http://dx.doi.org/10.20506/TT.2554

LUMPY SKIN DISEASE:

CURRENT SITUATION IN EUROPE AND NEIGHBOURING REGIONS AND NECESSARY CONTROL MEASURES TO HALT THE SPREAD IN SOUTH-EAST EUROPE

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Original: English

Summary: *Effective and safe vaccines against lumpy skin disease (LSD) are already commercially available. Large-scale vaccination combined with other appropriate control measures, can eliminate the outbreaks. In the absence of appropriate DIVA[3] vaccines, carrying out preventive vaccination against LSDV in disease free but at-high risk countries, inflicts heavy export restrictions on live cattle and their products, inhibiting these countries from vaccinating prior to incursion. Since despite massive vaccination in many countries there is no evidence of the vaccine strain regaining virulence or spreading of the disease via cattle products, lifting unnecessary trade restrictions should be advocated.*

As a sole control measure, stamping-out is rarely effective in stopping the spread of LSD and should be combined with vaccination. Culling infected and in-contact animals should remain as a primary measure when LSD is detected in a previously disease-free country. Removal of infected animals from the herds is feasible. However, discussions between Veterinary Authorities and policy makers should take place on the costs-benefits of total or partial stamping-out after vaccination campaigns have been initiated. Affected countries should be allowed to choose the most feasible culling policy for their circumstances, while respecting relevant international standards.

Regulation of cattle movements within and out of affected areas remains as a priority. Movement of unvaccinated cattle from affected and vaccinating zones should remain banned. However, in order to minimise the economic impact of the outbreaks and to increase farmers and traders cooperation, movement of fully immunised cattle should be allowed within or between vaccinated zones under strict supervision and according to the OIE international standards.

Current knowledge gaps on LSD need to be addressed. More funding is required to set up studies directly affecting disease control such as diagnostic methods, immunology, epidemiology, vectors and transmission.

Keywords: *Europe – lumpy skin disease.*

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1. Introduction

Lumpy skin disease (LSD) is a transboundary high-impact cattle pox disease characterised by fever, skin and visceral nodules. Lumpy skin disease virus (LSDV) shares the genus Capripoxvirus (CaPV) (family *Poxviridae*) with *Sheeppox virus* (SPPV) and *Goatpox virus* (GTPV) [1].

Despite implemented control and eradication measures, the disease is currently spreading widely in the Middle and Near East, South-East Europe and Northern Caucasus. Rapid and uncontrollable spread of LSD has found the cattle farming industry and Veterinary Authorities in many cases largely unprepared.

Successful control and eradication of LSDV relies heavily on early detection of outbreaks; swift laboratory confirmation of the tentative clinical diagnosis; rapid implementation of stamping-out of all or only those animals showing clinical signs of LSD; vaccination; strict animal movement control; quarantine; disinfection; vector control; and preventive bio security measures at affected farms and regions.

For many years LSD was confined to Africa. The disease was considered as an exotic cattle disease with minimal interest to the veterinary scientific community outside the endemic regions, with negligible research funding available. Consequently, there are major knowledge gaps on the characteristics of the causative agent, disease manifestation and the effectiveness of various disease control measures.

The aim of this report is to discuss the factors and challenges affecting successful control of LSD. In addition, the main gaps in our current scientific knowledge are identified.

2. Geographical distribution of LSD and the most recent outbreaks

LSD is widespread throughout Africa excluding Algeria, Morocco, Tunisia and Libya. In 1989 the disease was reported in Israel and since then sporadic outbreaks occurred in several Middle Eastern countries. In 2012, the disease appeared at the north-eastern border of Israel and spread since at an unprecedented scale within the Middle East. Outbreaks were reported from Lebanon, Palestinian Autonomous Territories, Jordan, Kuwait, Saudi Arabia, Iraq, and Iran. The first incursion of the disease in Turkey was reported in 2013, where LSD is currently an endemic disease. This was swiftly followed by outbreaks in the northern part of Cyprus, Azerbaijan, Armenia and Kazakhstan. Recently Dagestan, Chechnya and Krasnodar *kray* and Kalmykiyan Republic in southern Russia, as well as South Ossetia have reported LSDV outbreaks. As anticipated, in 2015 the disease spread from Turkey to Greece, followed by outbreaks in 2016 in Bulgaria, the Former Yugoslav Republic of Macedonia, Serbia, Albania, Montenegro and Kazakhstan. Currently, there is a high risk of further spread of LSD within the Caucasus region and South-East Europe.

3. Legal framework for the control of LSD

The *OIE Terrestrial Animal Health Code* (*Terrestrial Code*) Chapter 11.11 on lumpy skin disease (caused by group III virus, type Neethling) [2], which is currently under revision, establishes the international standards on disease control and safe international trade. Recommendations for diagnostic assays and vaccines are given in Chapter 2.4.13 of the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* [3].

Each country has its own national legislation applied to LSD. Within the European Union (EU), notification of the disease is regulated by the EU directive 82/894/EEC of 21 December 1982, intra-community trade in live animals and their products by EU 90/425/EEC of 26 June 1990, as well as control and eradication measures in EU 92/119/EEC of 17 December 1992.

Specific regulations for affected countries include Commission Implementing Decision (EU) 2016/1500 and 2055 concerning certain protective measures against lumpy skin disease in Greece and Commission Implementing Decision (EU) 2016/645 concerning certain protective measures against lumpy skin disease in Bulgaria.

4. Early detection of infected animals in the field

The incubation period of LSDV varies from four days to five weeks [4]. For the purpose of the *Terrestrial Code* the incubation period was established to be 28 days [2]. Approximately a week after experimental infection, animals develop high fever and show ocular and nasal discharges. Typical elevated LSD skin nodules are of 10–50 mm in diameter, and usually appear first in the skin of the head and neck but can be found anywhere. The number of nodules varies from few in mild cases to multiple nodules covering the entire body. Noticeably enlarged prescapular and precrural lymph nodes are a usual finding in infected animals. Small round necrotic pox lesions appear in the muzzle, tongue, oral and nasal mucous membranes. Internal pox lesions may spread throughout the entire digestive and respiratory tracts. Oral lesions may cause problems in eating and lesions in the digestive tract may hamper digestion and absorption of nutrients, leading to weight loss and emaciation. Deep skin nodules in the legs may cause severe lameness. Udder lesions can cause mastitis and scrotal lesions temporary infertility. In some animals painful ulcerative lesions can be found in the cornea of one or both eyes, causing blindness in severe cases [5].

Early detection of infected animals and rapid laboratory confirmation of the tentative field diagnosis are the cornerstones of successful control of the disease. Characteristic clinical signs of LSD are clearly recognisable in severely infected animals, yet early stages of infection and mild cases can easily go unnoticed, even by most experienced veterinarians. This is particularly the case when an outbreak occurs in cattle that are not frequently monitored or handled. In addition, skin lesions hidden under the longer winter coat of cattle are difficult to detect.

Thus, it is not rare that the index herd is only detected when some of the animals are already showing multiple skin nodules, each one containing high quantities of virus. At that point of time the virus has probably been circulating for weeks in the herd providing plenty of time for blood-feeding vectors to transmit the disease to nearby herds.

5. Awareness campaigns

The early recognition of the clinical signs of LSD in affected farms and understanding the modes of transmission are prerequisites for successful prevention, control and eradication of the disease. Awareness campaigns should be targeted to official and private, field and abattoir veterinarians, farmers, herdsmen, cattle traders, drivers of the cattle transport vehicles and artificial inseminators, who are all in a key position to identify infected animals on farms, slaughterhouses, cattle collecting holdings and resting stations and to notify the Veterinary Authorities of such clinical suspicions as soon as possible. It should be remembered that interests vary and motivation to report new disease cases differs between different stake holders and interested parties.

6. Diagnostic tools and reference laboratories

Diagnostic capacity of the national reference laboratories (NRL), a further prerequisite for successful control and eradication of LSD, relies on competent personnel and sufficient equipment, materials, reagents and funding. Availability of molecular, virological and serological diagnostic tools, according to the OIE international standards, allows swift confirmation of a tentative field diagnosis, epidemiological investigations during the outbreaks and post-outbreak sero-surveillance. Accreditation of methods according to appropriate quality assurance (QA) systems such as ISO 17025 is recommended and testing of samples should be performed according to good laboratory practise.

Routine tests for LSDV diagnostics include molecular group methods for the detection of a CaPV [6–11]. Several species-specific PCR methods have been published [12–15]. Species-specific tests are needed when typical clinical signs of LSD are detected in wild ruminants. When vaccine containing attenuated SPPV is used in cattle against LSDV, the species-specific assay can be used to differentiate if clinical signs detected in vaccinated animals are caused by the vaccine or field virus. However, these assays are not useful if vaccines containing LSDV are used.

If vaccines containing attenuated LSDV are used in cattle against LSDV, specific molecular tools for differentiating a virulent field strain from a LSDV vaccine strain have been developed [16, 17] and are used in some NRLs. Alternatively, sequencing of appropriate parts of the LSDV genome

can be used for this purpose [18]. Currently, for those vaccines containing attenuated LSDV a DIVA PCR kit is in its final step of becoming available on the market. The first PCR method suitable for portable thermocycler has been described [19]. There is an urgent need for an easy-to-use, affordable pen-side kit for LSDV.

Serological assays are suitable to investigate relatively recent outbreaks and can be used to demonstrate the disease-free status of a country provided that testing is carried out on regular intervals (every three to six months). Currently available tests include serum/virus neutralisation tests (SNT) which is a gold standard assay. In addition, immunoperoxidase monolayer assay (IPMA) [20] and indirect fluorescent antibody test (IFAT) [21] can be used for serological surveys. Although SNT is labour- and time-consuming, it can be modified slightly to increase a number of samples tested on one plate and to reduce the time to read the results [22]. Currently no ELISA for LSD is commercially available.

As there are no vaccines against LSDV which would contain a specific DIVA component, serology is not useful after the onset of vaccination campaigns. It is important to note that in those situations when the outbreaks have occurred more than a half year ago, the humoral response has diminished and immunity is already mainly cell-mediated. Consequently, cattle may be seronegative although they would have been infected and would be fully protected [5, 23].

LSD is already endemic in Turkey and there is a high risk that the disease becomes endemic in Europe as well. More and more expertise is swiftly building up in the NRLs within the affected region. In general, laboratory capacities are already at a good level, QA systems are in place and testing is performed according to good laboratory practice.

Substantial increase in sample quantities is expected when post-outbreak affected countries would wish to demonstrate their disease-free status, placing the existing international and national reference laboratories under pressure in regard their sample testing capacities. It should be investigated if there is a need for an international reference laboratory that would be located within the affected region, reducing time, costs and paperwork associated with sample transport. Current high sample transport costs and associated heavy administrative procedures are limiting the sample dispatch from those countries that have to operate with limited resources.

More European institutes with a wide collection of different LSDV isolates are required. Willingness to share the virus isolates for research purposes with international scientific community should be the basic requirement for all the institutes and laboratories supported by the international organisations.

7. Transmission of lumpy skin disease virus

7.1 Vector-borne transmission of LSDV

Transmission of LSDV occurs mechanically by numerous blood-feeding insect and tick vectors. Biological transmission has not been demonstrated but cannot be excluded. Due to the vector-borne nature of LSD, outbreaks in European climate are seasonal, more common but not restricted to hot and humid seasons with abundance of suitable active vectors.

Frequent and often interrupted feeding on several hosts is the basic requirement for vectors to be able to transmit the virus mechanically via their mouthparts from infected to naïve animals. The major arthropod vectors may vary between affected regions as different arthropod species favour different ecosystems. Viral transmission via insects from dead infected cattle to naïve live animals is a possible risk not sufficiently studied.

Global warming effect on insect and tick populations may be associated with the northbound spread of LSDV. However, existing local blood-feeding arthropod species are likely to be effective transmitters of the virus.

The common stable fly (*Stomoxys calcitrans*) has often been the culprit suspect for transmitting LSDV, although sound scientific evidence is still lacking. Transmission of the virus from infected to naïve cattle by female *Aedes aegypti* mosquitos has been experimentally demonstrated [24].

Experimental evidence have been published on the transmission of LSDV by African hard (ixodid) tick species (*Rhipicephalus* and *Amblyomma* spp) of which adult males feed several times and change hosts [25–27]. Transmission of the virus by tick vectors is likely to be mechanical as no evidence has so far been obtained for actual multiplication of the virus in ticks. Some evidence has been obtained on venereal transmission by tick vectors [28]. In case the virus can persist in tick eggs and second generation larvae, it may contaminate the environment such as grazing grounds and may partly explain where the virus resides between outbreaks and seasons.

Experimental demonstration of the virus transmission by vectors is challenging and expensive in a controlled laboratory environment. A challenge model for LSDV for vaccine efficacy studies has recently developed by the scientists at Coda-Cerva, Belgium [De Clercq, unpublished data] and can be utilised in vector studies as well.

7.2 Other modes of transmission

In endemic regions in Africa, LSD outbreaks typically occur in epidemics with several quiescent years between the outbreaks [29] and it is not known where the virus resides between the outbreaks. The index case can often be associated with legal or illegal transfer of cattle between farms, regions or even countries. This is also supported by observation that the outbreaks occur along the major cattle transport routes [5]. Efficacy of LSDV transmission by direct contact is considered to be relatively ineffective although more studies are required to confirm this statement. Iatrogenic intra- or inter-herd transmission may occur when clinical or sub clinical cattle already incubating the virus are vaccinated or treated by injection without changing needles between animals or herds. Affected animals, excreting infectious virus in saliva, nasal and ocular discharges [30] may contaminate shared feeding and drinking sites. Further research is required to investigate transmission via licking stones and mutual grooming between animals. LSDV is known to persist in semen of infected bulls and therefore natural mating or artificial insemination may be a source of infection for the females [31]. Importantly, vaccination using an attenuated LSDV containing vaccine prevented bulls from excreting the challenge virus in to the semen [32]. Infected pregnant cows are known to deliver calves with skin lesions [33]. Recently, the potential role of air currents in a long-distance transport of LSDV contaminated insects has been investigated in Israel [34].

8. Setting up protection and surveillance zones

Vector transmission highlights the importance of mass vaccination campaigns in control of LSD. If ring-vaccination is used, the radius of protection and surveillance zones should cover the flying range of the vectors. A minimum of 50-km-radius restricted zone should be implemented. However, since there are often several disease foci at the same time and area, the vaccination and protection zones should ideally be decided based on sound epidemiological and geographical parameters rather than the classical radius shape.

9. Control of vector populations

Efficient insect control on cattle or farm facilities may reduce the rate of mechanical transmission but cannot totally prevent it. In many countries cattle are free roaming or kept in fenced pastures, making repeated handling and restraint impractical or very costly. If insecticides are used registration and withdrawal time for milk and meat needs to be considered. Large-scale use of insecticides in the environment is not recommended as it may be harmful for the ecological balance and the risks for the environment are not fully understood. Limiting vector breeding sites, like standing water, slurry and manure is a sustainable, affordable and environmentally friendly way to reduce blood-feeding insect populations on and around cattle.

10. Animal movement restrictions

The onset of an outbreak is usually preceded by presence of naïve susceptible animals, legal or illegal/uncontrolled animal movements and abundance of active blood-feeding vectors, generating optimal conditions for the spread of LSDV. The index case (be it the first incursion or re-emergence of the disease) usually occurs as a consequence of introducing new animals into a herd

or to its close proximity. Transport of viraemic cattle with sub-clinical or unnoticed infections is one of the main risk factors for LSD spread. The literature states that the morbidity rate varies between 2 to 45% but it is often an underestimation due to undetected mild clinical cases [35]. Transhumance and nomadic farming practices further complicate disease control and vaccination of animals moving over long distances should be a priority.

As cattle transport vehicles and slaughterhouse yards are rarely insect-proof, animals originating from vaccinated herds from restricted area and shipped for slaughter in a disease-free area, need to be certified as free of LSD prior to dispatch. Properly vaccinated animals pose a low risk of spreading the disease. However, not all vaccinated animals develop full immunity and even vaccinated cattle have to be clinically checked and certified as LSD free prior to transport following the recommendations of the *Terrestrial Code* Chapter 11.11 on LSD.

The currently used homologous vaccines are shown to produce proper herd immunity. Yet detection of few sick animals in a vaccinated herd is possible due to various reasons from vaccine handling to vaccination execution and even immune-compromised individuals. Maternal antibodies may impede development of immunity in young calves [36]. In case a sheep pox vaccine is used in cattle, protection at an individual level is not as good as for LSDV vaccines [37]. Development of full immunity against LSDV takes approximately two to three weeks. Animals infected during that period may develop a clinical disease.

11. Biosecurity at farm level and disinfection of affected farms

During an outbreak, farm biosecurity should be raised to the highest practically possible level. As the disease spreads by vectors, it may not totally prevent the incursion but such risk can be reduced.

Purchase of new animals that are either incubating the disease or are viraemic without showing any skin lesions is a major risk for introducing the disease into a naïve herd. Therefore it should be limited to animals that fulfil the recommendations of the *Terrestrial Code* Chapter 11.11 on LSD and new animals should be examined to be free of clinical signs prior to movement and should be kept separated from the herd for 28 days.

Farm visits should be limited to essential services. All visitors should wear clean protective clothing and shoe covers before entering the holding.

LSDV is very stable and survives well freezing and drying and pH range from 6.3 to 8.3. Scabs from skin lesions are shed into the environment by infected animals and are known to harbour infectious virus for several months. Although LSDV is sensitive to most disinfectants and detergents, in order to effectively disinfect animal facilities and holdings, mechanical removal of surface material such as dirt, manure, hey and straw is required before disinfection. The disinfectant must be able to penetrate the organic material that the virus may be surrounded by in the environment. Efficacy study on disinfectants against LSDV should be performed.

12. Vaccination

Once LSD has entered a new country or region in more than a single site, a large-scale vaccination campaign is the most effective way to control further spread of LSDV. Mass vaccinations should be conducted around infected holdings and throughout the protection and surveillance zones. The vaccinated area should include the whole affected region targeting 100% vaccination coverage. No pockets of unvaccinated animals should be left within or between vaccinated zones. Vaccination is essential around slaughterhouses, live animal markets, cattle collection and resting places, carcass disposal and rendering plants. Prevention of the further spread of the virus to disease-free regions and countries should be prioritised.

Only live attenuated vaccines are currently available and their use needs to be authorised in non-endemic countries. Molecular characterisation should be mandatory for all vaccines used against LSDV. Two most commonly used vaccines produced by *Onderstepoort Biological Products* and by *MSD Animal Health* were confirmed to contain LSDV by the Pirbright Institute reference laboratory, using species-specific PCR method [Tuppurainen, unpublished data, 2014]. A Kenyan vaccine commonly used against LSDV and produced by *Kevevapi* was believed to contain LSDV.

However, recent study has demonstrated that the vaccine virus is actually a GTPV strain [38]. Kenyan sheep and goat pox (KSGP) virus O-240 and 180 vaccines were identified to be actually LSDV virus [13, 39–41].

Independent challenge experiments, evaluating safety and efficacy of all live vaccines currently used in cattle against LSDV and two newly developed inactivated vaccines, are on-going by the scientists at CODA-CERVA, Belgium [De Clercq, unpublished data]. Publication of the results is expected shortly.

Equally important is to confirm the purity of the vaccine as the currently available vaccines are manufactured using primary cells which makes quality assurance difficult and may cause issues with endogenous agents and other contaminants. As the primary cells usually originate from small ruminants and from regions where diseases such as foot-and-mouth disease, bluetongue, Rift Valley fever, peste des petits ruminants and rabies occur, rigorous purity testing and Good Manufacturing Process (GMP) are basic requirements for production of a vaccine used against LSDV. Currently, there are no commercially available vaccines against LSDV with a DIVA-component.

As there are only a few LSDV vaccine manufacturers, the sudden increase in demand of vaccines has led to slightly longer delivery times by the manufacturers and occasionally there is a waiting period of several weeks for supply. Internal legal processes in the affected country or lack of funding have also caused delay in the onset of vaccination campaigns.

Restrictions to or ban of international trade of live animals and their products are the major causes why countries at-risk are hesitating to start preventive vaccination campaigns prior to the actual incursion of the disease.

In some areas in the Middle East, farmers have used vaccines obtained from 'black markets' [42]. The use of unauthorised vaccines should be avoided as they are often unlabelled and the real identity and titre of the vaccine virus is unknown. These may have been diluted, contaminated with adventitious pathogens, expired or inappropriately stored.

13. Vaccines against lumpy skin disease

13.1 Live attenuated LSDV vaccines

The most commonly used live LSDV vaccines are derived either from the South-African LSDV Neethling strain or an attenuated LSDV field strain and are manufactured in South Africa. The efficacy of homologous LSDV containing vaccine is superior to that of SPPV vaccine [37]. Live LSDV vaccines are cheap (currently € 1.5–2.0 per dose) and although no vaccines can provide 100% immunity to every individual animal, these vaccines provide good protection if sufficient herd coverage is achieved (over 80–90%) and is maintained by annual boosters [36].

13.2 Live attenuated SPPV and GTPV vaccines against LSDV

LSDV, SPP and GTP viruses are very similar, more than 95% identical on a genome level [40, 43] but still phylogenetically different species that share cross-protection at a various degree.

SPPV and GTPV sourced vaccines can be used in cattle but it is essential that their safety and efficacy against LSDV is demonstrated by using a challenge experiment in a controlled environment. SPPV vaccines, such as the Yugoslavian RM65 SPPV (10 times stronger dose than used for sheep) and the Romanian SPP vaccine have been used also in cattle in the Middle East, and the Bakirköy SPPV (at three times sheep dose) is in use in Turkey.

13.3 Inactivated vaccines

It is believed that a replicating agent generates more broad protective immunity against LSDV than a non-replicating one. However, a recent study has shown that inactivated SPPV vaccines can produce a protective immunity in sheep, comparable to that provided by a live

SPPV vaccine [44]. An independent efficacy study on inactivated SPPV and LSDV vaccines against LSDV is on-going at the Coda-Cerva and results will be published soon.

14. Stamping-out policy

Total or partial stamping-out policies of infected cattle or herds have been implemented by various countries and are widely discussed by experts and decision makers.

Total stamping-out can be effective and practical if the first incursion to a country or defined region is detected and notified on time and the threat of repeated incursions is low. In real life scenarios, the time span between infection and detection of the disease can be several weeks, allowing the spread of the virus by vectors. Once the disease is well established the efficacy of total or partial stamping-out declines. The practicality of identifying all sick animals, especially mild and early cases, in all infected herds and implementing a total stamping-out in a short time may be extremely challenging and may prove to be both expensive and ineffective. Partial stamping-out by culling only generalised sick animals may reduce intra-herd infectivity but will not end the outbreak on its own [45].

The cost-benefit analysis of stamping-out versus vaccination should be evaluated for different scenarios, infected and vaccinated herds and different countries. From the experience of some countries it appears that wide enough vaccination using an effective vaccine, well ahead in time and place of the spread of LSD, is effective to bring an outbreak to a total halt without total or in some cases even partial stamping-out. The long term effect of stamping out on farmers livelihood, economy and sustainability, public perception and media involvement should be considered while decision making.

15. Surveillance programmes

Surveillance programmes are based on active and passive clinical surveillance and laboratory confirmation mostly by testing blood samples, nasal swabs or skin biopsies collected from suspected cases. Because in currently affected countries or zones the entire cattle population are vaccinated, serological surveillance cannot be used. However, serology is useful in case the presence of unnoticed/unreported outbreaks are investigated in disease-free regions either bordering or in close proximity to affected regions where cattle are not yet vaccinated. Presence of seropositive animals can be considered as an indication of recent outbreaks that have occurred within six months of time.

16. Identified knowledge gaps and opportunities for a research

- 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 occurrence 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.

17. Conclusions and recommendations for enhanced control and eradication of LSDV

Movement of cattle is a major risk for the spread of LSDV. Unnoticed mild infections and viraemic sub-clinical animals will effectively spread the disease via movement of breeding animals, seasonal grazing, trade and slaughter. Transboundary spread may occur via unauthorised trade of live animals and grazing in the border regions.

When the disease occurs for the first time in a disease-free country, culling of infected and in-contact animals is the recommended primary control measure and is the most efficient when the index case is detected at a very early stage of an outbreak, although it is known to be challenging in real life situations in many countries. Any time span between infection and stamping-out allows time for blood-feeding vectors to spread the virus locally.

Animals showing severe clinical signs with multiple skin lesions should be always removed from affected herds as these nodules contain high titres of virus. It is essential for a feasible stamping-out policy to clearly define the borders of the epidemiological unit, particularly when the outbreak occurs in a village where numerous small-holdings are in close proximity to each other and/or communal grazing is practiced.

However, in case a single animal showing characteristic clinical signs of LSD is detected in a vaccinated herd in areas where surrounding herds are vaccinated, efficacy as well as the pros and cons of culling the whole vaccinated herd need to be evaluated case by case. In these cases, the usefulness of total or even partial stamping-out is doubtful. The whole stamping-out process, including disposal of carcasses, staff costs, disinfection and compensation to farmers is expensive for governments and the inability to repopulate a farm with new cattle and renew business for several months is costly and stressful for farmers. In practice disposal of carcasses is challenging and the amount and capacity of rendering plants is usually limited. Burning or burying larger numbers of culled animals at the farm have both environmental and public health concerns although in some cases it is the most feasible or practical option.

Total stamping-out of a vaccinated herds may lead to decreased willingness of farmers to vaccinate or to report new cases. Sometimes skin lesions in vaccinated cattle may be caused by the vaccine but there are diagnostic methods available to differentiate between field and vaccine strains. Culling of herds is highly stressful for cattle owners, herdsmen and veterinarians. Money hardly compensates for years of farming tradition or breeding achievements. In any case, animals used for restocking should be vaccinated against LSDV prior to the introduction to a farm.

Total or partial restrictions of export of live animals and their products are the major causes why at-risk countries are hesitating to start preventive vaccination campaigns. Skeletal meat is considered as a safe commodity in the OIE *Code* LSD Chapter 11.11. However, no report exists on spreading of LSDV via cattle products that are appropriately pasteurised or otherwise treated to destroy the LSDV and originating even from affected countries. The actual likelihood for these products to come into contact with live susceptible cattle is very low. In order to increase the willingness of disease-free but at-risk countries to commence preventive vaccination campaigns in their territory, potential for temporary exemption or shortening the duration of export restrictions on live animals and their products should be investigated.

However, movement of unvaccinated live cattle from affected and vaccination zones should remain banned or strictly regulated. Movement of vaccinated animals after full immunity has been obtained could be allowed if sufficient control measures preventing accidental release of an infected animal are in place.

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