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Review: Lumpy Skin Disease

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Abstract

Lumpy skin disease, which is caused by lumpy skin disease virus, is among the major health problems affecting the livestock industry of most African countries. Skin lesions are the major sources of infection; although the virus is evacuated via different body secretions and excretions including semen. Thus, susceptible hosts contract the virus principally by mechanical means from hematophagous arthropods, including biting flies, mosquitoes and ticks. Transstadial and transovarial persistence in varies species of ticks is also possible. Following infection, characteristic lumpy skin disease lesions may explode from 7 to 14 days post infection under experimental conditions whereas in natural cases it takes 2 to 5 weeks. Lumpy skin disease is manifested by distinguishing firm, circumscribed, few (mild forms) to multiple (severe forms) skin nodules, which sometimes involve mucous membranes of respiratory system, urogenital system and other internal organs. Subsequently, milk production lessen, abortion, temporary or permanent sterility, damage to hide and deaths will occur which further contribute to a momentous economic loss in cattle producing countries. Therefore, large-scale vaccination combined with other appropriate control measures are the most effective way of limiting the spread and economic impact due to lumpy skin disease. This review is designed with the aim of providing, latest information on the biology of lumpy skin disease virus, mechanism of spread, clinical and pathological features of lumpy skin disease.

Keywords: Clinical signs; LSD; LSDV; Lesions; Pathogenesis; Transmissions

Introduction

Capripoxvirus (CaPVs) is one of the eight genera within the Chordopoxvirinae subfamily of the Poxviridae and is comprised of Lumpy Skin Disease Virus (LSDV), Sheep Pox Virus (SPPV), and Goat Pox Virus (GTPV). These viruses are responsible for most economically significant diseases of domestic ruminants in Africa and Asia [1]. CaPV infections have specific geographic distributions [2,3]. SPPV and GTPV is endemic in most African countries, the Middle East, central Asia and the Indian subcontinent. In contrast, LSDV occurs largely in southern, central, eastern and western Africa [4-7]; its occurrence in north Sahara desert and outside the African continent was confirmed for the first time in Egypt and Israel between 1988 and 1989, and was reported again in 2006, 2011 and 2014 in Egypt [8-10]. LSD occurrences have also been reported in the Middle Eastern, European and west Asian regions [11-13]. In 2015 and 2016 the disease spread to south-east Europe, the Balkans and the Caucasus [14].

Lumpy skin disease is caused by lumpy skin disease virus (LSDV) for which Neethling strain is the prototype. The principal method of transmission is mechanical by arthropod vectors [15,16]. Temporally LSD is shown to be aggregated during the warm and humid months of the year Gari et al. which is directly associated with vector abundance [17]. These authors also revealed the role of husbandry practices such as commingling of animals at communal grazing and watering points in the transmission of LSDV.

LSDV has a limited host range and does not complete its replication cycle in non-ruminant hosts [18]. Besides, LSD has not been reported in sheep and goats even when kept in a close contact with infected cattle although typical skin lesions, without systemic disease, have been produced experimentally in sheep, goats, giraffes, impalas, and Grant's gazelles [2]. Natural cases of lumpy skin disease were recorded in water buffalo (Bubalis bubalis) during an outbreak in Egypt in 1988, but morbidity was much lower than for cattle (1.6% vs. 30.8%) [16,19,20]. Among cattle *Bos taurus* is more susceptible to clinical disease than *Bos indicus*; the Asian buffalo has also been reported to be susceptible [14,21]. Cattle breeds of both sexes and all ages are susceptible to LSDV, but there is some evidence to support that young animal may be more susceptible to the severe form of the disease [22,23].

LSD symptoms in cattle are mild to severe; characterized by fever, multiple skin nodules covering the neck, back, perineum, tail, limbs and genital organs, the mucous membranes; the lesion may also involve subcutaneous tissues and sometimes musculature and internal organs. Affected animals also exhibit lameness, emaciation and cessation of milk production. Edema of limbs and brisket, and lymphadenitis are highly prominent and sometimes affected animals may die. In addition, pneumonia is a common sequel in animals with lesions in the mouth and respiratory tract [11,24].

Morbidity and mortality of LSD can vary considerably depending on the breed of cattle, the immunological status of the population, insect vectors involved in the transmission and isolates of the virus. In endemic areas morbidity is usually around 10% and mortality ranges between 1% and 3% [2,5]. In addition the incidence of LSD in Holstein Friesian and crossbred cattle was found to be significantly higher than in local zebu [25]. Recently, Abera and Elhaig showed that the prevalence of LSD is higher in adult cattle but, they observed no statistically significant association between the age groups in which they are equally exposed to risk [10,26]. Furthermore, LSD results in overwhelming economic losses due to severe reduction in milk yield, reduced hide quality, chronic debility, weight loss, infertility, abortion

and death. It also considered as notifiable disease, and in endemic countries, it results in serious restrictions to international trade [2,7,27]. The financial cost of clinical LSD has been computed by Gari et al. in Ethiopia and, the average financial cost in infected herds was estimated to be 6.43 USD per head for local zebu and 58 USD per head for Holstein Friesian or crossbred cattle [25]. Therefore, this review is aimed to highlight the biology of LSDV, mechanism of spread, clinical and pathological features of lumpy skin disease in cattle.

Biology of LSDV

The family Poxviridae contains the largest viruses which are able to cause disease naturally in most domestic animals, except in dogs. It is divided into two subfamilies, Chordopoxvirinae, the poxviruses of vertebrates, and Entomopoxvirinae, the poxviruses of insects (Figure 1) [28]. The family Poxviridae is featured by its large and complex genome consisting of a single, linear molecule of double stranded DNA (ds DNA) approximately coding for 200 proteins. The ends are ligated to each other so the DNA molecule is continuous, without free ends. Poxviruses are the only DNA viruses known to complete their replication cycle in the cytoplasm. In the cytoplasm, the dsDNA is used as a template for both mRNA production (for translation of proteins) and copies of the genome for progeny virions; viral enzymes largely mediate both processes. As the virions are large and complex, the mechanism associated with virion assembly is largely unknown. Virions are released from the cell by budding. Poxviridae families possess at least 10 major antigens with a common nucleoprotein antigen, which accounts for cross-reactivity among species. There are at least 10 viral enzymes contained within the virus particle, many of which function in nucleic acid metabolism and genome replication [29].

Capripoxvirus is the most economically significant in the Poxviridae family affecting domestic ruminants in Africa and Asia [1,30]. It comprises Lumpy skin disease virus (LSDV), Sheep pox virus (SPPV), and Goat pox virus (GTPV). They are ds DNA viruses containing around 150 kilo base pairs (Kbp) and are relatively large (230-260 nm). Their capsid or nucleocapsid is brick- or oval-shaped containing the genome and lateral bodies. There is extensive DNA cross-hybridization between species which account for serologic cross-reaction and cross-protection among members [30,31]. The LSDV is enveloped DNA virus, with 151-kbp genome and consists of a central coding region bounded by identical 2.4 kbp inverted terminal repeats and contains 156 putative genes. The virus encodes 30 homologues of poxviral proteins known to be structural or nonstructural which is antigenically and genetically closely related to sheep pox virus (SPPV) and goat pox virus (GTPV) with nucleotide sequence identities of 96% between species [32,33]. Although *Capripoxvirus*es are generally considered to be host specific, SPPV and GTPV strains can naturally or experimentally cross-infect and cause disease in both host species. In contrast LSDV can experimentally infect sheep and goats, but no natural infection of sheep and goats with LSDV has been described so far [34].

LSDV is remarkably stable for long periods at ambient temperature, especially in dried scabs. It can persist in necrotic skin nodules for up to 33 days or longer, desiccated crusts for up to 35 days, and at least 18 days in air-dried hides. It can remain viable for long periods in the environment. The virus is vulnerable to sunlight and detergents containing lipid solvents, but in dark environmental conditions, such as contaminated animal sheds, it can persist for several months. The virus can be inactivated at temperature of 55°C for 2 hours and 65°C for 30 minutes. In contrast it can be recovered from skin nodules kept at –80°C for 10 years and infected tissue culture fluid stored at 4°C for 6 months. It is susceptible to highly alkaline or acid pH but, no significant reduction in titer when held at pH 6.6-8.6 for 5 days at 37°C. The virus is susceptible to ether (20%), chloroform, formalin (1%), phenol (2% for 15 minutes), sodium hypochlorite (2-3%), iodine compounds (1:33 dilution) and quaternary ammonium compounds (0.5%) [16].

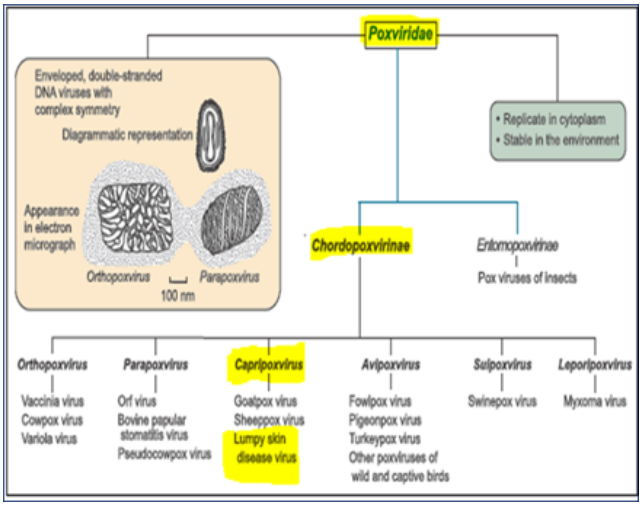

Figure 1: Poxviridae diagrammatic presentation. Source: [28].

Transmission and Pathogenesis

Transmission

Risk factors and sources of infection: In most of Sub Saharan Africa, the disease has been observed to appear following the seasonal rains, when there is always an increase in the population of different arthropod species. The onset of frosts in South Africa and Egypt results in a great fall in the number of cases of LSD, which virtually disappears over the winter to reappear again in the spring and summer. The outbreak in Egypt in 1989 is also associated with abundance of arthropod vector during summer, despite the total restrictions of animal movements. Further it spreads to Israel some 80-200 km away from active foci of LSD in Egypt, which indicates aerial movement of biting insects had occurred [1,24]. A study investigating the risk factors associated with the spread of LSD in Ethiopia showed that warm and humid agro-climate, conditions supporting abundance of vector population, was associated with a higher prevalence of LSD [17]. In addition it was shown that husbandry practices such as communal grazing and watering points, introduction of new animals to a herd are associated with the occurrence of LSD whereas cattle movements was not associated with the occurrence of the disease. This suggests that imposition of quarantines only does not prevent the spread of LSD infection as the aerial movement of vectors can significantly contribute to the blowout [24,31].

The most important source of infection to healthy animals is considered to be skin lesions or nodules since the virus persists in the lesions or scabs for long periods of time and has strong tropism to

dermal tissues [5]. The virus is also excreted via blood, nasal and lachrymal secretions, saliva, semen, and milk of infected animals (transmissible to suckling calves) that may be sources of infection to other susceptible cattle. Nodules that appear on the mucous membranes of the eyes, nose, mouth, rectum, udder and genitalia also ulcerate and shed sufficient viruses, which can serve as sources of infections [5,7]. Viraemic animals also play significant role as a source of infection especially that may last for up to two weeks [27]. Consequently, the hosts contract the virus via biting from blood-feeding arthropods, including biting flies, mosquitoes and ticks. Though rare, transmission also occurs through direct contact, and can also spread from contaminated feed and water [35]. Transmission or spread can also occur iatrogenically during mass vaccination in which single syringe and needle is used in several animals. Under this situation the needle can acquire the virus from crusts and other skin lesions and inoculate into healthy animals (possible means of spread has been summarized in Figure 2 below) [27].

The role of vectors: Evidence from different sources elucidated that LSDV can be mechanically transmitted by a variety of hematophagous arthropod vectors. Alike high morbidities are seen where mosquito populations are abundant and associated with warm and humid weather conditions, with 50-60% attack rates; and low, 5-15% morbidity in arid environments where there are fewer potential mechanical vectors [15,24,35]. Recent studies in ticks have shown transstadial and transovarial persistence of LSDV in *Rhipicephalus decoloratus*, *Rhipicephalus appendiculatus* and *Amblyomma hebraeum*, and mechanical or intrastadial transmission by *Rhipicephalus appendiculatus* and *Amblyomma hebraeum* [36-38]. On the other hand, mechanical transmission of LSDV has been experimentally demonstrated in female *Aedes aegypti* mosquitoes; however, clinical disease recorded in most of the animals exposed to infected mosquitoes was generally of a mild nature [39]. In the mechanical mode of transmission, the virus is transmitted via contaminated mouth parts of vectors without actual replication of the virus in the arthropod cells or tissues. *Aedes aegypti* has been incriminated in airborne transmission over long distance in disease free areas, which is thought to complicate the control measures by movement restriction [27]. The virus has been also recovered from *Stomoxys*, *Biomyia*, *Musca*, *Culicoides* and *Glossina* species that may have a potential to transmit LSD, as all feed voraciously upon domestic cattle [21,40]. Although the virus was detected in *Anopheles stephensi*, *Culex quinquefascuatus*, *Stomoxy calcitrans* and *Culicoides nebeculosis*, attempts to transmit LSD mechanically to susceptible animal is failed [41]. In recent times, the potential role of the *Culicoides* spp. in the transmission of LSDV was investigated by Sevik and Dogan and revealed that *Culicoides* punctatus could have played role in transmitting LSDV during 2014-2015 outbreak in Turkey [42]. Therefore, it is clear that various arthropods feeding on cattle can transmit the LSDV and spread the virus.

Other means of transmission: Another attempts to transmit LSDV via the manual handling of infected animals immediately prior to contact with susceptible cattle, or keeping naive and infected animals in the same pen, failed. This leads to the conclusion that direct or indirect contact between infected and susceptible animals is an inefficient method of transmission [27,31]. In previous reports transmission of LSDV through semen (natural mating or artificial insemination) has not been experimentally demonstrated, but LSDV has been isolated from semen of experimentally infected bulls [40,43]. Conversely, a recent study by Annandale et al. showed that experimental transmission of LSDV via semen from infected cattle is possible; however, whether this also occurs during natural mating or artificial insemination needs further investigation [44].

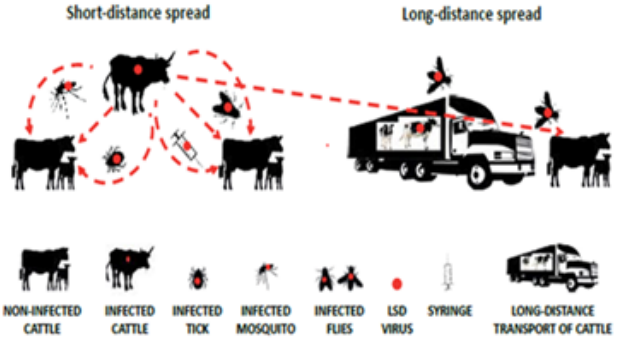

Figure 2: Schematic summary of LSD spread [27].

Pathogenesis

There have been few studies conducted on the pathogenesis of LSD in cattle [34]. In the generalized form there is viremia and fever, followed by localization in the skin and development of inflammatory nodules [20]. Following Subcutaneous or intradermal inoculation of cattle with LSDV, localized swelling at the site of inoculation developed 4 to 7 DPI which is varying in size from 1 to 3 cm and covering up to approximately 25% of the skin surface. Enlargement of the regional lymph nodes and generalized eruption of skin nodules usually follows 7 to 19 DPI. Viremia and Low levels of viral shedding in oral and nasal secretions was detectable between 6 and 15, and 12 and 18 DPI, respectively following febrile reaction. LSDV is also demonstrated in saliva, semen and skin nodules for at least 11, 42 and 39 days after the development of fever, respectively [3,22]. Viral replication in microphages, fibroblasts, pericytes, endothelial cells and probably other cells in blood vessel and lymph vessel walls causes vasculitis and lymphagitis in some vessels in affected areas, while thrombosis and infarction may result in severe cases [3]. In natural infection, very young calves, lactating cows, and malnourished animals seem to develop more severe disease that may be due to an impaired humoral immunity. Antibodies was detectable 21 DPI using serum neutralization tests [5]. Immunity after recovery from natural infection is life-long; calves of immune cows acquire maternal antibody and are resistant to clinical disease for about six months [22,45]. Eventually, affected animals clear the infection and there is no known carrier state for LSDV [27].

Clinical Manifestations and Pathology

Clinical manifestations

The time between inoculation and first observation of generalized clinical signs ranges from 7 to 14 days in experimentally infected cattle, irrespective of the route of infection [21] and between 2 to 5 weeks in natural cases [21,45]. LSD can be classified into mild and severe forms based on the number of lumps (nodules) and occurrence of complications, dose of the inoculum as well as the susceptibility of the host and the density of insect population. Accordingly appearance of one or two lumps (Figure 3B) or nodules within 2 days after onset of the fever (1 to 5 cm in diameter), depression, anorexia, excessive

salivation, ocular and nasal discharge, agalactia and emaciation are clinical manifestation of mildly affected cattle. Also, nodular lesions which is painful and hyperemic may be observed on the animal body especially in the skin of the muzzle, nares, back, legs, scrotum, perineum, eyelids, lower ear, nasal and oral mucosa, and tail [9]. In severe cases that may persist for 7-12 days, continuous high pyrexia (40-41.5°C), serious depression, anorexia and a characteristic several (more than hundreds) nodules and usually fairly uniform in size in the same animal, all over the animal body is observed (Figure 3A) [40].

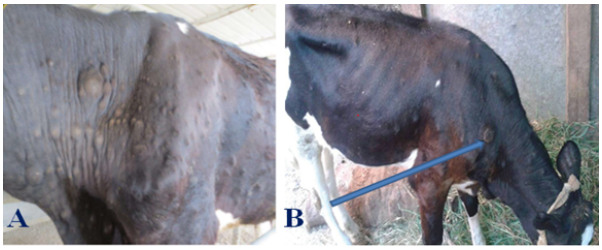

Figure 3: Characteristic LSD nodular lesion indicating severity: Lesion covering the whole body in severe form (A) and LSD with few skin nodules in mild form (B), adapted from [46,47].

The nodules are firm and slightly raised above the surrounding normal skin from which they are often separated by a narrow ring of hemorrhage (Figure 4A). They involve the epidermis, dermis, adjacent subcutis and musculature. Nodules may disappear, but they may persist as hard lumps or become moist, necrotic, and slough or ulcerated (Figure 4B). Lesions where skin is lost may remain visible for long periods. When lesions coalesce, large areas of raw tissue can be exposed, and these are susceptible to invasion with screwworm fly larvae [20]. The sloughed away lesion may create a hole of full skin thickness and characteristic lesion of "inverted conical zone" of necrosis, known as "sit fast" (Figure 4C) [48].

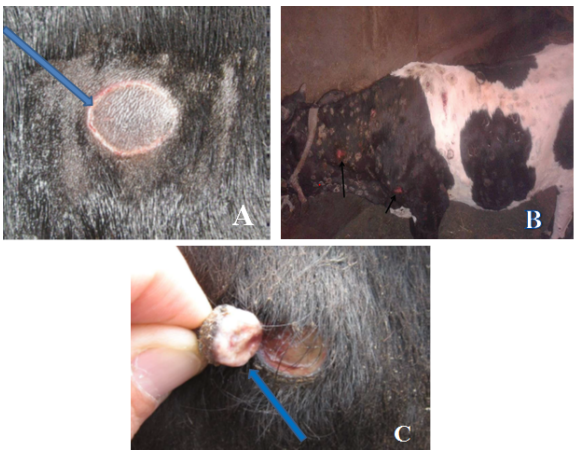

Figure 4: Distinguishing lesions of LSD: Raised and separated narrow ring of hemorrhage" (A), skin lesions leaving ulcer (B) and "sit fast" like "inverted conical zone" of necrosis (C), adapted from [46,48].

Affected animals also exhibit excessive salivation, lacrimation, nasal discharge and emaciation due to necrotic plaques and typical LSD lesions in oral cavity, conjunctiva and nasal cavity, respectively. Enlargement of superficial lymph nodes and lymphadenopathy are also feature of LSD. In addition, lactating cow's milk production may lessen and mastitis occurs and possibly abortion in some pregnant cows; calves with extensive skin lesions, presumably acquired by intrauterine infection may be delivered. Swelling of the testicles and orchitis are also occurring in infected bulls. Following lesions in reproductive organs, temporary or permanent sterility may occur in bulls and cows [20]. Edematous and inflammatory swellings of the brisket (Figure 5B), face (Figure 5A) and one or more limbs may be seen and can severely restrict movement (Figure 5C), deep ulcerative skin lesions, keratitis (unilateral or bilateral) are also seen in some of infected cows [9-12,23]. Pox lesions may also be present in the pharynx, larynx, trachea, lungs and throughout the alimentary tract. The lesions in the respiratory tract are often followed by pneumonia [5].

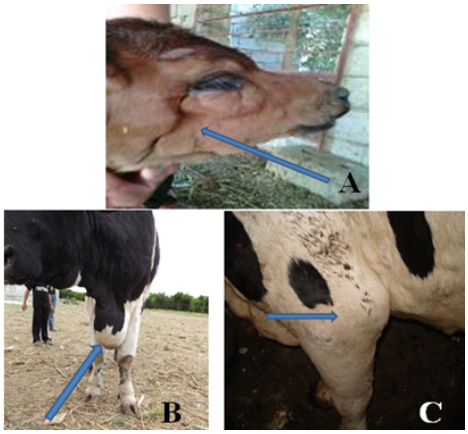

Figure 5: Edematous and inflammatory swelling on different parts of the body; on the face (A), brisket (B) and limb (C) of affected cattle adapted from [23,48].

Severe cases of LSD are highly characteristic and easy to recognize, but early stages of infection and mild cases may be confusing with other diseases affecting the skin. For instance Pseudo lumpy skin disease also known as Allerton virus caused by bovine herpes virus-2 (BHV) has related skin lesions with LSD and requires laboratory confirmation to distinguish. Pseudo lumpy skin disease has circular superficial lesions which may cover the entire body and up to 2 cm in diameter. It has distinctive intact central area (Figure 6B) and raised edges, accompanied by loss of hair. Urticaria, Streptotrichosis (*Dermatophilus congolensis* infection), ringworm, *Hypoderma bovis* infection, photosensitization, bovine papular stomatitis, foot and mouth disease, bovine viral diarrhea, and malignant catarrhal fever are all considered as differential diagnosis of LSD [20,27,47].

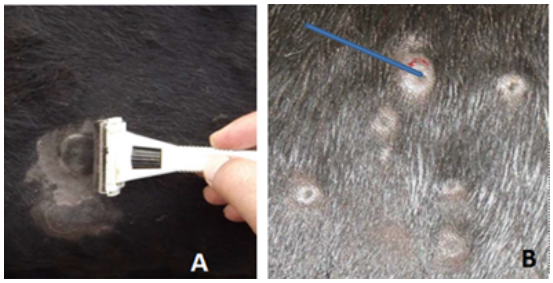

Figure 6: Illustrative clinical feature of LSD (A) and BHV (B), with characteristic intact central area (blue arrow).

Pathology

Gross pathological lesions: Skin nodules are usually uniform in size, firm round and raised, but some may fuse into large irregular and circumscribed plaques, when incised the surface of the nodule is reddish-gray and edematous in the sub-cutis layer. A necrotic lesion which is circular in nature may be observed in different parts of alimentary, respiratory and urogenital tract (Figure 7). For instance, muzzle, nasal cavity, larynx, trachea, bronchi, inside of lips, gingiva, dental pad, abomasum, uterus, vagina, teats, udder and testes may be involved [12,27]. Regional lymph nodes become enlarged (up to 10 times than their usual size), edematous, congested and having pyaemic foci, in addition to local cellulitis [9]. Pleuritis and enlargement of mediastinal lymph nodes are also involved in severe cases. The LSD typical nodular lesions also encompass the musculature and the fascia over limb and appear grey-white surrounded by red inflammatory tissue. Furthermore, the lesions are separated from the necrotic epithelium far from the healthy tissue and leave an ulcer that slowly heals by granulation. Severely infected animals may show secondary bacterial pneumonia, tracheal stenosis, acute and chronic orchitis, mastitis with secondary bacterial infection, and similar lesions in the female reproductive tract [49].

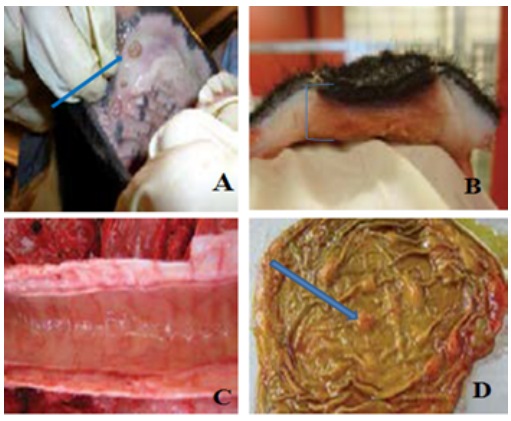

Figure 7: Internal lumpy skin lesions: Ulcerative lesions in the oral cavity (A) and cross-section of skin lesion (B); lesions in the trachea (C) and gall bladder (D), adapted from [27].

Histopathological findings: Histopathological findings of the LSD are typical and provide a basis for diagnosis. The pathognomonic LSD lesion eosinophilic intracytoplasmic inclusion bodies may be detected microscopically in the keratinocytes, macrophages, endothelial cells and pericytes from skin nodules in addition to ballooning and degeneration of the cell layers. Inflammatory cells including macrophages, lymphocyte and eosinophils are infiltrated the affected area. In addition, widespread vasculitis which reflects the viral tropism for endothelial cells is seen histologically [20,50]. If there is muscular damage during the course of LSD, histopathologically sever coagulative necrosis in subcutaneous muscle may be observed [51].

Hematological and serum biochemical changes: Hematological and serum biochemical analysis of animals naturally and experimentally infected by LSDV were recently studied and described [46,51,52]. The results of Neamat-Allah, revealed that there is a significant decrease in red blood cells, hemoglobin, packed cell volume, and mean corpuscular hemoglobin concentration with a significant increase in mean corpuscular volume in experimentally infected animals which is interpreted as a macrocytic hypochromic anemia [46]. On the other side leucogram results showed leucopenia and lymphopenia which may be due to viral infection and granulocytic leukocytosis which could be due to secondary acute bacterial infections, especially pyogenic bacterial infections. LSD was also reported to be associated with inflammatory thrombocytopenia, hyperfibrinogenemia, decreased creatinine concentration, hyperchloremia and hyperkalemia in naturally infected cattle [52]. Neamat-Allah and Abutarbush studies showed the existence of a significant decrease in total protein and albumin in serum, however; there was a significant increase in globulin, especially gamma globulins in LSD infected cows [46,52]. In addition the results of Sevik et al. on serum biochemical analysis of LSD infected cattle showed that aspartate aminotransferase and alkaline phosphatase increase in addition to globulin protein and creatinine concentrations [51]. Finally, the studies concluded that the alteration in serum biochemical analysis might be due to liver and kidney failures, severe inflammatory process and disease complications such as anorexia and reduced muscle mass during LSDV infection.

Economic Importance of LSD

The morbidity and mortality rate of LSD varies widely, depending on the presence of insect vectors and host susceptibility. Generally high milk-producing European cattle breeds are highly susceptible and severely affected compared to indigenous African and Asian animals. The morbidity rate of the disease may ranges from 3% to 85% and in endemic areas it is usually around 10%. Although the disease is not associated with high mortalities (1-3%), the economic losses accompanying LSD eruption is higher. It results in great economic losses due to decreased feed intake, milk production, weight conversion, abortion and infertility, and damaged hides. In addition, the disease is an important notifiable disease and hampers the international trade [31,48,53]. Lumpy skin disease virus is recently considered as a potential agent of agro terrorism because of its endowed ability to spread out of Africa to the outside world [47]. Abutarbush et al. study during an outbreak in Jordan estimated the average cost of supportive antibiotic treatment to be 27.9 British pounds per head [48]. The financial cost of clinical LSD based on questionnaire survey distributed to livestock farmers, in Oromia regional state of Ethiopia, was studied [25]. 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 average financial cost in

infected herds was estimated to be 6.43 USD per head for local zebu and 58 USD per head for Holstein Friesian or crossbred cattle [25].

Diagnostic Techniques

The diagnosis of LSD can be established based on the typical clinical signs or generalized nodular skin lesions and enlarged superficial lymph nodes in affected animals combined with laboratory confirmation of the presence of the virus or antigen. For laboratory confirmation various diagnostic techniques (Table 1) which require different types of samples need to be performed. The gold standard method for the detection of capripox viral antigen and antibody are electron microscopy examination and serum or virus neutralization tests, respectively [36].

The clinical diagnosis of LSD can be confirmed using conventional or real-time PCR methods [10,36,45]. 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 [36]. A study to compare the different diagnostic tests in experimentally infected cattle was conducted and specified PCR was a fast and sensitive method in demonstrating viral DNA in blood and skin samples [45]. However, it is time consuming to use for instance, viremia was detected from 1-12 days using virus isolation, while 4–11 days using PCR. LSDV will grow in tissue culture of bovine, ovine or caprine origin, although primary or secondary culture of bovine dermis cells or lamb testis cells are considered to be the most susceptible [14]. It causes characteristic cytopathic effect and intracytoplasmic inclusion bodies and is distinct from BHV-2 which producing syncytia and intranuclear inclusion bodies [5].

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. Antibody ELISAs have been developed with limited success [36]. Indirect fluorescent antibody test (IFAT) can be used for LSD diagnosis and screening however, the test requires longer time and may be more costly as compared to ELISA technique [54].

Test Purpose	Methods	Epidemiological investigation	Screening prior to movement	Contribute to eradication	Confirmation in clinical cases	Prevalence of infection surveillance	Immune status in individual animals or populations post vaccination
Agent identification	Virus isolation	+	++	+	+++	+	–
	PCR	++	+++	++	+++	+	–
	Electron microscopy	–	–	–	+	–	–
Detection of immune response	IFAT	+	+	+	+	+	+
	VN	++	++	++	++	++	++

Table 1: Key:+++=recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – =not appropriate for this purpose; although not all of the tests listed as category +++ or ++ have undergone formal validation, their routine nature and the fact that they have been used widely without dubious results, makes them acceptable. PCR=polymerase chain reaction; VN=virus neutralization; IFAT=indirect fluorescent antibody test, adapted from OIE.

Treatment, Prevention and Control

The treatment of LSD is only symptomatic and targeted at preventing secondary bacterial complications using antimicrobial therapy [48]. Treatment trials performed by Salib and Osman, with the aim of preventing LSD complications and saving life has been successful using combination of antimicrobials, anti-inflammatory, supportive therapy and anti-septic solutions [9]. The complications encountered during the trial including corneal opacity (keratitis), mastitis, dysentery, lameness, pneumonia and myasis have been recovered within 3 days to 2 weeks. However, the treatment of LSD (its complications) is costly as well as does not ensure full recovery therefore; prevention is more beneficial to avoid the substantial economic losses due to hide damages, loss of milk due to mastitis and loss of animal product due to death, abortion, fever and myiasis. Gari et al. study on epidemiological aspects and financial impact of lumpy skin diseases in Ethiopia illuminates the importance of vaccination in controlling LSD in endemic areas [25]. The authors also enumerates vaccination can enable the financial costs due to LSD to be reduced by 17% per head in local zebu herds and 31% per head in Holstein Friesian or crossbred herds.

Therefore vaccination is the only effective method to control the disease in endemic areas as movement restrictions and removal of affected animals alone are usually not effective. Effective vaccines against LSD exist and the sooner they are used the less severe the economic impact of an outbreak is likely to be [27]. Members of the *capripoxvirus* are known to provide cross protection. Hence, homologous (Neethling LSDV strain) and Heterologous (sheep pox or goat pox virus) live attenuated vaccines can all be used to protect cattle against LSD infection [16]. Commercially available *capripoxvirus* (CaPV) vaccine strains include 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 [47]. Recently, a study by Gari et al. on efficacy of three CaPV strains against LSD in Ethiopia revealed that the Gorgan GTP vaccine can effectively protect cattle against LSDV and that the Neethling and KSGP O-180 vaccine were incompetent and suggests the need for further molecular characterization for those ineffective vaccines [55]. In countries previously free of LSD and which use sheep pox vaccine to protect sheep against sheep pox, it is recommended to use the same vaccine during LSD outbreaks, because of potential safety issues associated with the live attenuated LSDV vaccine use [15]. In addition, rapid confirmation of a clinical diagnosis is essential so that

eradication measures, such as quarantine, slaughter-out of affected and in-contact animals, proper disposal of carcasses, cleaning and disinfection of the premises and insect control can be implemented as soon as possible during the eruption [20,45]. Moreover, rigorous import restrictions on livestock, carcasses, hides, and semen from endemic areas must be in place in disease free areas.

Conclusion and Recommendations

Lumpy skin disease (LSD), which is a vector borne disease caused by genus CaPV, is previously restricted to sub-Saharan Africa. However, in recent times it is slowly invading new territories including Europe. Clinically the disease is characterized by distinctive nodular lesions principally on the skin and underlying tissues of affected animals with occasional involvement of different parts of the body including; conjunctiva, alimentary, respiratory and urogenital tracts. The lesions consequently, results in overwhelming economic losses due to reduced hide quality, chronic debility, reduced milk yield, weight loss, infertility, abortion and death. These may also impose dramatic effects on rural livelihoods, which are strongly dependent on cattle, with significant production losses. Disease consequences are also devastating at national level since its presence has triggered strict trade restrictions. Therefore, in order to come across these alarming situations, the following recommendations are forwarded;

- Clinico-hematological and biochemical profile of cattle affected by LSD need to be identified in addition to typical clinical signs.
- Accurate on time diagnosis is needed for control measurements.
- Annual vaccination strategy with homologous strain of the LSDV is obligatory in endemic areas.
- Vector control and animal movement restriction during active period of insect movement is important.
- Bulls used for breeding need to be diagnosed for LSDV.

References

1. CFSPH (2008) Center for Food Security and Public Health, Iowa State University. Lumpy Skin Disease. Accessed on July 17, 2017.
2. Davies GF (1991) Lumpy skin disease of cattle: A growing problem in Africa and the NearEast. FAO Corporate Document Repository, Agriculture and Consumer protection.
3. Coetzer JAW, Tuppurainen E (2004) Lumpy skin disease. In: Infectious diseases of livestock. Oxford University Press, Southern Africa 2: 1268-1276.
4. Bhanuprakash V, Indrani BK, Hosamani M, Singh RK (2006) The current status of sheeppox disease. Comp Immunol Microbiol Infect Dis 29: 27-60.
5. Babiuk S, Bowden T, Boyle D, Wallace D, Kitching RP (2008b) *Capripoxvirus*es: an emerging world wide threat to sheep goats and cattle. Transbound Emerg Dis 55: 263-272.
6. Fassi-Fehri MM (2010) Sheep pox and Goat Pox. Infectious and Parasitic diseases of Livestock. Lavoisier Paris, 392.
7. Lefèvre PC, Gourreau JM (2010) Lumpy Skin disease. In: Lefèvre PC, Blancou J, Chermette R, Uilenberg G (Eds.) Infectious and Parasitic diseases of Livestock. OIE -407.
8. Brenner J, Haimovitz M, Oron E, Stram Y, Fridgut O, et al. (2006) Lumpy skin disease in a large dairy herd in Israel. Israel Journal of Veterinary Medicine 61: 103.
9. Salib FA, Osman AH (2011) Incidence of lumpy skin disease among Egyptian cattle in Giza Governorate, Egypt. Veterinary World 4: 162-167.
10. Elhaig MM, Selim A, Mahmoud M (2017) Lumpy skin disease in cattle: Frequency of occurrence in a dairy farm and a preliminary assessment of its possible impact on Egyptian buffaloes. Onderstepoort J Vet Res 84: 1393.
11. Tageldin MH, Wallace DB, Gertdes GH, Putterill JF, Greyling RR, et al. (2014) Lumpy skin disease of cattle: an emerging problem in the Sultanate of Oman. Trop Anim Health Prod 46: 241-246.
12. Al-Salihi KA, Hassan IQ (2015) Lumpy Skin Disease in Iraq: Study of the Disease Emergence. Transbound Emerg Dis 62: 457-462.
13. Sameea P, Mardani K, Dalir-Naghadeh D, Jalilzadeh-Amin G (2016) Epidemiological Study of Lumpy Skin Disease Outbreaks in North-western Iran. Transbound Emerg Dis 64: 1782-1789.
14. OIE (2017) World Organization for Animal Health. Lumpy Skin Disease. Terrestrial Animal Health Code.
15. Tuppurainen E, Oura C (2012) Review: Lumpy skin disease: An emerging threat to Europe, the middle east and Asia. Transbound Emerg Dis 59: 40-48.
16. OIE (2013) World Organization for Animal Health. Lumpy Skin Disease. Technical Disease Card.
17. Gari G, Waret-Szkuta A, Grosbois V, Jacquiet P, Roger F (2010) Risk factors associated with observed clinical lumpy skin disease in Ethiopia. Epidemiol Infect 138: 1657-1666.
18. Shen YJ, Shephard E, Douglass N, Johnston N, Adams C, et al. (2011) A novel candidate HIV vaccine vector based on the replication deficient *Capripoxvirus*, Lumpy skin disease virus (LSDV). Virol J 8: 265.
19. El-Nahas EM, Habba AS, El-bagoury GF, Radwan EI (2011) Isolation and Identification of Lumpy Skin Disease Virus from Naturally Infected Buffaloes at Kaluobia, Egypt. Global Veterinaria 7 : 234-237.
20. Constable PD, Hinchcliff KW, Done SH, Grundberg W (2017) Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. 11th edn. Elsevier, UK, p: 1591.
21. Carn VM, Kitching RP (1995) The clinical response of cattle experimentally infected with lumpy skin disease (Neethling) virus. Arch Virol 140: 503-513.
22. Al-Salihi KA (2014) Lumpy Skin disease: Review of literature. Mirror of Research in Veterinary Sciences and Animals 3: 6-23.
23. Jameel GH (2016) Determination of complications decrease the risk factor in Cattle infected by lumpy skin disease virus in diyala province, Iraq. International Journal of Micro Biology, Genetics and Monocular Biology Research 2: 1-9.
24. AU-IBAR (2013) African Union - Interafrican Bureau for Animal Resources: lumpy skin disease. Selected content from the Animal Health and Production Compendium.
25. Gari G, Bonnet P, Roger F, Waret-Szkuta A (2011) Epidemiological aspects and financial impact of lumpy skin disease in Ethiopia. Prev Vet Med 102: 274-283.
26. Abera Z, Degefu H, Gari G, Kidane M (2015) Sero-prevalence of lumpy skin disease in selected districts of West Wollega zone, Ethiopia. BMC Vet Res 11: 135.
27. Tuppuraine ES, Alexandrov T, Beltran-Alcrudo D (2017) Lumpy skin disease field manual - A manual for veterinarians. FAO Animal Production and Health Manual 20: 1-60.
28. Quinn PJ, Markey BK, Leonard FC, Fitzpatrick FS, Fanning S (2016) Concise Review of Veterinary Microbiology. 2nd edn. John Wiley and Sons Ltd, UK, p: 142.
29. Carter GR, Wise DJ, Flores EF (2005) A Concise Review of Veterinary Virology. Accessed on July 14, 2017.
30. King AM, Adams MJ, Carstens EB, Lefkowitz EJ (2012) Virus Taxonomy. Classification and Nomenclature of Viruses. Ninth Report of the International Committee on Taxonomy of Viruses, pp: 289-307.
31. EFSA (2015) European Food Safety Authority. Scientific Opinion on Lumpy Skin Disease. EFSA Panel on Animal Health and Welfare (AHAW). EFSA Journal 13: 3986.
32. Tulman CL, Afonso ZLU, Zsak L, Kutish GF, Rock DL (2001) Genome of Lumpy Skin Disease Virus. J Virol 75: 7122-7130.
33. Tulman CL, Afonso ZLU, Zsak L, Kutish GF, Rock DL (2002) The genomes of sheeppox and goatpox viruses. J Virol 76: 6054-6061.

34. El-Kenawy AA, El-Tholoth MS (2010) Sequence analysis of attachment gene of lumpy skin disease and sheep poxviruses. Virol Sin 25: 409-416.
35. Ali H, Ali AA, Atta MS, Cepica A (2012) Common, emerging, vector-borne and infrequent abortogenic virus infections of cattle. Transbound Emerg Dis 59: 11-25.
36. Tuppuraine ES, Stoltsz WH, Troskie M, Wallace D, Oura CA, et al. (2011) A Potential Role for Ixodid (Hard) Tick Vectors in the Transmission of Lumpy Skin Disease Virus in Cattle. Transbound Emerg Dis 58: 93-104.
37. Lubinga JC, Tuppuraine ES, Stoltsz WH, Ebersohn K, Coetzer JA, et al. (2013) Detection of lumpy skin disease virus in saliva of ticks fed on lumpy skin disease virus-infected cattle. Exp Appl Acarol 61: 129-138.
38. Lubinga JC, Tuppuraine ES, Coetzer JA, Stoltsz WH, Venter EH (2014) Evidence of lumpy skin disease virus over-wintering by transstadial persistence in *Amblyomma hebraeum* and transovarial persistence in *Rhipicephalus decoloratus* ticks. Exp Appl Acarol 61: 77-90.
39. Chihota CM, Rennie LF, Kitching RP, Mellor PS (2001) Mechanical transmission of lumpy skin disease virus by *Aedes aegypti* (Diptera: Culicidae). Epidemiol Infect 126: 317-321.
40. Weiss KE (1968) Lumpy skin disease virus. In: Virology Monographs. Springer Verlag, Vienna, New York, pp: 111-131.
41. Chihota CM, Rennie LF, Kitching RP, Mellor PS (2003) Attempted mechanical transmission of lumpy skin disease virus by biting insects. Med Vet Entomol 17: 294-300.
42. Sevik M, Dogan M (2015) Epidemiological and Molecular Studies on Lumpy Skin Disease Outbreaks in Turkey during 2014-2015. Transbound Emerg Dis 64: 1268-1279.
43. Irons P, Tuppurainen E, Venter E (2005) Excretion of lumpy skin disease virus in bull semen. Theriogenology 63: 1290-1297.
44. Annandale CH, Holm DE, Ebersohn K, Venter EH (2014) Seminal Transmission of Lumpy Skin Disease Virus in Heifers. Transbound Emerg Dis 61: 443-448.
45. Tuppuraine ES, Coetzer JA, Venter EH (2005) The detection of lumpy skin disease virus in samples of experimentally infected cattle using different diagnostic techniques. Onderstepoort J Vet Res 72: 153-164.
46. Neamat-Allah ANF (2015) Immunological, hematological, biochemical, and histopathological studies on cows naturally infected with lumpy skin disease. Vet World 8: 1131-1136.
47. Abutarbush SM (2017) Lumpy Skin Disease (Knopvelsiekte, Pseudo-Urticaria, Neethling Virus Disease, Exanthema Nodularis Bovis). In: Bayry J (eds.) Emerging and Re-emerging Infectious Diseases of Livestock. Springer International Publishing, Gewerbestrasse 11, 6330 Cham, Switzerland, pp: 309-326.
48. Abutarbush SM, Ababneh MM, Al Zoubil IG, Al Sheyab OM, Al Zoubi MG, et al. (2013) Lumpy Skin Disease in Jordan: Disease Emergence, Clinical Signs, Complications and Preliminary-associated Economic Losses. Transbound Emerg Dis 62: 549-554.
49. El-Neweshy MS, El-Shemey TM, Youssef SA (2013) Pathologic and immunohistochemical findings of natural lumpy skin disease in Egyptian cattle. Pakistan Vet J 33: 60-64.
50. Body M, Pal Singh K, Hammid Hussain M, AL-Rawahi A, Al-Maawali M, et al. (2011) Clinico-Histopathological Findings and PCR Based Diagnosis of Lumpy Skin Disease in the Sultanate of oman. Pakistan Vet J 32: 206-210.
51. Sevik M, Avci O, Dogan M, Ince O (2016) Serum Biochemistry of Lumpy Skin Disease Virus-Infected Cattle. BioMed Res Int 2016: 6257984.
52. Abutarbush SM (2015) Hematological and serum biochemical findings in clinical cases of cattle naturally infected with lumpy skin disease. J Infect Dev Ctries 9: 283-288.
53. Babiuk S, Bowden TR, Dalman B, Parkyn G, Copps J (2008a) Quantification of lumpy skin disease virus following experimental infection in cattle. Transbound Emerg Dis 55: 299-307.
54. Gari G, Biteau-Coroller F, LeGoff C, Caufour P, Roger F (2008) Evaluation of indirect fluorescent antibody test (IFAT) for the diagnosis and screening of lumpy skin disease using Bayesian method. Vet Microbiol 129: 269-280.
55. Gari G, Abiea G, Gizawa D, Wubetea A, Kidanea M, et al. (2015) Evaluation of the safety, immunogenicity and efficacy of three *capripoxvirus* vaccine strains against lumpy skin disease virus. Vaccine 33: 3256-3261.