CONTROL AND ERADICATION OF LUMPY SKIN DISEASE IN SOUTH-EASTERN EUROPE – TECHNICAL ITEM II

by

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OUTLINE

- Part I
  - Current knowledge of the disease
  - Knowledge gaps
  - Situation in Europe
- Part II
  - Outbreak in Israel
  - Field experience and dilemmas

LEGAL FRAMEWORK FOR LSD

- National legislation applied to LSD varies according to a Member State and in most countries a general contingency plan is applied to LSD
- Within the European Union, the general framework is given by the EC Directive 92/119/EEC and notification by the Council Directive 82/894/EEC
- Commission Implementing Decisions have been applied to individual countries (EU 2016/1500 and 2055 for Greece and EU 2016/645 for Bulgaria)
- International trade - The OIE Terrestrial Animal Health Code (Terrestrial Code) Chapter 11.11 on lumpy skin disease
- Manual of Diagnostic Tests and Vaccines for Terrestrial Animals LSD Chapter 2.4.13

FEASIBLE CONTROL AND ERADICATION OF LSD

- Varies between different countries and geographic regions due to different farming practices
- North – farms density is low, herds don't mix and are daily monitored, cattle spending most of the year inside during a long winter time with no insect activity
- South – Small-holdings are located in close proximity to each other, using communal and seasonal grazing, making the whole village as one epidemiological unit or free-ranging beef cattle kept on remote regions and are not frequently handled or monitored
- Swift culling of all infected and in-contact animals without vaccinations would work well in the North - whereas in southern countries partial stamping-out combined with 100% vaccination coverage is more feasible



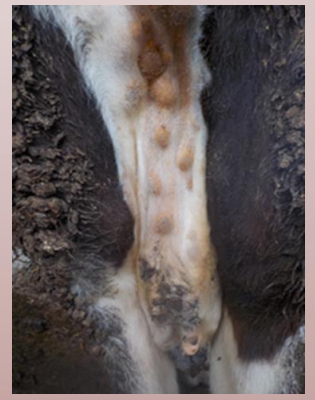

AWARENESS CAMPAIGNS - EARLY DETECTION AND PREVENTING OF MOVEMENT OF INFECTED ANIMALS

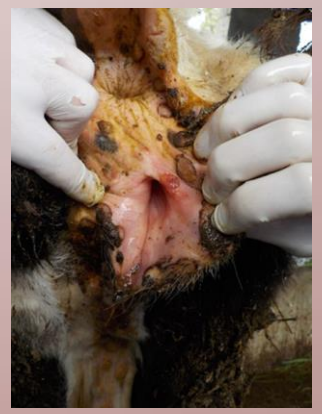
- Early detection is one of the major challenges – mild and early infections difficult to recognize even for most experienced veterinarians
- In free-ranging herds that are not monitored daily outbreaks may remain undetected for weeks
- Awareness campaigns should be targeted to personnel in key position to identify infected animals at a farm or prior to movements
- Official and private field vets, cattle owners, cattle traders, drivers of the cattle transport vehicles, slaughterhouse veterinarians and personnel of cattle collecting holdings and resting stations, as well as artificial inseminators
- Interests and motivation to report a new disease cases may vary between different stakeholders and interested parties

Photo courtesy Dr Milovanovič

TRANSMISSION OF LSDV REQUIRES FURTHER RESEARCH

- 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 – mutual grooming may play a role





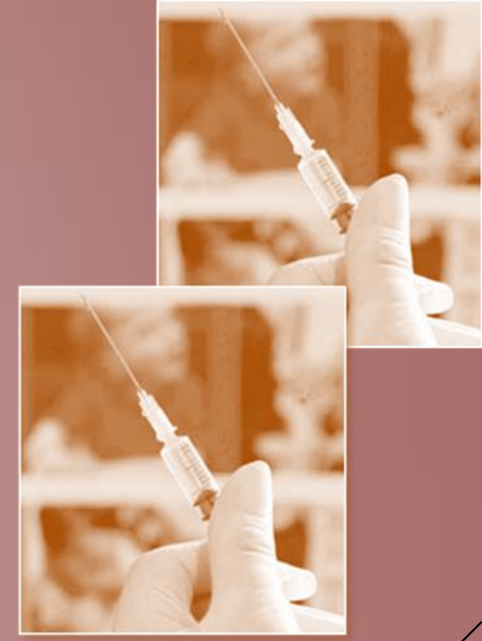
VECTOR CONTROL IN AFFECTED HOLDINGS

- Reducing number of vectors is likely to reduce the infection rate in cattle but it cannot prevent the spread of the disease
- Dips, sprays and spot-on product on animals (withdrawal period applies)
- Spray-on formulations used on housing and vehicles can give protection for up to three days
- Environmentally friendly way to reduce the number of vectors is by removal of suitable breeding sites
  - Improving drainage in the farm and removal of standing water sources
  - Removal of dung heaps
- Large-scale use of insecticides in the environment is debatable
- Potential harmful effect to ecological balance should be considered
- May affect honeybees and/or end up into honey and food chain

CHOOSING A VACCINE AGAINST LSDV

- Live attenuated LSDV vaccines provide good protection in cattle and is superior to sheeppox virus (SPPV) vaccines (Ben-Gera *et al* 2015)
- Only vaccines with demonstrated efficacy and safety should be used – independent vaccine challenge experiment at CODA CERVA
- 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

VACCINES ON THE MARKET



- LSDV containing vaccines:
  - LSDV Neethling strain by Onderstepoort Biological Products (OBP)
  - Attenuated LSDV field strain by MSD Animal Health
- SPPV containing vaccines against LSDV:
  - Yugoslavian RM65 SPPV vaccine (at a 10 times stronger dose than used for sheep) is commonly used for cattle in the Middle East
  - Romanian SPPV vaccine for cattle in Egypt
  - Bakirköy SPPV (3 times sheep dose) used in cattle in Turkey
  - Russian SPPV
- No DIVA (Differentiation of Infected from Vaccinated Animals) vaccine available
- Inactivated vaccines are expected to appear on the market shortly
- Huge increase in demand of vaccines has led to longer waiting times to obtain vaccines from manufacturers

VACCINATION REGIME AND ADVERSE REACTIONS

- Annual vaccinations
- Regional vaccinations should be preferred to ring vaccinations
- All animals should be vaccinated (100%) including pregnant females and young calves
- Calves from vaccinated mothers are vaccinated between 3 to 4 months of age
- Local reaction at the vaccination site should be accepted
- Some animals show general reaction caused by the vaccine virus; so called “Neethling disease”
- Diagnostic PCR assay available to differentiate between field and vaccine viruses

Photo courtesy Dr Shlomi Levi

WHY CLINICAL SIGNS ARE SOMETIMES DETECTED IN VACCINATED ANIMALS

- Herd is already incubating the disease when vaccinated
- Animals get the infected after vaccination but before the immunity has fully developed in vaccinated animals
- Insufficient vaccination coverage –pockets with unvaccinated animals left within vaccinated zones
- “Missing” of some animals during mass vaccination, particularly with free-ranging beef cattle
- Failure of the vaccine virus to protect, immunocompromised animals or over-attenuated vaccine
- Inappropriate storage or a failure of the cold-chain
- Poorly administrated vaccine or an incorrect dosage (mass vaccinations, free-ranging beef cattle not used to handling)
- Interfering maternal antibodies in calves less than four to six months of age

DIAGNOSTIC TOOLS AND REFERENCE LABORATORIES

- Tests:
  - For primary detection of the LSD virus - validated, specific and highly sensitive group-specific PCR methods
  - If clinical signs are detected in cattle vaccinated with a LSDV containing vaccine - PCR method to differentiate the attenuated vaccine from the virulent field strain
  - If clinical signs are detected in cattle vaccinated with a SPPV containing vaccine or in wild ruminants - Species-specific genotyping PCR methods
- National ref labs:
  - Competent staff, facilities, funding, equipment, kits, materials, reagents
  - Testing performed according to good laboratory practice
  - Appropriate QA system in place
- International reference laboratories provide diagnostic service, training, research and biobank of different strains/isolates – willingness to share the isolates for research purpose to address the current knowledge gaps on LSDV
- Proficiency testing (2016) is organized by the Austrian institute AGES together with the APHL of the Joint FAO/IAEA Division
- High transport costs of infected samples and heavy administrative procedures limit the sample dispatch from those affected countries that have to operate with limited resources
- Need to evaluate if current national and international reference laboratory capacities are sufficient for increasing sample numbers

CLINICAL, VIROLOGICAL AND SEROLOGICAL SURVEILLANCE

- Active and passive clinical surveillance can be challenging because of
  - Logistical problems to inspect cattle farms in remote mountainous areas, time-consuming hampering frequent monitoring
  - Free-ranging cattle that kept in remote regions are difficult to round up
  - Mild infections are difficult to detect from a distance and are easily missed if covered by a long winter coat
  - Farmers' capability to recognize the clinical signs of a new disease may be low
  - Lack of funding to employ sufficient numbers of veterinary inspectors and field veterinarians
- In general, molecular methods are highly specific and sensitive
  - In cattle showing mild infections viraemic stage may be only a few days and at low level, leading to false negative test
  - Sample collection should include blood, nasal swabs and skin (if showing lesions) samples from each animal, they can be mixed if three samples/animal cannot be afforded

LIMITATIONS OF SEROLOGY

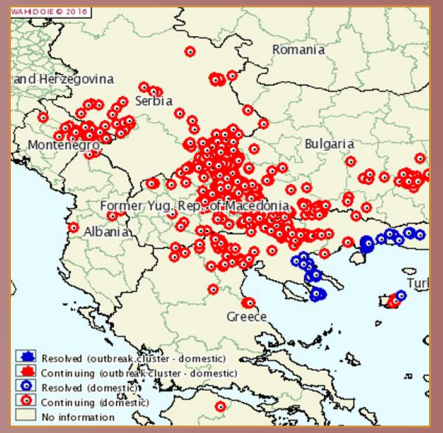
- In regions where vaccinations have not been practised, serological assays can be a used in high risk regions to look for unnoticed infections or potential under-reporting
- In vaccinated regions
  - Naturally infected cattle can not be serologically differentiated from vaccinated animals (no DIVA vaccine available)
  - Antibodies can be usually detected for three to six months after natural infection
  - After vaccination, antibodies appear within 15 days and reach the highest level in 30 days, dropping then below detectable levels, some vaccinated animals do not seroconvert although fully protected
  - Some individuals showing mild disease may develop only a low levels of neutralizing antibodies that cannot be detected using currently available neutralization test - Interpretation negative test result is challenging.
- Neutralization test is gold-standard but time- and labour-consuming and requires working with live virus and cell cultures, limited to bio security level 3 labs (IPMA validated in Coda Cerva)
- Urgent need for a DIVA vaccine against LSD as well as ELISA and an assay detecting cell-based immunity

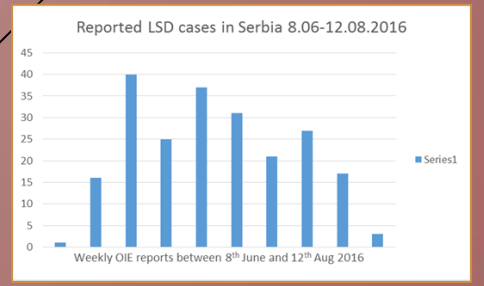
LIST OF KNOWLEDGE GAPS

- DIVA and inactivated vaccines
- Efficacy and duration of protection provided by different vaccines and vaccination protocols
- Efficacy of a LSDV vaccine for Asian water buffalo
- The efficacy and duration of passive (maternal) immunity on protection of young calves
- Duration of humoral response after natural infection and vaccination
- ELISA or other serological methods suitable for large-scale testing
- Cell based test to evaluate immunity against LSDV
- Simple and affordable pen-side test
- Presence of viraemic sub-clinical animals in affected herds
- Biological transmission occur in arthropod vectors
- Vector capacity of the European or Middle Eastern insect and tick species
- Effect of climatic and environmental changes to insect and tick populations and to the spread of LSDV
- Natural immunity against LSDV in cattle
- Susceptibility of European and Middle-Eastern wild ruminants and potential role of wildlife as a reservoir
- Susceptibility of different age groups
- Efficacy of the commonly used disinfectants against LSDV
- Presence of virus in different commodities

EFFECT OF VACCINATION IN THE BALKAN REGION

- Vaccination of the whole cattle population has been completed in
  - Bulgaria – by 15th July - the last outbreak on 1st August
  - Serbia –by 31st August - a total of 8 outbreaks in August mainly in unvaccinated animals and the last one 1st September
  - Montenegro – by 18th August, some outbreaks still on-going but are expected to cease
  - Former Yugoslav Republic of Macedonia – 99% of cattle vaccinated, the spread of the disease has stopped but a few sporadic cases reported
- Croatia – preventive vaccination campaign in high risk counties was started on 8th of Aug 2016
- Greece – vaccination of whole cattle population in good progress but hampered by lack of sufficient numbers of vaccines and funding. Number of outbreaks has decreased but are on-going in unvaccinated cattle





THANK YOU FOR YOUR ATTENTION!

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