about 80% effective
• Full protection is achieved 30 days post vaccination
• Models and field data show that LSD outbreaks can be fully controlled with good coverage.
• Transient adverse effects 0.5% of cows = negligible
• Drawbacks- vaccine contaminants, non- GMP
• Price? Availability ?
“The facts of today are the fallacies of tomorrow”

thank you
Live bovine movements 2008-2014
Countries reporting LSD in 2011-2014 according to OIE

EFSA Journal 2015; 13(1):3986