Food and Agriculture Organization of the United Nations

FAO ANIMAL PRODUCTION AND HEALTH



position paper

SUSTAINABLE PREVENTION, CONTROL AND ELIMINATION OF LUMPY SKIN DISEASE

Eastern Europe and the Balkans

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2

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Eastern Europe and the Balkans

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS
Rome, 2017

Recommended Citation
FAO. 2017. *Sustainable prevention, control and elimination of Lumpy Skin Disease – Eastern Europe and the Balkans*. FAO Animal Production and Health Position Paper. No. 2. Rome, Italy.

ISBN 978-92-5-109937-7

Table of contents

Summary

The benefits of effective disease control must be balanced against the costs of the control measures applied. Lumpy skin disease (LSD) is recognized as a major threat to cattle and cattle production, with substantial impacts on livelihoods and food security, particularly among smallholders. It is also a World Organisation for Animal Health (OIE) -listed disease, absence of which may provide trade advantages. But LSD is not a zoonotic disease and hence poses no direct risk to human health. As it is primarily transmitted mechanically, by biting arthropods, import controls on livestock and products cannot fully mitigate the risk of the causative agent (LSD virus, or LSDV) being introduced across borders from neighbouring, infected regions. Vaccination of cattle under all production systems with live, attenuated LSDV vaccines is the most effective way to prevent the spread and persistence of the virus and should be combined with controls on movements of susceptible animals which can seed infection into non-affected areas. Stamping out can help improve control measures if the disease is recognized and reported promptly, especially when it was introduced into a previously infection-free country and vaccination has either not been, or was inadequately, applied. However, the frequency of subclinical infection and the absence of good serological tests undermine the reliability of surveillance. Conversely, if vaccination is applied comprehensively, i.e. using high coverage in a large enough area, only modest additional benefits (in terms of certainty and speed of eradication) can be expected from stamping out. The strategy may thus be hard to justify where reintroduction of the disease remains a constant threat, especially considering the damage caused by this measure to livelihoods, and its high economic cost. Furthermore, if vaccination is applied comprehensively, partial stamping out (i.e. humane culling of only clinically affected animals) is likely to be nearly as effective as a full-scale stamping-out programme, although at significantly less expense. While no relevant cost-benefit studies have been undertaken yet, it seems that preventive vaccination in a sufficiently wide buffer zone is a logical approach to protecting a disease-free country from LSDV contagion when the virus is present across a border, taking into account geographical contours, vehicle transport access and host population densities.

Lumpy skin disease

Lumpy skin disease is caused by a Capripox virus (LSD virus – LSDV) closely related to goat pox virus (GTPV) and sheep pox virus (SPPV). The clinical disease is characterized by the appearance of highly visible nodules on the skin of cattle. Other findings may include fever, oedema, lymph node enlargement, and pox lesions on mucous membranes and internal organs. Production losses stem from lower milk yields and body condition, damage to hides, abortion and infertility. Cattle are the primary host, but LSDV can sometimes infect Asian water buffalo (El-Nahas *et al.*, 2011) and, rarely, small ruminants, the latter asymptomatically. Those inexperienced in recognizing LSD can mistake it for many other conditions, for instance bovine herpes virus 2 (Allerton) infections; delayed hypersensitivity reactions following foot-and-mouth disease vaccinations; insect bites; streptothricosis; hypodermal bovids; besnoitiosis; or demodicosis (Davies, 1991). Laboratory confirmation is therefore essential.

Transmission

Transmission of LSDV is mainly associated with mechanical transfer of virus by an incompletely characterized range of biting arthropods, such as mosquitoes (*Aedes aegypti*), stable flies (*Stomoxys calcitrans*) and possibly ticks, feeding on live infected hosts (Carn and Kitching, 1995; Coetzer, 2004; Tuppurainen and Oura, 2012; Tuppurainen *et al.*, 2013). Spread of the disease is facilitated by warm, moist conditions that favour insects. Movements of cattle and vectors may allow virus to jump over long distances, and airborne spread of disease by vectors over more than 100 km has been suggested (Yeruham *et al.*, 1995). There is little evidence that topography interferes with virus spread and outbreaks have been reported in Turkey at altitudes of 1300 m (Saraç *et al.*, unpublished). It is not known if non-biting arthropods that feed on live or dead animals can also transmit virus mechanically. Large herd sizes and proximity to lakes have been associated with an increase in LSD prevalence in Turkey, and European cattle breeds are found to be particularly susceptible (Sevik and Dogan, 2016).

Spread of LSDV from animal to animal without a vector seems to be very inefficient. Meat is not considered to be a significant transmission risk, but infection through milk and semen is possible. The risk posed by milk not destined for animal consumption is probably negligible and can be mitigated by pasteurization and transportation in closed containers. Raw hides are more likely to be contaminated with virus than meat or milk and the OIE Terrestrial Animal Health Code requires 40 days' storage of raw hides prior to importation from LSD-infected countries (OIE, 2016). As noted, LSD is not a zoonotic disease, i.e. LSDV cannot be transmitted from cattle to humans and hence poses no direct risk to human health.

Geographical Distribution

LSD was first described in southern Africa, where it has occurred sporadically, attributed to changes in vector insect abundance and population immunity (Hunter and Wallace, 2001). The disease has spread northwards through sub-Saharan Africa, where it probably occurs in all countries except Libya, Tunisia, Algeria and Morocco (Figure 1). It was first reported in Ethiopia in 1983 (Mebratu *et al.*, 1984), Egypt in 1988 (House *et al.*, 1990), and emerged in the Middle East in Israel in 1989 (Yeruham *et al.*, 1995). LSD was reported again in Egypt in 2006 and rapidly spread throughout the country (Tuppurainen and Oura, 2012). Further outbreaks occurred in southern Israel in 2006 and 2007, with first appearance in the north of the country in 2012 (Sharir, 2012, unpublished report). In the same year, outbreaks occurred in neighbouring Lebanon, possibly due to infected animals imported from Sudan. Oman has reported cases from 2010 onwards and since 2011 LSD has become widespread in the Middle East, aided by civil unrest. The disease was reported from Turkey, Iraq, Jordan and Palestine in 2013 (Ababneh *et al.*, 2013), Iran and Kuwait in 2014 and Bahrain and Saudi Arabia in 2015.

Figure 1
Map showing when lumpy skin disease was
first reported in different countries
(LSD may be endemic throughout sub-Saharan Africa)

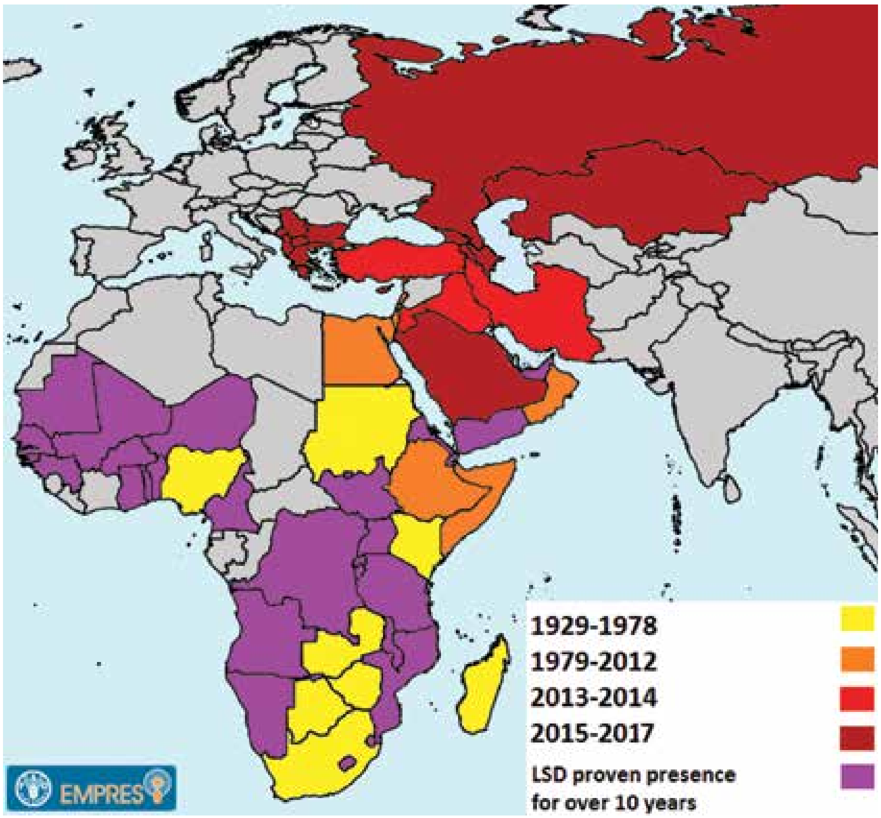
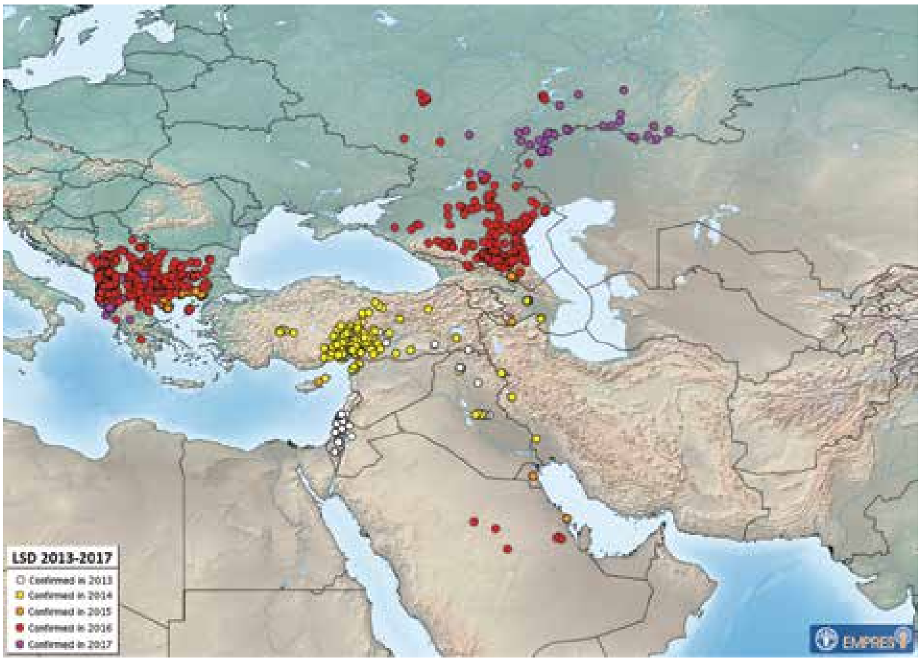


Figure 2
Map showing the recent outbreaks in the Middle East ,
Turkey, the Balkans and Eastern Europe/ Central Asia (2013-2017)



With outbreaks continuing in Turkey, the virus spread to Cyprus (2014) and has travelled northeast through the Caucasus, affecting Azerbaijan (2014), Armenia and the Russian Federation (2015) and Georgia and Kazakhstan (2016). In 2015, following occurrences in the Turkish region of Thrace, Greece became infected and, although there were no new cases during in the winter, they resumed in April 2016. That year, the virus spread to Bulgaria, the former Yugoslav Republic of Macedonia (FYROM), Serbia, Montenegro, Kosovo[1] and Albania (OIE WAHIS Interface). Currently there is a threat to Central Asia and Europe.

Analysis of incursion risk

Collection of full information about outbreaks, risk factors, epidemiological enquiries, vaccination coverage, vaccine breakdowns, etc. is essential in order to establish and quantify risk factors for the spread of infection. Countries should have a cattle identification database that includes vaccination and laboratory test results at both individual and herd levels. Given the vector-borne nature of the disease, this should be combined with geographical information (lakes, rivers, roads, topography, etc.) and climatic data.

[1] This designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244 and the International Court of Justice opinion on the Kosovo Declaration of Independence.

Understandably, outbreak response and control operations, particularly in emergencies, tend to take priority over activities directed at improving future understanding and prevention efforts. For example, during culling, sampling of statistically sound sample sizes of animals to evaluate the performance of diagnostic tests, as well as vector investigations, may be neglected despite their importance.

Collaboration should be established between veterinary services of affected and at-risk countries and national and international specialists in epidemiology, modelling, diagnosis and vector biology, as well as with the private sector. Such collaboration makes it possible to evaluate questions that can only be answered during outbreaks, such as which vectors are carrying LSD virus and how far they can fly, what is the attack rate of animals in affected herds, or what are the antibody dynamics of immune response to infection and to vaccination. Small longitudinal studies to follow up outbreaks or vaccination are also required and a portfolio of study designs could be drawn up. Potential sources of funding for such studies should be identified from interested stakeholders in the government, private sector or international organizations. Socio-economic studies on how LSD outbreaks impact on the whole value chain, as well as cost-benefit analyses of different prevention and control strategies, are also important as an additional tool for policy and decision makers.

Vaccines

Live, attenuated capripoxviruses are used to prevent clinical signs and to control transmission or persistence of the wild-type virus. The attenuated Neethling strain of LSDV was developed in South Africa and has been used as a vaccine for many years. Some vaccinated animals develop a vaccine reaction known as "Neethling disease" (Ben-Gera *et al.*, 2015). The duration of post-vaccination immunity is poorly understood so annual revaccination is recommended by vaccine manufacturers. Additional studies are therefore needed to fill this important knowledge gap so as to develop appropriate vaccination strategies. The vaccine is given subcutaneously, usually in 1 or 2 ml doses, depending on the type of vaccine used. Maternal immunity can block an acquired immune response in vaccinated calves under six months of age (Hunter and Wallace, 2001). Calves from unvaccinated cows may be vaccinated at any age. If possible, all animals should be vaccinated during spring before vector activity begins. New vaccines are under development, but with current formulations it is not possible to distinguish antibody responses from infection with wild-type virus from those determined by vaccination (DIVA testing). The practical value of post-vaccination monitoring using serology should therefore be closely evaluated. Nevertheless, serological studies with vaccinated cattle have shown that many animals resist challenge with virulent LSD when they have no detectable neutralizing antibody to the virus. However, most animals do show a serological response after field infections with LSDV and, by 28 days after vaccination, animals should develop protective immunity and should not transmit infection. Most outbreaks occurring in vaccinated holdings in Greece, Bulgaria and Serbia in 2016, where reactive vaccination was used, took place within 14 days of vaccination, although a clinical case was reported in Serbia after 19 days. This should be taken into consideration when applying emergency vaccination in at-risk herds. Further, the relative risk of transmission from recently vaccinated animals that become subclinically infected remains to be determined. As the Neethling-strain vaccine is manufactured in South Africa and is not licensed in Europe, it cannot be guaranteed to meet European Good Manufacturing Practices (GMP) requirements. To mitigate this, batch quality testing for potency and innocuity should be conducted locally, as has been done in Israel (Bumbarov *et al.*, 2016), or in collaborating reference laboratories.

Heterologous SPPV or GTPV vaccines have been used instead of attenuated LSDV as well, often at increased dosage compared to the one for small ruminants. Field studies during LSD outbreaks in Israel in 2013 showed that the Neethling vaccine was more effective in preventing LSD morbidity than the RM65 SPP vaccine at ten times the small-ruminant dose, as determined by clinical observation. There was a low incidence of Neethling disease (0.5%), but no observed transmission of the Neethling strain to non-Neethling vaccinated cows (Ben-Gera *et al.*, 2015).
Vaccination remains the cornerstone of LSD control in Eurasia and Africa. In Israel, in 2013, vaccination proved effective in controlling LSD with only limited use of stamping out. All of the Balkan countries affected by LSD in 2016 used the Neethling vaccine, either obtained from EU reserves or directly sourced from two South African manufacturers. In the Russian Federation and The former Yugoslav Republic of Macedonia, modified stamping out was used in vaccinated herds and only clinical cases were culled, whereas in Albania, stamping out is not applied in vaccinated herds. The EU Commission Implementing Decision 2016/2008 was established to allow preemptive vaccination but it still requires Member States to cull all animals in an infected herd, even if the herd was vaccinated (Commission Implementing Decision, 2016). Unfortunately, trade penalties for countries vaccinating preemptively act as a disincentive to regional disease control and hence should be evaluated from a cost-benefit perspective. Commission Implementing Decision (EU) 2016/2008 allows the movement of vaccinated animals, under specified conditions, and may reduce some of these drawbacks. It also provides rules for movement of products that are considered to risk transmitting LSD (dairy products, semen, ova and hides). A distinction is made between zones where animals have been vaccinated preventively in the absence of disease (free zones with vaccination) and zones where disease has been reported (infected zones). Milk and dairy products from free zones with vaccination are not restricted. There are exemptions, with specific conditions that should be consulted carefully, for moving consignments of vaccinated animals and risky products from free zones with vaccination and, with greater stringency, from infected zones. In all cases, there is a requirement for at least 28 days to elapse after vaccination.

In the light of current evidence, it is clear that vaccination, combined with movement controls, is crucial to combating the spread of the virus. In countries applying emergency vaccination, the zones of vaccination and movement control should be large enough to prevent spread to other regions. Commission Implementing Decision (EU) 2016/2008 requires the establishment of an increased surveillance area of at least 20 km around the area where vaccination is practiced, in which intensified surveillance is conducted and the movement of cattle is subject to official controls. Countries facing a threat of LSDV introduction should urgently establish a preemptive vaccination programme. Contingency plans for vaccination should include quality checks on vaccines purchased for future use. Countries using vaccination should aim for 100 percent coverage in the affected areas and closely monitor what is achieved using clinical surveillance. A recently published guideline on foot-and-mouth disease (FMD) vaccination provides examples of methods for recording and monitoring vaccination progress (FMD Post-Vaccination Monitoring Guide, 2016), some of which could be adapted for LSD vaccination monitoring, particularly with regard to sample size calculation and sampling methods. There is a need to collate data on antibody responses to vaccination and on levels of adverse reactions to vaccination, including incidence of cases presenting clinical signs similar to LSD (so-called Neethling disease).

Further, preventive vaccination in Bosnia and Herzegovina, and northern Serbia would complete a buffer zone, which would help to protect Hungary, Romania and beyond, even if not entirely. A new vaccination campaign in 2017 in all vaccinating countries and especially including all unvaccinated young animals is necessary to avoid the re-emergence and further spread of LSD once the new vector season starts. Newly affected countries should be encouraged to extend their vaccination zones beyond the initial foci of infection and thus stop the disease from spreading beyond their borders. Modelling studies may be helpful in defining vaccination zones and identifying and correcting potential gaps.

Movement Control

While OIE guidelines specify that protection (3 km), surveillance (10 km) and restriction (at least 50 km) zones need to be established around outbreaks to prevent infected animals carrying the virus into uninfected areas, a more risk-based management approach, with surveillance taking place within larger distances, may be considered. Vaccinated animals have a greatly reduced risk of becoming infected or of spreading infection once sufficient time (at least 28 days) has elapsed for immunity to develop. It should be possible to move animals between vaccination zones of equivalent health status as long as they are not within protection and surveillance zones. However, due to the potential for vector-borne spread of LSD, transiting non-vaccinated animals or animals vaccinated less than 28 days before through a zone of higher health status is an unacceptable risk, even for slaughter, especially if such transit takes place in other countries. All animals to be moved should be subjected to veterinary inspection, and health and vaccination certification. Movement of dairy products, semen, ova and hides should also be strictly regulated, depending on the vaccination status of the animals and the area of origin. The EU Commission Implementing Decision 2016/2008 foresees several exemptions allowing the movement of animals and animal products according to strict conditions and channelling procedures.[2] This can encourage countries to use preemptive vaccination and hence protect local livelihoods, particularly those of small-scale producers.

2 http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv%3AOJ.L_.2016.310.01.0051.01.ENG

Stamping Out

Killing cattle on affected holdings removes virus at source, before onward transmission by biting arthropods can take place. However, the negative impact on peoples' livelihoods, food security, mental health and welfare should not be underestimated, particularly as concerns the most vulnerable producers whose few animals are often their main source of income. Considering that in many of the affected countries most of the cattle owners have less than ten cows, the socio-economic impact of stamping out is even larger. Humane slaughter and safe, prompt and appropriate disposal of carcasses, plus cleansing and disinfection of holdings, will ensure that virus does not spread by other indirect means or resume after restocking. But mechanical virus transmission, by non-biting arthropod vectors that feed on infected carcasses, cannot be excluded, even if no studies have been published. Widespread depopulation of cattle species, to reduce the numbers of susceptible at-risk animals ("fire-break", or pre-emptive culling), is clearly discouraged due to its socio-economic impact and questionable benefit in controlling the spread of the disease. For stamping out to be effective, cases must be clinically recognized, preferably confirmed by the laboratory, humanely culled and disposed of appropriately and as soon as possible. According to the European Food Safety Authority (EFSA),[3] low reporting rates of clinical disease (~50%) reduces the possible benefits of this approach. Reporting decreases even more when compensation for stamping out is not timely, fair, well-regulated or consistently applied. As LSD clinical cases represent the greatest risk for virus spread, humane culling and destruction is the top priority. Subclinical infection is common (possibly around 50 percent of infected animals (Tuppurainen and Oura, 2014), but the role of subclinically infected animals in transmission is uncertain. Assuming that subclinically infected animals pose a lower risk of transmission, stamping out may be modified to include only clinically diseased cattle, especially in a vaccinated population, where the susceptibility of potential recipients to become infected will also be reduced.

In modified stamping out, unaffected animals remain on the premises, and normal animal husbandry activities continue. This creates the rarely discussed problem of how to conduct the full range of necessary cleaning and disinfection procedures that should be performed after disposal of the clinically infected animals. More information is needed on how this problem can be tackled so that recommendations on best practices can be made.

Culling of clinical cases in vaccinated herds could be supplemented by laboratory tests on the remaining animals, subject to available laboratory capability. Despite their limited interpretive value due to cell-mediated immune response to LSDV, serological tests could also be used to check post-vaccination immunity, together with virological testing to identify and cull viraemic animals subclinically infected with wild-type LSD virus. Identifying subclinical infections will improve understanding of LSD dynamics in vaccinated herds and also provide insight into the value or effectiveness of partial or modified stamping out. However, false negative test results for viraemia are possible and there will be a time delay between sampling and test

3 http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2015.3986/epdf

results, during which further spread of the virus might occur. In this regard, animal identification and animal movement controls are crucial to prevent any further virus spread.

In the absence of DIVA serology, laboratory testing by differential PCR or sequencing is the only certain way to distinguish vaccine and wild-type virus (Menasherow *et al.*, 2016). However the time needed for testing may delay slaughter of affected animals, especially if samples have to be referred to specialized laboratories in other countries. In the absence of confirmatory tests, decisions will need to be made based on the history and clinical picture. Nevertheless, Neethling disease is rare, happens for a short period after vaccination, and looks different from clinical LSD skin lesions. If confusion indeed arises, it is recommended to quarantine the herd and prevent animal movements until verification by laboratory within 24-48 hours.

Carcass Disposal

The practicality of different forms of carcass disposal depends on many factors, including the numbers of animals involved, the environment, particularly soil structure and hydrology, the availability of resources and facilities, and the level of risk arising from residual virus contamination. Some affected countries rely on normal veterinary services and lack specialist teams for such operations. Alternatives to on-site burial include various on-site and off-site disposal methods. On-site incineration by pyres or mobile incinerator units may be possible in some circumstances. Burning or burying cattle is considered a source of pollution in many countries (Scudamore *et al.*, 2002) and conflicting regulations from the Ministry responsible for disease control and the Ministry of Environment can hamper disposal seriously. Off-site alternatives include moving suspected or apparently healthy herds for slaughter at abattoirs to provide heat-treated meat products. This practice has been used in the Russian Federation, depending on the availability of on-site disposal units. The risk of vector-borne spread from live animals during transit and at the abattoir is reduced by killing all severely affected animals on site, followed by transportation of carcasses to incinerating facilities. On-site killing followed by movement of carcasses for rendering, burial, or incineration, etc. might carry some residual risk due to the possible feeding of non-biting arthropod vectors on the carcasses prior to their disposal. Hence, important consideration should be given to the proper transport of carcasses, including spraying insecticide on body surfaces.

In conclusion, different options exist, although movement of live or culled animals showing clinical disease is a higher-risk operation than local burial, if environmental conditions allow. Further, measures should be taken to prevent access of potential vectors to carcasses prior to disposal, including spraying with disinfectant and insect repellent, and deep burial to lessen the risk of access by scavengers. Subsequent timely and thorough cleaning and disinfection of affected premises is essential.

Restocking

LSD virus, as other poxviruses, can survive for prolonged periods in the environment, although for how long has not been directly quantified. However, the risk of infection from environmental contamination is low (especially for vaccinated animals) and should be greatly diminished by proper cleansing and disinfection of farm premises, including barns and milking parlours. The possibility of long-term virus survival in vector populations cannot be excluded, so vector control and the use of repellents on cattle is recommended.

Conditions for restocking with non-vaccinated animals would most likely require a long waiting period, possibly two vector seasons under prevailing Eastern Europe temperate conditions. Restocking with vaccinated animals that have had sufficient time to become immune greatly reduces the risk of infection recurring, whether from residual infectivity on depopulated, cleaned, and disinfected premises, or from virus activity on neighbouring premises or regions. Therefore, restocking should be possible after a minimum waiting period of 21 days, as specified in current EU legislation (Council Directive 92/119/EEC), providing that the restocked animals have been vaccinated at least 28 days before and that thorough cleansing and disinfection has been carried out and certified. This of course can impose a major burden on smallholders whose livelihoods solely depend on their livestock. Hence, conducting appropriate research on the possibility of reducing this waiting period should be evaluated. Where culling has been used without vaccination, or where the use of vaccination has been limited, there may be logistical difficulties in finding vaccinated animals for repopulating premises after stamping out. The net result could be an increase in the price of vaccinated animals, and governments might need to contribute more to compensate for the overall costs of depopulation and restocking.

Vector Control

This is part of the response of most countries to LSD outbreaks. However, it is not known what impact these measures have had on reducing the incidence of the disease. Vector control is difficult, since there are many potential species for LSDV transmission, and the ones that are most important in any particular region are generally not known. Massive spraying with insecticides damages the environment and also harms valuable non-target species such as bees. To avoid needless environmental degradation, insecticides use aimed at limiting vector breeding sites in standing water, slurry and manure should be applied in a proportionate, targeted and regulated manner. Regular removal of manure piles, stagnant water bodies and other potential breeding sites for insects in and around farms can also help reduce vector densities. The lack of clear guidelines and policies in some countries can exacerbate the environmental impact, and hence these gaps should be filled with appropriate research and legislation. The use of repellents could be beneficial and have less impact on the environment. Insecticide-impregnated netting is being investigated as a way of reducing vector attacks on livestock and might be helpful where husbandry systems make it practical (FAO, 2013).

Laboratory support

Countries without the laboratory capacity to differentiate vaccine from wild-type virus and to undertake serology should seek support for referral of samples for testing by OIE, EU or FAO reference laboratories, or other centres of excellence.

Options for combining vaccination, movement control and stamping out

While stamping out is essential for LSD control in unvaccinated cattle populations, the need for full or even modified stamping out if cattle have been vaccinated has been contentious in several countries. This approach may be most easily justified in countries infected for the first time before vaccination is applied. Current EU legislation requires Member States to stamp out all animals in an infected herd even if that herd has been vaccinated, and this controversial aspect of the legislation can be revised only in 2019 as it requires a new animal health law.

Culling of vaccinated animals is not well accepted by livestock keepers and may jeopardize vaccination or other counter-epidemic measures, as well as the reporting of clinical cases. Reluctance or refusal to vaccinate cattle has a negative impact on disease control and solidarity for preventive vaccination to protect neighbouring countries. Furthermore, the measures required for eliminating infection as quickly as possible during an emergency may differ from those needed for cost-effective disease control and eventual eradication in more endemic settings. Thus, for example, rigorous culling might be justified in a country with major animal exports and at low risk of reintroduction of disease.

In many African countries, LSD control has relied mainly on vaccination, with few movement controls and very little, or no use of, stamping out. Vaccination has been voluntary and mainly aimed at clinical protection rather than decreasing and eventually eliminating virus circulation. The effectiveness of some vaccines has been questioned, but valuable clinical protection is clearly possible (Ayelet *et al.*, 2013; Hunter and Wallace, 2001). The intermittent nature of the threat posed by endemic LSD can lead to vaccination being neglected. A vaccination cover with a 25–50 km radius around the infected focus has been recommended, with all cattle movements stopped within that zone (Davies, 1991).

No country in sub-Saharan Africa, however, has succeeded in eradicating LSD after an outbreak. Recent recommendations are to establish a vaccination zone of at least 50 km radius around any upsurges (Anonymous, 2016), ensuring a very high and homogeneous vaccine coverage (minimum 90 percent). However, in local contexts, especially where multifocal outbreaks occur, the vaccination and protection zones are likely to deviate from the classical circular shape to take account of epidemiological and geographical parameters. Strict movement restrictions should be applied for live animals, semen and other genetic material to infected and at-risk herds in affected zones. Within infected zones, only vaccinated animals (more than 28 days) should be allowed to move.

In Israel, different culling approaches have been combined with vaccination, from complete stamping out in the first outbreak in 1989 through modified stamping out and vaccination in 2004, to annual vaccination of the whole country's cattle population, with very limited culling in 2012-2013, and then only of the most severe clinical cases. This latest approach was found to be effective at controlling the disease, which has not recurred, enabling vaccination to be changed from compulsory to voluntary in 2016 (Dr Galon, Israel Chief Veterinary Officer, May 2017).

After the LSD incursion into Bulgaria, the former Yugoslav Republic of Macedonia and Serbia in 2016, the implementation of large restriction zones with vaccination, movement control and full or modified stamping out has proved effective so far in preventing or limiting the spread of LSDV to neighbouring countries. As of 8 June 2017, only two isolated outbreaks have been reported in the region – in the former Yugoslav Republic of Macedonia – following the vaccination campaigns.

In Turkey, the policy developed involves compulsory notification and slaughter of clinically affected animals, with the rate of compensation increased in 2015 from 50 percent to 100 percent. A locally produced, live SPPV vaccine was used in 2013-2014 and the dose was increased in 2015 to three times that recommended for small ruminants. Ring vaccination was not effective at preventing the spread of the LSDV throughout Turkey because traffic of cattle and vehicles was poorly regulated during increased movements associated with the Kurban religious festival. The number of cattle vaccinated increased from 1.6 million in 2014, to 8 million in 2015, and the plan is for all animals over three months of age and not in the last month of pregnancy to be vaccinated annually. No animals can be moved until 28 days after vaccination, but border controls on animal entry from neighbouring infected countries are problematic. The incidence of LSD in Turkey seems to have peaked in the summer of 2014 (Saraç *et al.*, unpublished). LSDV was detected in non-engorged female midges (Culicoides punctatus) from affected areas within a radius of 2 km from LSDV-infected herds (Sevik and Dogan, 2016). While Culicoides are known to be poor flyers, they are highly liable to be carried by winds (>100 km).

In Greece, in 2015, a stamping out policy was applied, with culling of all cattle on affected holdings and on nearby farms with cattle or buffalo. Carcasses were destroyed by sanitary burial on the premises. Protection and surveillance zones with a minimum radius of 3 and 20 km respectively, were established around each infected holding, which was more than the 10 km surveillance zone required by Council Directive 92/119/EEC. Supplementary measures included animal movement control, quarantine, vector control and disinfection of infected establishments and vehicles. Three weeks after clinical signs of LSD were reported, emergency vaccination with Neethling vaccine began and once immunity had been established, further outbreaks occurred only in unvaccinated cattle. For up to ten days after vaccination, some cattle developed a painful local swelling at the injection site and reduced milk production and appetite (Tasioudi *et al.*, 2014). The lack of government funding for the purchase of LSD vaccine in good time hampered the LSD control programme.

Other vector-borne diseases such as bluetongue in Europe have been controlled using mass country- or region-wide vaccination without culling, but applying strict movement controls. This incorporated a waiting period of 60 days post vaccination (dpv) before allowing movement, or 28 dpv after serological testing, or 14 dpv after testing using PCR. More data on the onset of post-vaccination immunity and duration of post-infection viraemia are urgently needed to allow the same kind of flexible approach for LSD.

In some recently affected countries, such as the Russian Federation, the former Yugoslav Republic of Macedonia, and Serbia, modified stamping out is used in vaccinated herds and only clinical cases are culled. It is not yet possible to evaluate the effectiveness of such an approach in these countries. The experience of the Russian Federation in fighting LSD in 2015 (totally stamping out diseased and apparently healthy, in-contact animals), was that this approach was effective but very costly. Since its introduction in the Russian Federation near the border with Azerbaijan in July 2015, the epidemic had spread northwest up to the border with Ukraine by October 2016.

An EFSA report describes the results of modelling the comparative impacts of combinations of different stamping-out and vaccination approaches for LSD control in Greece and Bulgaria, based on vector dynamics and infection pressures deduced from the study of the Israeli LSD outbreaks in 2012/13 (EFSA, 2016). Stamping out on affected holdings was either "total stamping out" or "modified stamping out". The authors assumed 50 percent as the rate of outbreak reporting. Vaccination options were either "no vaccination", "preventive vaccination" (completed at least 21 days before a first incursion of LSD) or "reactive vaccination" (from 15 days after a detected LSD incursion). Vaccination coverage was assumed to be 95 percent and vaccination effectiveness either 75 percent or 40 percent. Options without vaccination were by far the worst compared to any other vaccination approach; however, in the absence of vaccination, total stamping out was significantly more beneficial than modified stamping out. When vaccination was used, the additional benefits of stamping out were quite small, with the benefits of modified stamping out almost

indistinguishable from total stamping out, when vaccination effectiveness was 75 percent. Based on the experiences of countries and the EFSA publication, FAO recommends that if vaccination is implemented comprehensively, even with a moderately effective vaccine, then the benefits of total stamping out are small. In these cases, modified stamping out of clinical cases only is recommended.

Areas of uncertainty

Until recently, LSD has not been a research priority for the developed countries with the most advanced research and development capacities. Consequently, there are many knowledge gaps about the biology, host responses and epidemiology of this disease. Future collaboration between subject specialists, reference centres, veterinary services, and international and regional organizations in infected and threatened regions is needed. Among the most urgent priorities are to better understand the following:

1. The epidemiological significance of animals with subclinical infection (due to innate or acquired immunity or to a low infection rate, and including small ruminants) in the spread or maintenance of the LSDV;
2. The vector species involved in transmission in different regions, and the distance and time span over which they can transmit infection;
3. The risk of transmission by means other than biting arthropods, including direct and indirect contact between cattle, and spread by non-biting arthropods;
4. How the virus survives in inter-epizootic periods;
5. The rate of onset and duration of immunity and protection derived from vaccination;
6. The presence, survival and significance for transmission of virus in animal products, the environment, and different vectors;
7. Development and validation of an affordable assay for differentiating wild-type from vaccine virus, and for high-throughput serological assays.

References

Ababneh, M.M., Al Zoubi, I.G., Al Sheyab, O.M., Al Zoubi, M.G., Alekish, M.O. & Al Gharabat, R.J. 2013. Lumpy skin disease in Jordan: disease emergence, clinical signs, complications and preliminary-associated economic losses. *Transbound. Emerg. Dis.*, 62: 549–554.

Abutarbush, S.M., Hananeh, W.M., Ramadan, W., Al Sheyab, O.M., Alnajjar, A.R., Al Zoubi, I.G., Knowles, N.J., Bachanek-Bankowska, K. & Tuppurainen, E.S. 2016. Adverse Reactions to Field Vaccination Against Lumpy Skin Disease in Jordan. *Transbound Emerg Dis.*, 63(2): e213-9.

Ayelet, G., Abate, Y., Sisay, T., Nigussie, H., Gelaye, E., Jemberie, S. & Asmare, K. 2013. Lumpy skin disease: preliminary vaccine efficacy assessment and overview on outbreak impact in dairy cattle at Debre Zeit, central Ethiopia. *Antiviral Res.*, 98: 261–265.

Ben-Gera, J., Klement, E., Khinich, E., Stram, Y.& Shpigel. N. Y. 2015. 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. *Vaccine* 33, (38): 4837-4842. doi: 10.1016/j.vaccine.2015.07.071.

Bumbarov, V., Golender, N., Erster, O. & Khinich. Y. 2016. Detection and isolation of Bluetongue virus from commercial vaccine batches. *Vaccine* 34, (28): 3317-3323. doi: 10.1016/j.vaccine.2016.03.097.

Carn, V. M. and Kitching, R. P. 1995. An investigation of possible routes of transmission of lumpy skin disease virus (Neethling). *Epidemiol Infect.*, 114(1): 219-26.

Coetzer, J. A. W. 2004. Lumpy skin disease. In *Infectious Diseases of Livestock*, 2nd Edition, eds: Coetzer, J. A. W., Tustin, R. C. pp. 1268-1281. Oxford University Press.

Davies, F. G. 1991. Lumpy skin disease of cattle: A growing problem in Africa and the Near East. *World Animal Review*, 68, 37-42. Available at FAO Corporate Document Repository: http://www.fao.org/docrep/u4900t/u4900t0d.htm

EFSA. 2016. Urgent advice on lumpy skin disease. EFSA Panel on Animal Health and Welfare. ADOPTED: 29 July 2016. EFSA Journal. doi: 10.2903/j.efsa.2016.4573.

El-Nahas, E., El-Habbaa, A., El-bagoury, G. & Radwan, M.E. 2011. Isolation and identification of lumpy skin disease virus from naturally infected Buffaloes at Kaluobia, Egypt. *Global Veterinaria*, 7: 234-237.

EU Commission Implementing Decision 2016/2008 of 15 November 2016
concerning animal health control measures relating to lumpy skin disease in certain Member States. Available at http://eur-lex.europa.eu/eli/dec_impl/2016/2008/oj

EU Council Directive 92/119/EEC of 17 December 1992 introducing general Community measures for the control of certain animal diseases and specific measures relating to swine vesicular disease. Available at http://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX:31992L0119

FAO. 2013. Netting flies and mosquitoes protects livestock, boosts milk yields. Available at http://www.fao.org/news/story/en/item/173224/icode/

FAO and OIE. *Foot and mouth disease vaccination and post-vaccination monitoring. Guidelines*. 2016. Eds: Metwally, S. and Münstermann, S. Available at http://www.fao.org/documents/card/en/c/56c4f441-1aad-46b5-bc7a-c0ba17c1a11d/

FOA/OIE. Global Framework for Progressive Control of Transboundry Animal Diseases (GF-TADs). 2016. Final Recommendations. First Standing Group of Experts on Lumpy Skin Disease in South-East Europe under the GF-TADs umbrella. First meeting (SGE LSD1), Brussels, Belgium, 4-5 July 2016. Available at http://web.oie.int/RR-Europe/eng/Regprog/docs/docs/LSD1/LSD%20SGE1%20(Brussels%20%20July2016)%20-%20Conclusions%20and%20recommendations%20(Final).pdf

House, J. A., Wilson, T. M., el Nakashly, S., Karim, I. A., Ismail, I., el Danaf, N., Moussa, A. M. & Ayoub, N. N. 1990. The isolation of lumpy skin disease virus and bovine herpesvirus-4 from cattle in Egypt. J. Vet. *Diagn. Invest*., 2: 111–115.

Hunter, P. and Wallace, D. 2001. Lumpy skin disease in southern Africa: a review of the disease and aspects of control. *J. S. Afr. Vet. Assoc.*, 72: 68–71.

Mebratu, G. Y., Kassa, B., Fikre, Y. and Berhanu, B. 1984. Observation on the outbreak of lumpy skin disease in Ethiopia. *Rev Elev Med Vet Pays Trop.*, 37(4): 395-9.

Menasherow, S., Erster, O., Rubinstein-Giuni, M., Kovtunenko, A., Eyngor, E., Gelman, B., Khinich, E. & Stram. Y. 2016. A high-resolution melting (HRM) assay for the differentiation between Israeli field and Neethling vaccine lumpy skin disease viruses. *J Virol Meth.*, 232:12-15. doi: 10.1016/j.jviromet.2016.02.008.

OIE Terrestrial Animal Health Code, Chapter 11.11., Lumpy skin disease (Caused by Group III Virus, Type Neethling), 2016. Available at http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_lsd.htm

OIE WAHIS Interface. Animal Health Disease Information. Available athttp://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/Diseasetimelines

Onderstepoort Biological Products. Neethling Vaccine Datasheet. Available at http://www.obpvaccines.co.za/Cms_Data/Contents/OBPDB/Folders/Product/~contents/PZBJ3K5TLC47W3BJ/2223_LumpySkin_PI.pdf

Saraç, F., Gülyaz, V., Satır, E., Uzar, S. & Sayı, O. 2016. Lumpy Skin Disease Situation, Surveillance and Control Activities in Turkey. Unpublished Report. Ministry of Food, Agriculture and Livestock, Pendik Veterinary Control Institute, İstanbul,Turkey. Lead Author: fahriye.sarac@tarim.gov.tr

Scudamore, J.M., Trevelyan, G.M., Tas, M.V., Varley, E.M. & Hickman, G.A. 2002. Carcass disposal: lessons from Great Britain following the foot and mouth disease outbreaks of 2001. Rev Sci Tech., 21(3):775-87.

Sevik, M. and Dogan, M. 2016. Epidemiological and Molecular Studies on Lumpy Skin Disease Outbreaks in Turkey during 2014–2015. *Transbound Emergo Dis.* doi:10.1111/tbed.12501.

Sharir, B. 2012. Lumpy skin disease outbreak in Israel 2012. Available at: http://www.hachaklait.org.il/articles/files/3594794742.pdf

Tasioudi, K. E., Antoniou, S. E., Iliadou, P., Sachpatzidis, A., Plevraki, E., Agianniotaki, EI, Fouki, C., Mangana-Vougiouka, O., Contoocook, E.& Dile, C. 2016. Emergence of Lumpy Skin Disease in Greece, 2015. *Transbound Emerg Dis.*, 63(3):260-5. doi: 10.1111/tbed.12497.

Tuppurainen, E. S. and Oura, C. A. 2012. Review: lumpy skin disease: an emerging threat to Europe, the Middle East and Asia. *Transbound. Emerg.* Dis., 59: 40–48.

Tuppurainen E.S. and Oura, C. 2014. Lumpy skin disease: an African cattle disease getting closer to the EU. Vet Rec., 175(12):300-301. doi: 10.1136/vr.g5808.

Tuppurainen, E.S., Lubinga, J. C., Stoltsz, W. H., Troskie, M., Carpenter, S. T., Coetzer, J. A., Venter, E. H. & Oura, C. A. 2013. Mechanical transmission of lumpy skin disease virus by Rhipicephalus appendiculatus male ticks. *Epidemiol Infect.*, 141(2): 425-30. doi: 10.1017/S0950268812000805.

Yeruham, I., Nir, O., Braverman, Y., Davidson, M., Grinstein, H., Haymovitch, M. & Zamir, O. 1995. Spread of lumpy skin disease in Israeli dairy herds. *Vet. Rec.*, 137: 91–93.

ISBN 978-92-5-109937-7

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I7827EN/1/09.17