Lumpy Skin Disease (Knopvelsiekte, Pseudo-Urticaria, Neethling Virus Disease, Exanthema Nodularis Bovis)

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14.1 Introduction

Lumpy skin disease (LSD) is an acute viral disease of cattle that is caused by lumpy skin disease virus, of the genus *Capripoxvirus*, within the subfamily *Chordopoxvirinae* of the family *Poxviridae* (Buller et al. 2005). The LSDV prototype strain is the Neethling virus and it has only one serotype (Alexander et al. 1957). The virus has close antigenic relationship to sheep pox and goat pox viruses, which are also in the same genus, and the three viruses cannot be distinguished by routine virus neutralization or other serological tests (Radostits et al. 2007; Burdin 1959). The clinical syndrome of LSD was first described in Zambia (formerly Northern Rhodesia) in 1929 and was initially thought to be the result of poisoning or insect bite hypersensitivity (Mac-Donald 1931; Davies 1991). The disease is endemic in most African countries and some of the Middle East countries, with a recent incursion into other territories that were not known to have the disease before. Epizootics interspersed with periods of sporadic occurrence. LSD currently poses a serious threat to Europe and the rest of the world (Davies and Atema 1981; Davies 1991; Tuppurainen and Oura 2012).

LSD is associated with high morbidity and low mortality in cattle. It causes serious economic losses due to severe reduction in milk production, feed intake, and weight conversion. Furthermore, it causes abortion, infertility, and damage to cattle hide. LSD is considered a notifiable disease, and in affected countries, it results in serious restrictions to international trade (Davies 1991; Tuppurainen and Oura 2012). The incubation period is reported to be between 1 and 4 weeks (Haig 1957;

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Coetzer 2004). Not all affected animals show clinical sings. High fever, lachrymation, and enlarged palpable lymph nodes are the first clinical signs reported. Soon after the fever, few to several variable-sized cutaneous nodules appear on different regions of the body. The entire body of the animal can be covered with nodules, and lesions may be seen in the mouth and nose as well as the mucous membranes of the eye in affected animals (Haig 1957; Coetzer 2004; Babiuk et al. 2008).

In postmortem, LSD lesions may be seen throughout the gastrointestinal and respiratory tracts. Pox lesions may be widespread and seen in each organ. In some cases limb edema can be seen in one or more limbs (Babiuk et al. 2008).

Diagnosis of LSD is based on characteristic signs, histopathology, and virus isolation as well as polymerase chain reaction (PCR) (Davies 1991; Tuppurainen and Oura 2012).

In endemic regions, vaccination is the only effective method of control (Hunter and Wallace 2001). There are commercial vaccines that are currently used to control the disease. Broad-spectrum antibiotics are used to control secondary bacterial infections (Salib and Osman 2011).

14.2 Epidemiology

14.2.1 Occurrence

The disease used to be confined to sub-Saharan Africa (Radostits et al. 2007). Over the years, LSDV has spread out to most of the African countries. The disease was reported in Egypt (Ali et al. 1990) and Israel (Yeruham et al. 1994). Outbreaks have been reported in the Middle East since 1990 (Kuwait in 1991, Lebanon in 1993, Yemen in 1995, United Arab Emirates in 2000, Bahrain in 2003, Israel in 2006–2007, and Oman in 2010) (Tuppurainen and Oura 2012). In 2006, the disease was reported again in Egypt and Israel (ProMed report no. 20060421.1167 and no. 20060627.1786, 2006). In 2012, the disease reoccurred again in Israel (ProMed report no. 20120729.1219223, 2012). In 2013, the disease spread in the region and was reported in Lebanon (ProMed report no. 20130118.1505118, 2013), Palestinian authority (ProMed report no. 20130311.1581763, 2013), Jordan (Abutarbush et al. 2013), Turkey (ProMed report no.20130918.1951299, 2013; Wainwrigh et al. 2013), Iraq (ProMed report no.20131128.2079065, 2013; Al-Salihi and Hassan 2015), and Egypt (ProMed report no.20131213.2111947,2013). In 2014, the disease was reported in Iran (ProMed report no.20140623.2561202, 2014), Azerbaijan (ProMed report no.20140719.2621294, 2014), and Cyprus (ProMed report no.20141209.3022793, 2014). In 2015, the disease was reported in Kuwait (ProMed report no. 20150105.3072591, 2015), Saudi Arabia (ProMed report no.20150430.3333997, 2015), Greece (ProMed report no. 20150821.3594203, 2015), and Russia (ProMed report no. 20150904.3622855, 2015). The disease continues to spread into new territories, and current methods of control and prevention do not appear to be efficient enough to stop it.

14.2.2 Morbidity, Mortality, and Case Fatality Rates

Generalized severe infections and a high mortality are seen in some field outbreaks. Other outbreaks are associated with few obviously affected animals and no deaths. In general, outbreaks are more severe with the initial introduction of the infection to a region and then abate, probably associated with the development of widespread immunity (Radostits et al. 2007). Morbidity, mortality, and case fatality rates are influenced by many factors including the immune status of the affected cattle and the abundance of the vectors (Thomas and Mare 1945; Tuppurainen and Oura 2012).

Morbidity rates of 1–2 % may reach 80–90 % in different situations (Davies 1991). Morbidity rates reach 80 % during epizootics, but are close to 20 % in enzootic areas. Morbidity rates of 31 % and 10 % were recorded in some outbreaks in Egypt and in 1994 in Israel, respectively. Much lower morbidity rate and milder disease were seen in Kenya (Radostits et al. 2007). Mortality rates of 10–40 % and even higher may be reported on occasion, but the much lower range of 1–5 % is more usual (Davies 1991). In natural outbreaks, the morbidity and mortality rates were reported to range from 3 to 85 % and from 1 to 3 %, respectively (Thomas and Mare 1945; Coetzer 2004). In recent outbreaks, the overall morbidity and mortality rates in Jordan were 26 % and 1.9 %, respectively (Abutarbush et al. 2013). Case fatality rate average is 2 %, but varies with the outbreak. The case fatality rate in the Jordanian outbreak was 7.5 %. In disease outbreak in Egypt, the case fatality rate was reported to be 1.8 % (Salib and Osman 2011). In Israel in 1994, no direct mortality from the disease was reported.

The disease has been reappearing in South Africa in the past decade probably due to higher rainfall and a decrease in the use of vaccination due to previous low incidence in the area (Hunter and Wallace 2001).

14.2.3 Origin of Infection and Transmission

Cattle can be infected by drinking water, but ingestion and direct contact transmission are not common routes, even though the virus is present in nasal and lacrimal secretions, semen, and milk of infected animals. Experimental seminal transmission of LSDV in cattle has been reported recently (Annandale et al. 2014). Although not commonly seen, the disease can be transmitted by direct contact (cutaneous lesions, saliva, respiratory secretions, milk, and semen) and using of contaminated needles (Davies 1991; Hunter and Wallace 2001). Most cases are believed to result from transmission by an arthropod vector. Historically, LSD virus has been isolated from *Stomoxys calcitrans* and *Musca confiscata* and transmitted experimentally using *S. calcitrans*, but other vectors are also suspected including *Biomyia*, *Culicoides*, *Glossina*, and *Musca* spp. However, in a recent study, despite the detection of virus in mosquitoes (*Anopheles stephensi*, *Culex quinquefasciatus*), the stable fly, and a biting midge (*Culicoides nebeculosis*) after they had fed on cattle with lumpy skin disease, the infection did not transmit to susceptible cattle when these arthropods were allowed to refeed on them (Chihota et al. 2003).

Although the specific vector of the disease was not confirmed yet, there is a strong evidence supporting LSD to be mechanically transmitted by arthropods. Lumpy skin disease virus was detected in saliva samples of both *Amblyomma hebraeum* and *Rhipicephalus appendiculatus* ticks (Lubinga et al. 2013). Previous studies showed successful transmission by *Aedes mosquitoes* (Chihota et al. 2001) and by African brown ear ticks (*Rhipicephalus appendiculatus Neum.*) (Tuppurainen et al. 2012). Another study showed evidence of transstadial and transovarial transmission of LSDV by *Rhipicephalus (Boophilus) decoloratus* ticks and mechanical or intrastadial transmission by *Rhipicephalus appendiculatus* and *Amblyomma hebraeum* ticks (Tuppurainen et al. 2011). Further evidence of mechanical/intrastadial and transstadial transmission of LSDV by *Amblyomma hebraeum* implicating *A. hebraeum* as a possible maintenance host in the epidemiology of the disease was reported (Lubinga et al. 2015).

Some more evidence is derived from a study which found that direct contact between infected and susceptible cattle in an insect-free environment does not lead to infection (Carn and Kitching 1995). Moreover, a recent study used a mathematical model to analyze the development of an LSD outbreak that took place at a dairy farm in Israel was reported. The model described the different forms of contact between the cattle groups and concluded that the virus spread could be attributed mostly to indirect transmission via insect vectors (Magori-Cohen et al. 2012).

14.2.4 Risk Factors

14.2.4.1 Animal Risk Factors

All ages and types of cattle are susceptible to the causative virus, except animals recently recovered from an attack, in which case there is a solid immunity lasting for about 3 months. In outbreaks, very young calves, lactating and malnourished cattle develop more severe clinical disease (Hunter and Wallace 2001). Introduction of a new animal to the herd, herd size, and utilization of communal grazing and watering points were found to be risk factors for contracting the disease in a recent study (Hailu et al. 2014).

Bos taurus cattle, imported from Europe, are far more susceptible than the indigenous *Bos indicus* cattle (Davies 1991). British breeds, particularly *Channel Island* breeds, are much more susceptible than zebu types, both in numbers affected and the severity of the disease. In an Ethiopian study (Gari et al. 2011), the annual cumulative incidence of LSD infection in Holstein Friesian/crossbred (33.93 %) was significantly higher than that of local zebu cattle (13.41 %). Also, the annual mortality was also significantly higher in Holstein Friesian/crossbred (7.43 %) than in local zebu cattle (1.25 %) (Gari et al. 2011).

Wildlife species are not affected in natural outbreaks, although there is a concern that they might be reservoir hosts. Typical skin lesions, without systemic disease, have been produced experimentally with Neethling virus in sheep, goat, giraffe, impala, and Grant's gazelle, but wildebeest were resistant. Serological evidence of naturally acquired infection has been observed only in African buffalo (*Syncerus*

caffer) (Davies 1982). Natural occurrence of LSD has also been reported in water buffalo (*Bubalis*).

14.2.4.2   Environmental Risk Factors

Outbreaks tend to follow waterways, and extensive epizootics are associated with high rainfall and concomitant high levels of insect activity with a peak of disease in the late summer and early autumn (Hunter and Wallace 2001).

14.2.4.3   Pathogen Risk Factors

Capripox viruses are generally resistant to drying and survive freezing and thawing. Resistance to heat is variable but most are inactivated at temperatures above 60 °C. LSDV has shown to be very resistant to physical and chemical agents. In necrotic skin, the virus persists for at least 33 days. At ambient temperature, the virus remains viable in lesions in air-dried hides for at least 18 days (Weiss 1968a, b). From intact skin nodules kept at −80 °C, the virus was recovered for 10 years (Weiss 1968a, b). It is stable at pH range between 6.6 and 8.6 and sensitive to chloroform and ether, readily inactivated by dodecyl-sulfate (Weiss 1968a, b; Plowright and Ferris 1959).

14.2.4.4   Experimental Production

Experimental transmission can be accomplished using ground-up nodular tissue and blood or tissue culture virus. Disease is produced following intranasal, intradermal, or intravenous challenge (Prozesky and Barnard 1982). While LSD is characterized by generalized nodular skin lesions, less than 50 % of natural or experimental infections develop generalized skin nodules, and the length of the viremic period does not correlate with the severity of the clinical disease (Radostits et al. 2007). A recent study has shown experimental seminal transmission of LSDV in cattle (Annandale et al. 2014).

14.2.4.5   Economic Importance

Economic loss associated with LSD outbreaks is high. Although the disease is not associated with high mortalities, it results in great economic losses due to decreased feed intake, milk production, weight conversion, abortion and infertility, and damaged cattle hides. Secondary mastitis predisposed by the development of lesions on the teats may occur. In addition, this disease is an important notifiable disease and affects international trade (Abutarbush et al. 2013). Lumpy skin disease was proven to be one of the high-risk diseases for spread out of Africa to the outside world and is a potential agent of agroterrorism.

In an outbreak in Jordan, the cost of supportive antibiotic treatment ranged from 0 to 84.3 (mean = 27.9) British Pound/animal (Abutarbush et al. 2013). In another study, the total cost of treatment and losses per animal (including the total value of the animal in case of death) in the holding, as estimated by the owner, was 27–2210 £ (mean = 486) in non-vaccinated cattle and 0–2210 £ (mean = 78) in vaccinated cattle (Abutarbush 2014).

The financial cost of clinical LSD based on questionnaire survey distributed to livestock farmers, in Oromia region of Ethiopia, was studied (Gari et al. 2011). The

annual financial cost included the average production losses, due to morbidity and mortality arising from milk loss, beef loss, traction power loss, and treatment and vaccination costs at the herd level. The financial cost in infected herds was estimated to be USD 6.43 (5.12–8) per head for local zebu and USD 58 (42–73) per head for Holstein Friesian/crossbred cattle (Gari et al. 2011).

14.3   Pathogenesis

Viremia accompanied by a febrile reaction and localization in the skin occurs with development of inflammatory nodules in generalized disease (Radostits et al. 2007). Local lesions can develop at the site of challenge, without viremia and generalization of the infection, in the experimental disease after intradermal inoculation, (Prozesky and Barnard 1982).

14.4   Clinical Findings

LSD is an acute infectious disease of cattle of all ages. There have been five instances of clinical cases of LSD in *Bubalus bubalis*, the Asian water buffalo (Ali et al. 1990). No other domestic ruminant species becomes infected naturally during field outbreaks. The incubation period is reported to be between 1 and 4 weeks (Haig 1957; Coetzer 2004). An incubation period of 2–4 weeks is common in field outbreaks and 7–14 days following experimental challenge (Carn and Kitching 1995). In severe cases there is an initial rise of temperature (40–41.5 °C), which lasts for over a week, sometimes accompanied by depression, lacrimation, nasal discharge, salivation, and a reluctance to move. Shortly afterward, the characteristic skin lumps develop. Multiple nodules appear suddenly about a week later, the first ones usually appearing in the perineum. They are intradermal, round, circumscribed, and firm. In most cases, they are confined to the skin area, varying from 5 to 50 mm in diameter, and are flattened, and the hair on them stands on end. They vary in number from a few to hundreds (Fig. 14.1). They may cover the whole body or be restricted to the head, neck, perineum, udder, genitalia, or limbs (Figs. 14.2 and 14.3). The distribution of the lesion, in a decreasing order, is seen on the body, neck, perineum, udder, head, vulva, and mouth (Abutarbush et al. 2013). They are firm and slightly raised above the surrounding normal skin from which they are often separated by a narrow ring of hemorrhage (Fig. 14.4). The lesions are of full skin thickness involving the epidermis, dermis, and adjacent subcutis. Nodules may disappear, but they may persist as hard lumps or become moist, necrotic, and slough (Radostits et al. 2007). Lesions may harden and remain in situ. They may also slough away to leave a hole of full skin thickness and characteristic lesion of "inverted conical zone" of necrosis, also known as "sitfast" (Abutarbush et al. 2013) (Fig. 14.5).

The regional superficial lymph nodes are enlarged and edematous. Nasal and oropharyngeal secretions are seen and may be associated with the development of lesions on the muzzle and in the mouth (Davies 1991) (Fig. 14.6). Lesions may be

Fig. 14.1 Characteristic skin lumps in cattle infected with LSDV

Fig. 14.2 Skin nodules in the udder region of cattle infected with LSDV

found anywhere in the oropharynx, in the upper respiratory tract, throughout the alimentary tract, in the subcutis, in the muscle fascia, and in the muscle itself. The lesions on the mucous epithelium are round (usually 4–40 mm in diameter) and have a ring shape and separated from the normal tissue (Davies 1991). Necrosis follows quickly and the ulcers become infected. Other manifestations that may be observed in severe cases include respiratory obstruction and snoring (Radostits et al. 2007). Conjunctivitis and keratitis may be seen.
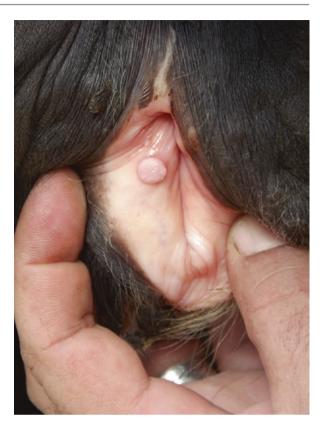
Fig. 14.3 Skin nodules in
the genitalia of cattle
infected with LSDV

Mouth lesions may interfere with feeding and dehydration and starvation
may be seen in some cases. Milk production is reduced and may cease, and
udder and teat lesions may result in serious infections with the sloughing of
necrotic tissue and mastitis (Davies 1991; Abutarbush et al. 2013). Edematous
and inflammatory swellings of the brisket and of one or more limbs may be
seen and can severely restrict movement (Fig. 14.7). The sheath of bulls can be
similarly affected and may interfere with their ability to serve for many weeks.
In addition, estrus may be suppressed during the periods of severe debility
(Davies 1991). Secondary bacterial infections and myiasis can develop at the
lesion site (Abutarbush et al. 2013) (Fig. 14.8). Pneumonia is a common sequel
in animals with lesions in the mouth and respiratory tract. Nodular lesions may
have quite extensive surrounding areas of interstitial pneumonia in the lung,
and inhalation pneumonia frequently occurs (Radostits et al. 2007; Davies
1991). Pregnant cows may abort, and calves have been born with extensive skin
lesions, presumably acquired by intrauterine infection (Radostits et al. 2007;
Davies 1991).

Emaciation can be seen and affected cattle may require humane euthanasia.
Debility status remains for 1–3 months and sometimes for up to 6 months (Davies
1991). A convalescence of 4–12 weeks is usual (Radostits et al. 2007).

Fig. 14.4 A narrow ring of hemorrhage that separates normal skin from LSD lesion

Fig. 14.5 Lesion of "inverted conical zone" of necrosis ("sitfast") on the LSDV-infected cattle skin

Fig. 14.6 Lesions on the
muzzle and mouth of
LSDV-infected cattle

Fig. 14.7 Edematous and
inflammatory swellings of
the brisket and of limbs of
LSDV-infected cattle

Fig. 14.8 Myiasis of skin lesion in LSDV-infected cattle

14.5   Clinical Pathology

14.5.1 Hematology and Serum Biochemical Analysis

Hematological and serum biochemical findings associated with natural clinical infection of LSD in cattle were recently studied and described (Abutarbush 2015). LSD was reported to be associated with inflammatory leukogram, anemia, thrombocytopenia, hyperfibrinogenemia, hyperproteinemia, decreased creatinine concentration, hyperchloremia, and hyperkalemia. These abnormalities were attributed to the associated severe inflammatory process and disease complications such as anorexia and reduced muscle mass (Abutarbush 2015).

14.5.2 Antigen Detection and Serology

The gold standard methods for the detection of capripox viral antigen and antibody are electron microscopy examination and serum/virus neutralization tests, respectively (Tuppurainen et al. 2011). Typical capripox virions in full thickness skin biopsies or scabs can be seen by electron microscopic examination (Radostits et al. 2007). The clinical diagnosis of LSD can be confirmed using conventional or real-time PCR methods (Tuppurainen et al. 2005; Orlova et al. 2006; Zheng et al. 2007; Tuppurainen et al. 2011). When compared to real-time PCR, gel-based PCR is more time and labor consuming. However, it is a cheap, reliable method and useful in countries with limited resources (Tuppurainen et al. 2011). PCR and immunohistochemistry can be used for the diagnosis of LSD in formalin-fixed paraffin-embedded tissue samples from skin nodules and lymph nodes of affected cattle (Awadin et al. 2006).

In a study to compare the different diagnostic tests in experimentally infected cattle (Tuppurainen et al. 2005), the incubation period in infected animals varied from 4 to 5 days. The PCR was a fast and sensitive method in demonstrating viral DNA in blood and skin samples. Although sensitive and reliable, virus isolation from blood and skin samples was too time consuming to use. However, it is required if infectivity of the LSD virus is to be determined. Virus isolation was successful in detecting viremia from 1 to 12 days, while PCR was successful from 4 to 11 days. The latter could demonstrate viral DNA until day 92 postinfection. The virus was isolated from skin biopsies until 39 days postinfection (Tuppurainen et al. 2005).

Virus can be cultivated from lesions. Antigen can also be detected by antigen detection ELISA with samples taken early in the course of the disease before the development of neutralizing antibodies and by fluorescent antibody tests and PCR. The AGID test can be used but the antigen will also react with parapox virus (Radostits et al. 2007; Tuppurainen et al. 2005).

The host immunity against LSDV is mainly cell mediated, and, therefore, serological testing may not be sensitive enough to detect mild and long-standing infections or antibodies in vaccinated animals (Kitching et al. 1987). Antibody ELISAs have been developed with limited success (Tuppurainen et al. 2011). Indirect fluorescent antibody test can also be used (Gari et al. 2008). AGID tests may be associated with false-positive reactions due to cross-reaction with other viruses such as bovine papular stomatitis and pseudocowpox viruses (Radostits et al. 2007).

14.6   Necropsy Findings

Typical LSD lesions, described previously in the clinical signs section, are seen on the skin, mouth, pharynx, trachea, skeletal muscle, bronchi and stomachs, and there may be accompanying pneumonia (Radostits et al. 2007). Superficial lymph nodes are usually enlarged. Respiratory obstruction by the necrotic ulcers and surrounding inflammation in the upper respiratory tract and/or concurrent aspiration pneumonia may be seen. Widespread vasculitis reflects the viral tropism for endothelial cells is seen histologically. Microscopic examination of the lesion of affected cattle with LSD reveals a granulomatous reaction in the dermis and hypodermis. Intracellular, eosinophilic inclusion bodies can be seen in the earlier acute stages of the disease. Intracytoplasmic viral inclusion bodies may be seen in a variety of cell types (Prozesky and Barnard 1982; Radostits et al. 2007).

14.7   Differential Diagnosis

The clinical signs, rapid spread of the disease, and the sudden appearance of lumps on the skin after an initial fever are characteristics for LSD infection (Radostits et al. 2007). However, pseudo-lumpy skin disease, also known as Allerton virus infection and general infection of cattle with bovine herpesvirus-2, the agent of bovine mammillitis, can be confused with LSD. Pseudo-lumpy skin disease causes circular, up

to 2 cm in diameter, multifocal cutaneous lesions involving the superficial layer only and are distributed over the body. These lesions are associated with loss of hair, an intact central area, and raised edges. Sometime, the lesions show a circular ring of necrosis around a central scab, which falls off leaving discrete hairless lesion, which may be depigmented. The duration of the disease is approximately 2 weeks with usually no mortality (Radostits et al. 2007).

Streptotrichosis (*Dermatophilus congolensis* infection), ringworm, *Hypoderma bovis* infection, photosensitization, insect bites, urticaria, bovine papular stomatitis, foot and mouth disease, bovine viral diarrhea, and malignant catarrhal fever are all considered as differential diagnosis of LSD.

14.8 Treatment

Treatment is mainly symptomatic and supportive and no specific treatment is available. The use of antibiotics to prevent secondary bacterial infection is highly recommended (Abutarbush et al. 2013).

14.9 Control

Lumpy skin disease is usually introduced into new territory mainly by the movement of infected cattle or possibly by wind-borne vectors (Yeruham et al. 1995). Further spread is suspected to be via an insect vector. Cattle movement control from uninfected to infected territories is a critical control measure. Beyond that, vaccination is the main control method (Radostits et al. 2007).

Members of the capripox virus family are known to provide cross protection. Live attenuated sheep pox, goat pox, and LSDV vaccines can all be used to protect cattle against LSD infection (Kitching 1983). Available commercial vaccines are live attenuated. Live attenuated capripox virus (CaPV) vaccine strains that are used for cattle to control LSD include lumpy skin disease virus (LSDV) Neethling strain, Kenyan sheep and goat pox virus (KSGPV) O-240 and O-180 strains, Yugoslavian RM65 sheep pox(SPP) strain, Romanian SPP, and Gorgan goat pox (GTP) strains (Kitching et al. 1987; Kitching 2003). In countries previously free of LSD and use sheep pox vaccine to protect sheep against sheep pox, it is recommended to use the same vaccine in LSD outbreaks, because of potential safety issues associated with the live attenuated LSDV vaccine use (Tuppurainen and Oura 2012).

Field trials of the vaccines used in LSD prevention are few in the literature, and their efficacy has been questioned (Brenner et al. 2009; Ayelet et al. 2013). However, new reliable studies have been published recently. In a recent study to assess the value and efficacy of vaccination against a natural outbreak of LSD, epidemiological data were collected from 101 vaccinated and unvaccinated farms in Jordan (Abutarbush 2014). In the unvaccinated holdings, the overall morbidity rate was 42.6 %, mortality rate 10.2 %, and case fatality rate 23.9 %, compared to the overall morbidity rate of 4.7 %, mortality rate of 1 %, and case fatality rate of

22.9 % in vaccinated holdings. Decreased feed intake, decreased milk production, and fever were seen in 100 %, 76.9 %, and 92.3 % of the cattle farms in unvaccinated holdings, respectively, compared to decreased feed intake of 23.8 %, decreased milk production of 21.4 %, and fever of 23.8 % seen in vaccinated holdings. The percentage reduction in milk production in unvaccinated holdings ranged from 0 to 100 % (mean = 38.5 %, SE ± 9.6 %), and the total loss/animal in the farm ranged from £27 to £2210 (mean = 486, SE ± 162), compared to 0 to 100 % (mean = 6 %, SE ± 1.8 %) range of decrease in milk production and total loss/animal that ranged from 0 to 2210 £ (mean = 78, SE ± 29) in the vaccinated holdings (Abutarbush 2014).

In one study, 11.1 % of the cattle vaccinated with RM65 vaccine developed skin lesions after natural exposure to the disease. However, the number of affected cattle with clinical disease was five times higher compared with the unvaccinated cattle (Brenner et al. 2009). In another study, the authors concluded that Kenyan sheep pox vaccine strain used to protect cattle from LSDV infection did not confer good protection against LSDV infection. In this study 22.9 % of animals were clinically affected, while 2.31 % died of the disease (Ayelet et al. 2013). In a recent study three vaccines were evaluated (lumpy skin disease virus (LSDV) Neethling, Kenyan sheep and goat pox (KSGP) O-180 strain vaccines, and a Gorgan goat pox (GTP) vaccine). The Neethling and KSGPO-180 vaccines failed to protect vaccinated cattle against LSDV, whereas the Gorgan GTP vaccinated calves did not show clinical signs of LSD. In addition, incomplete protection of cattle vaccinated by live attenuated KSGP O-240 strain was reported during the 2006 outbreak in Egypt (Marshall 2006). In a randomized controlled field study to compare the efficacy of Neethling lumpy skin disease virus and x10 RM65 sheep pox live attenuated vaccines (10$^{3.5}$TCID50/dose) for the prevention of lumpy skin disease (Ben-Gera et al. 2015). However, enrolled cattle in both groups were vaccinated 2–5 months prior to study onset with a single dose of 10$^{2.5}$TCID50 of RM65 attenuated sheep pox vaccine. LSD morbidity rate was significantly lower in the Neethling-vaccinated cattle when compared to that of the x10RM65 vaccinated cattle. In the same study, an incidence of 0.38 % of Neethling-associated disease was reported among Neethling-vaccinated cows, while no such disease occurred in x10RM65 vaccinated cows (Ben-Gera et al. 2015).

Cattle vaccinated with a recombinant capripox-rinderpest vaccine are immune to experimental challenge with both viruses but for a different length of time with each agent (Ngichabe et al. 2002).

Incomplete protection and adverse reactions have been associated with the use of capripox virus vaccines against lumpy skin disease virus (LSDV). The South African Onderstepoort Neethling vaccine strain administration causes a local reaction at the injection site (Weiss 1968a, b). However, no large-scale systemic or generalized reactions have been reported after the use of sufficiently attenuated LSDV vaccines. The Kenyan sheep and goat pox (KSGP) vaccine [also known as Kenya sheep-1 (KS-1)] was derived from the O-240 sheep isolate and is used against LSD. This vaccine has been associated with adverse clinical reactions in certain cattle species (Yeruham et al. 1994; Kitching 2003). The resulting clinical

signs in dairy cattle were reported to be similar to those seen with natural LSD infection and included fever, skin lesions, and decreased milk production (Yeruham et al. 1994; Ayelet et al. 2013). However, this strain has been used effectively in sheep and goats in Kenya without severe or generalized reactions being observed (Kitching et al. 1987).

Currently available vaccines in the market against LSD include LSD vaccine by Onderstepoort Biological Products, South Africa (LSDV Neethling strain); Lumpyvax – Merck, Intervet, SA (attenuated LSDV field strain); Herbivac LS – Deltamune, South Africa (LSDV Neethling strain); Yugoslavian SPPV RM-65 (Jovac/Jordan and Abic/Israel) (10 × sheep dose); Bakirköy SPPV strain (Turkey, 3 to 4× sheep dose); and Romanian SPPV strain. KSGP O-240 and O-180 strains have been characterized as LSDV (Tulman et al. 2002; Le Goff et al. 2009; Davies 1976, Davies and Otema 1978), and vaccines using these strains are not recommended for cattle against LSDV until safety and efficacy have been tested using challenge experiments (Personal communication, Tuppurainen ES, FAO and EuFMD on line meeting, 2015).

In a recent field study to investigate the adverse reactions that were reported after vaccine administration, 63 dairy cattle farms, with a total of 19,539 animals, were included in the study (Abutarbush et al. 2014). Of those, 56 farms reported adverse clinical signs after vaccine administration, while the rest did not. The duration between vaccine administration and appearance of adverse clinical signs ranged from 1 to 20 days (mean = 10.3, SD ± 3.9). Reported clinical signs were similar to those observed in natural cases affected with LSD. Reported clinical signs were mainly fever, decreased feed intake, decreased milk production, and variable-sized cutaneous nodules (a few millimeters to around 2 cm in diameter) that were seen anywhere on the body (head, neck, trunk, perineum), udder, and/or teats. Nodules were raised and firmed initially and then formed dry scabs that could be peeled off the skin. The characteristic deep "sitfast" appearance was rarely seen, and most lesions were superficial. Some cattle had swollen lymph nodes, while a few pregnant animals aborted. The percentage of affected cattle ranged from 0.3 to 25 % (mean = 8, SD ± 5.1). Fever, decreased feed intake, and decreased milk production were seen in 83.9, 85.7, and 94.6 % in cattle on the affected farms, respectively. All affected cattle displayed skin nodules over their entire bodies, while 33.9 and 7.1 % of the affected farms reported nodular lesions present on the udder and teats, respectively. No mortalities were reported due to vaccine adverse reactions. Duration (course) of clinical signs ranged from 3 to 20 days (mean = 13.7, SD ± 4.1). In the same study, two types of LSD vaccines were used by the farmers: sheep pox virus (SPPV) vaccine derived from the RM65 isolate and a strain of LSDV vaccine with unknown source (Abutarbush et al. 2014).

Vaccination of cattle with sheep pox virus may result in a small percentage of cattle that develop granulomatous local reactions, but there is no spread of the sheep pox to sheep running with the cattle (Radostits et al. 2007). Vaccination of a herd at the start of an outbreak has limited efficacy as most animals will already be incubating the disease and poor needle hygiene in these circumstances may spread the disease (Radostits et al. 2007). However, in a recent study, a small number of farms

were vaccinated after the onset of the LSD clinical signs (Abutarbush et al. 2014). In those, morbidity and mortality rates, percentage of decrease in milk production, duration of illness (days), and the total cost of treatment and losses per animal in the holding (£) were all lower than those reported for unvaccinated farms. This suggests that using vaccine after the appearance of clinical signs may have some benefits. However, the case fatality rate was similar in the two groups of farms, and abortion rate was almost six times higher in the vaccinated group after clinical signs compared with the unvaccinated group (Abutarbush et al. 2014).

Slaughter of affected and in-contact animals and destruction of contaminated hides, coupled with vaccination of at-risk animals, are used when the disease gains access to a previously free country (Radostits et al. 2007).

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