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# Lumpy skin disease: A comprehensive review

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## Abstract

Lumpy skin disease (LSD) is a viral disease affecting cattle worldwide, causing significant economic losses in dairy farming. This review summarizes the latest updates on LSD, including its epidemiology, pathophysiology, transmission, clinical signs, diagnosis, treatment, and prevention. LSD is characterized by fever, skin nodules, and lymph node swelling, with a morbidity rate of 45-100% and mortality rate of 10-40%. The disease is transmitted mechanically through arthropod vectors and can also spread through direct contact. Vaccination is the primary control measure, with live attenuated strains of capripoxvirus used as vaccines. The economic impact of LSD is substantial, with losses due to reduced milk yield, abortion, and hide damage. Understanding the epidemiology and pathophysiology of LSD is crucial for developing effective disease management strategies. This review aims to provide a comprehensive overview of LSD, highlighting its significance as a major transboundary animal disease.

**Keywords:** Lumpy skin disease virus (LSDV); Capripox virus; Cattle; Skin lesions; Vaccine

## 1. Introduction

Lumpy skin disease (LSD) is an emerging viral disease affecting bovine population world including India. It is spreading rapidly in various parts of world and causing severe economic losses in dairy farming due to reduced milk yield, abortion and hide damage [1]. The increasing emergence or recurrence of major trans-boundary and emerging animal diseases in recent decades has become a matter of great economic and public health concern worldwide [2]. Livestock is an integral component of rural society of India. In 2020-21, the contribution of livestock was 6.17% to 30.87% to national and agricultural Gross Value Added (GVA) respectively. The Dairy sector proves to be the backbone of rural economy. Among all the agricultural commodities in India, milk is the highest grossed commodity with 66.76% of contribution in the total value output from livestock sector [3]. LSD was reported for the very first time in 1929 (in Zambia) since then, it was confined to various areas of Africa. The first occurrence of LSD outside of Africa was reported in Israel between 1986 and 1988 and has gradually spread to the Middle East, then Eastern Europe and Russia. In 2019, new cases were reported in South and East Asia [2]. Bangladesh was identified as the first hotspot in South Asia, with the first incident occurring on July 14, 2019 [4]. In 2021, the disease was confirmed in Pakistan, Mongolia, Vietnam, Thailand, Laos, Cambodia, and Malaysia. Starting from March 2022, it was officially reported by Indonesia, Afghanistan, and Singapore. LSD is the best example of an emerging infectious disease owing to its recent rapid spread and geographic expansion in disease-free Asian countries. Initially limited to Africa, since 2019, the disease has spread through China and Southeast Asia [5]. The reasons of the disease spread to India are unknown but it may be due to livestock movement across international borders or may be due to vectors movement from the neighbouring countries. In recent years, LSD has been reported from countries neighbouring India like China and Bangladesh. Therefore, understanding the epidemiology of exotic diseases becomes necessary for timely planning effective disease management. This review summarizes the latest updates about the LSD [6].

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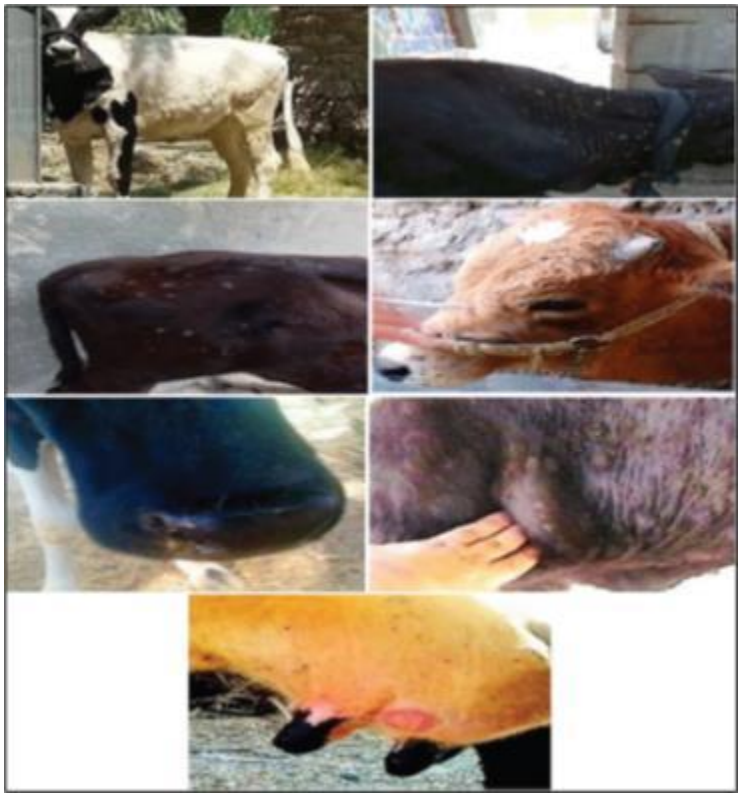

**Figure** 1 Skin lesions in different body areas of cattle [1]

Lumpy skin disease (LSD) is highly contagious viral infection of cattle that is caused by the lumpy skin disease virus (LSDV) [7]. The incidence of LSD occurrence is high during wet seasons when biting-fly populations are abundant and it decreases or ceases during the dry season. Direct transmission can also occur between infected animals, but such transmission is rare and of low epidemiological significance [8]. The transmission pathways may vary among different genera within the Poxviridae family [9]. LSD is associated with high morbidity but low mortality. LSD is a vector-borne, nonzoonotic disease [7]. It is characterized by fever, lymph node swelling, circumscribed nodules on skin causing severe emaciation, reduction in milk production, infertility. Overall, it affects the economic value of animal as it will affect the meat and milk production, hide quality, draft power of animals and reproductive efficiency [9]. In difference, LSDV can experimentally infect sheep and goats, but no natural infection of goats with LSDV has been reported [10].

## 2. Etiology

LSD virus from the Poxviridae family that is divided into two subfamilies, poxviruses affecting insects (Entomopoxvirinae) and vertebrates (Chordopoxvirinae) causes lumpy skin disease [11, 12]. Lumpy skin disease (LSD) is caused by LSDvirus (LSDV), a virus in the family Poxvirus, genus Capripoxvirus as well as sheep pox virus (SPPV) and goat pox virus (GTPV) [13]. This genus is made up of the goat pox virus (GTPV), sheep pox virus (SPPV), and lumpy skin disease virus (LSDV). GTPV infects goats, sheep are infected by SPPV, and LSDV infects cattle and buffalo. There is only one serotype of LSDV, which is phylogenetically distinct but serologically related to SPPV and GTPV [5]. These three viruses could cause transboundary disease with serious consequences among the ruminants, causing a major threat to the global animal husbandry [14]. LSDV is narrow vertebrate host range that mainly affects cattle, both Bos indicus and Bos taurus among which, Bos taurus is more susceptible and vulnerable to clinical disease compared to Bos indicus and also, domestic water buffalo (Bubalus bubalis) and responsible for devastating economic and production loss and negative impacts [15].

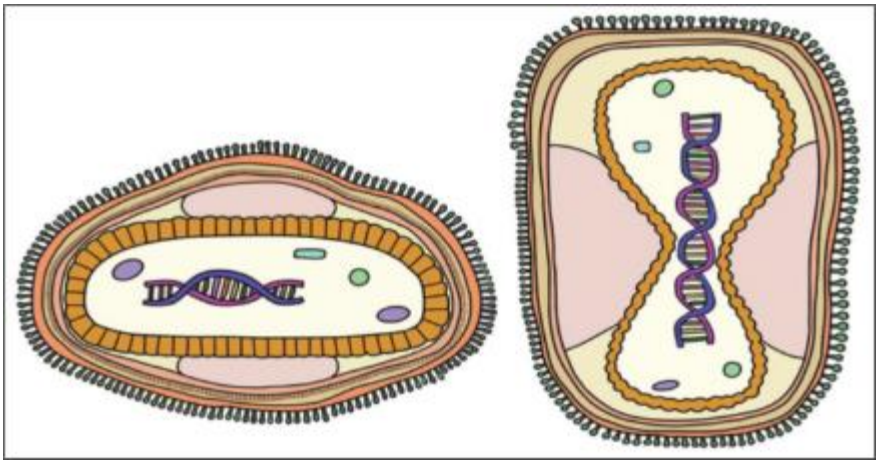

**Figure 2** Schematic diagram of the poxvirus structure [13]

LSDV is pleomorphic, enveloped, brick or oval-shaped dsDNA virus with a molecular size of 350*300nm and a molecular weight 73 to 91 KDa. An LSDV genome sequence is 145 to 152 [16]. The viral DNA contains roughly 146 conserved genes that are critical in driving molecular processes like DNA replication, transcription, virion production, and assembly. However, LSDV completely depends on the host cellular machinery to translate viral mRNA. Also, the LSDV genome contains homologous genes such as G protein-coupled CC chemokine receptor (GPCR), interleukin-10 (IL-10), IL-1 binding proteins and epidermal growth 3 factor-like protein, which are commonly observed in related poxviruses [7]. LSDV is very stable and survives well in extremely cold and dry environments within the pH range 6.3-6.8 [17]. The virus is susceptible to ether (20 %), chloroform, formalin (1 %) and some detergents, e.g., sodium dodecyl sulphate. It is susceptible to phenol (2 % for 15 minutes), sodium hypochlorite (2–3%), iodine compounds (1:33 dilution), Virkon® (2%) and quaternary ammonium compounds (0.5%) [18]. LSDV has more than 97% nucleotide sequence homology with GTPV [14]. The Capripoxvirus have oval profile shape that is a larger size than Orthopoxvirus so that this virus can grow on the different type of tissue, like chicken embryo fibroblasts, thyroid gland, rabbit kidney, skin and equine lungs, through primary isolation of virus the cytopathic effect may take up to 11 days accompanied to various kinds of serotype, except one types that are closely related serologically to poxvirus of goats and sheep and not easy to distinguish by routine technique [19]. LSDV can persist in skin plugs for approximately 42 days [20].

## 3. Risk factors

It has been documented that wild animal such as African buffaloes, eland, blue wildebeest, giraffe, greater kudu and impala are the source of LSD spreading [21]. The automatic spread of the LSD virus has mainly associated with flying insects and all the possible clue confirms the field observations that epidemics of LSD occur at periods of greatest biting insect activity [22]. Young animals are severely affected, and clinical symptoms are rapid to appear, Lactating cows appearing to be severely affected and result in a sharp drop in milk production because of high fever caused by viral infection itself and secondary bacterial mastitis. LSD can also spread through the host factors, pathogenic factors and environmental factors [23].

## 4. Transmission of LSD

The direct spread of LSD can happen when animals use the same feeding and drinking areas, leading to contamination by nasal and salivary discharges from infected animals or ingestion of contaminated food [20]. LSD-infected cattle can affect uninfected cattle by vectorial or non-vectorial transmission [10]. Poxvirus, LSD is a host-specific disease that is transmitted mechanically through arthropod vectors, with its infective host(s) being bovine animals like cows and buffaloes, LSD is a non-zoonotic disease with no traceable history or evidence of human infection to date [16]. The disease can also be transmitted through infected milk to suckling calves. LSD virus sexual transfer was seen from infected bull semen to the heifer and even congenitally to the foetus [24]. The transmission of LSD are shown in figure no. 3.

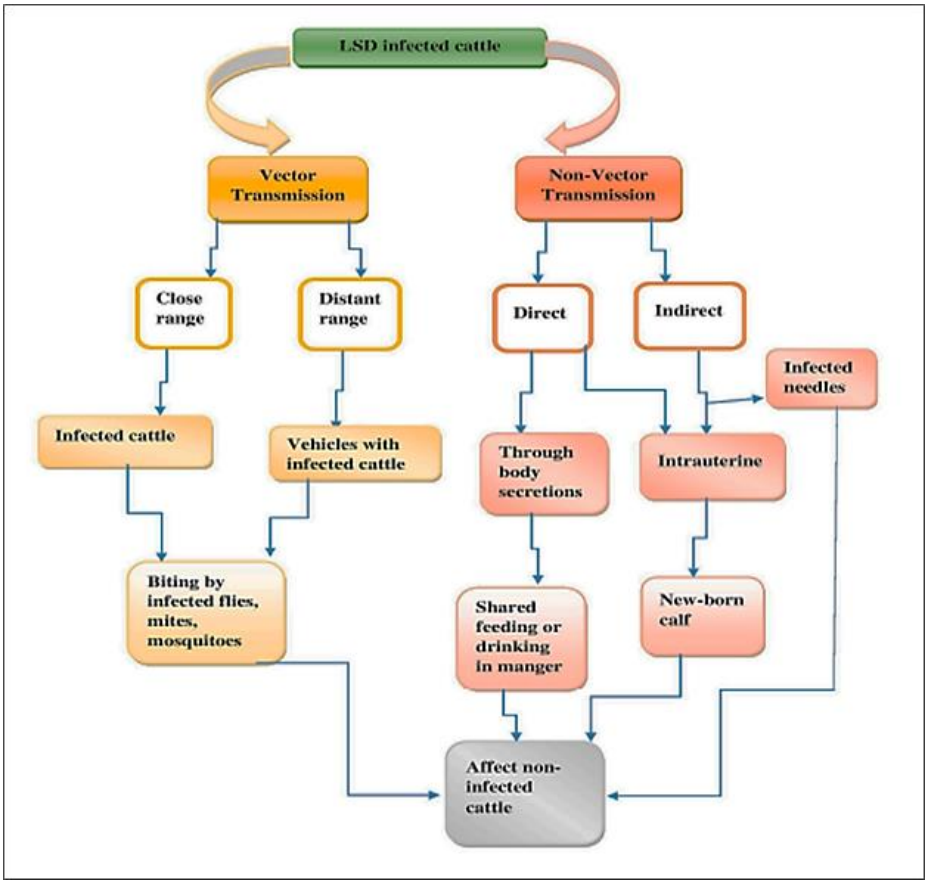


**Figure 3** Transmission of LSD [9]

## 5. Morbidity and mortality rate

Morbidity and mortality rate of LSD varies according to climatic conditions. Morbidity and mortality rate of LSD varies between 45%-100% and 10%-40% [21]. The morbidity of the disease is highest in wet, warm weather and decreases during the dry season, Reported morbidity rates during outbreaks range from 1-2% to 80-90%, while mortality rates are often between 1% and 6%, but are occasionally higher or lower. The overall morbidity rates during recent outbreaks in the Middle East and Europe were generally < 30%, and sometimes much lower; however, control measures may have limited the number of cases. Jordan reported morbidity and mortality rates of 43% and 10%, respectively, in unvaccinated cattle, compared to 5% morbidity and 1% mortality in vaccinated cattle [25, 26].

## 6. Pathogenesis

Pathogenesis studies have involved examining clinical manifestations and distribution of the virus in the body by inoculation via subcutaneous, intradermal, intravenous and intranasal routes [18]. LSDV replicate inside the host cell such as the macrophages, fibroblasts, pericytes and endothelial cells in the lymphatics and blood vessels walls lead to vasculitis and Lymphangitis, in severe cases thrombosis and infarction may also develop [27]. There have been few studies confirmed on the pathogenesis of LSD; in general, there is fever and viremia, followed by localization in the skin and development of nodules. Following subcutaneous inoculation with LSDV, swelling at the site of inoculation developed 4 to 7 day, which is varying in size from 1 to 3 cm [19]. Lumpy skin disease skin nodules may exude serum initially but develop a characteristic inverted grayish pink conical zone of necrosis [25]. During the initial days of viral infection, the nodules appear grayish-white (internally) and may also exude serum. However, following disease progression (~ 14 days), the nodules may develop a cone-shaped central core or sequestrum of necrotic material called the "sit-fast". A clinical study on LSDV surfaced previously, indicating the oxidation-anti-oxidation state imbalance in infected cattle, thereby invoking a significant rise in the levels of pro-inflammatory cytokines, extending negative consequences on animal health [7].

## 7. Clinical sign and symptoms

The disease is characterized by fever, nodules on the skin, mucous membranes, and internal organs, emaciation, enlarged lymph nodes, edema of the skin, and sometimes death. The characteristic skin lesions are multiple, well-circumscribed to coalescing, 0.5–5 cm in diameter, firm, flat-topped papules, and nodules [5]. The most common sites of nodules are head, neck, perineum, genitalia, limb and udder; involve skin, cutaneous tissues and sometime underlying part of the muscle [16]. Fever which may exceed 42°C along with anorexia, depression, and lethargy is observed. Corneal opacity and blindness may be observed in some cases. Pregnant animals may abort [17]. In lactating cattle there is a marked reduction in milk yield [27]. The incubation period of the disease is 2-5 weeks [23]. The following figure no. 4 and no. 5 show the lesions of skin in cattle.

**Figure 4** A cow showing typical lumpy skin disease skin lesions (arrow) [5]

**Figure 5** Lesions on skin of cattle [23]

## 8. Diagnosis of LSD

Based on symptoms seen in the animals, LSD can be diagnosed. Depending on the animal health, the symptoms may be severe, minor or long-lasting. The severity of disease in the 10% of affected cattle in the herd can vary from mild to fatal [24]. Clinically, it can be identified by the characteristic nodular lesions on the skin, which may be present as raised areas of hair, as well as nodules around the nostrils, mouth, vulva, and prepuce, these nodules can either persist as hard lumps or become moist, necrotic, and sloughed [20]. For laboratory confirmation various diagnostic techniques (Table 1) which require different types of samples need to be performed [28]. There are other methods that could be utilized

for the diagnosis of LSD including (a) the isolation of virus, (b) electron microscopy, (c) agar gel immunodiffusion, (d) polymerase chain reaction (PCR), (e) fluorescent antibody tests, (f) Enzyme-linked immunosorbent assays, (g) real time PCR [9].

**Table 1** The various diagnostics techniques of LSD [28]

| **Test Purpose** | **Methods** | **Epidemiological investigation** | **Screening prior to movement** | **Contribute to eradiation** | **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 | ++ | ++ | ++ | ++ | ++ | ++ |

In the above table the symbol are show +++ = recommended method; suitable method; + = may 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 fluorecent antibody test, adapted from OIE.

Disease can be confirmed with a laboratory diagnosis, with tests available to detect the DNA of the virus or antibodies. LSD can be confused with many diseases, including Pseudo lumpy skin disease (caused by Bovine Herpesvirus 2), Bovine papular stomatitis (Parapoxvirus), Pseudocowpox (Parapoxvirus), Cowpox, cutaneous tuberculosis, Demodicosis (Demodex), insect or tick bites, urticarial, photosensitisation, Papillomatosis (Fibropapillomas, "warts"), Rinderpest, Dermatophilosis, Besnoitiosis, Hypoderma bovis infection and Oncocercosis. Signs such as fever and milk drop are non-specific and can be seen with many other diseases [23].

## 9. Treatment and prevention of LSD

There is no specific treatment for lumpy skin disease. Nonspecific therapy using antibiotics, anti-inflammatory drugs, and vitamin injections is typically used to treat secondary bacterial complications, inflammation, and fever, as well as to increase the animal's appetite [5]. Because movement restrictions and the removal of affected animals are typically ineffective, vaccination is the only practical and economically viable strategy for controlling the spread of the disease and improving cattle productivity in endemic areas, Vaccinating animals every year might keep LSD under control [29].

Four live attenuated strains of capripoxvirus are currently used as vaccines to control LSD; these includes,

- Kenyan sheep- and goat-pox strain (KS-1),
- Yugoslavian RM 65 sheep-pox strain,
- Romanian sheep-pox strain,
- South African neethling LSDV strain.

Because of antigenic homology and cross-protection between sheep pox, goat pox and LSD viruses, any of these viruses can be used as a vaccine strain to protect cattle against LSDV [16]. The complications encountered during the trial including corneal opacity (keratitis), mastitis, dysentery, lameness, pneumonia and myiasis have been recovered within 3 days to 2 weeks [28].

Specific national control plans vary from country to country, so advice should be sought from relevant authorities and veterinarians. Infections can be treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and also with antibiotics (topical +/- injections), such as

- Antiviral treatment with methylene blue.

- Use of non-steroidal anti-inflammatory drugs to treat the inflammatory condition.
- Use of paracetamol for high fever.
- Administration of antibiotics to fight secondary infections [10].

The following figure no. 6 shows the medicine used in treatment of LSD. The treatment of LSDV is very costly and not accessible to every farmer in the country, so proper preventive measures should be adopted which give effective control of virus and minimize the milk loss, hide, skin damage and the substantial economic losses [21].

Primary routes of drug administration in veterinary medicine, mirroring human models, include oral, intramuscular and topical applications like 'pour-on' and 'spot-on' pesticides and antiparasitics (e.g., fenthion, ivermectin). Notably, transdermal delivery, utilizing patches, has gained traction, though limited literature exists in veterinary practice. An understanding of skin anatomy and physiology across species is crucial for effective patch design. Skin structure varies significantly among species, impacting patch design considerations. Skin, a complex organ, plays a vital role in drug absorption, making it imperative to grasp its intricacies for transdermal delivery success. Electrically driven transdermal iontophoretic systems are emerging for controlled peptide drug delivery. The literature on transdermal patches for humans is extensive, underscoring the need for further development and research in the veterinary domain [30]. LSD control can be done only by vaccination or immunoprophylaxis. According to OIE, four live attenuated strains of capripoxvirus have been used as vaccines specifically for the control of LSD. However in India Live Goat Pox Vaccine Uttarkashi strain has been used to mass vaccinate the animals against LSD disease. The vaccine is recommended for use as early as 4 months or above. Recently indigenous vaccine Lumpi-ProVacInd against LSD has been developed by the National Equine Research Center, Hisar Haryana in collaboration with the Indian Veterinary Research Institute, Izatnagar Bareilly Uttar Pradesh for the vaccination of livestock animals against LSD disease. To prevent the spread/occurrence of LSD disease animals should not be left for grazing in the vector borne areas, complete restriction on movement of the animals at village or district or state level. The affected animals should be kept in separate insect proof paddocks and fed separately. Use of fly repellents at the farms to prevent entry of insects. Proper disposal of farm manure and urine on regular basis. Any stagnation of water in nearby places should be avoided. Smoking of farm with raw leaves especially during evening hours would help to reduce the nuisance. In conclusion the animal should be stall fed and should not be left open for grazing. Cow sheds should be made mosquito/insect proof to prevent the occurrence of disease. Mass vaccination/Immunization of the susceptible livestock animals seems to be the best strategy to prevent occurrence of the LSD disease [31,6].


**Figure 6** Some medicine used in treatment of LSD [10]

## 10. Economic Impact of LSD

Although the mortality rate caused by LSD is usually low, the disease is of major economic importance owing to production losses [32]. LSD is an economically important disease of cattle, serious economic losses from outbreaks that have a high morbidity and can produce a chronic debility in infected cattle [12]. Fine-skinned breeds of cattle such as

Holstein-Friesian and Jersey breeds are more susceptible to this disease. The morbidity and the mortality rate of LSD usually vary by the breed and immunological status of the animal but generally has variable morbidity (2%-45%) and low mortality (<10%). In addition, permanent damage to the skin and hide due to deep skin lesion causes economic loss in the leather industry [33]. Asian cattle and buffalo account for more than 30% and 97% of the global population, respectively and these animals play an important role in the socio-economic fabric of Asia. Economically, Asia accounts for 31 percent and 98% +of global cow and buffalo milk production respectively and 29% of the cattle slaughtered globally for meat production [34]. The disease has subsequent effects on cattle production including a decrease in feed intake, weight losses, abortion, infertility and decreases milk production [19].

## 11. Conclusion

Control and management of LSD in India is challenging due to the limited availability of vaccines and the absence of effective treatment options. The best way to control the spread of the disease is through early detection quarentine and culling of infected animals. Additionally, measures such as improving hygiene and sanitation, as well as avoiding the movement of cattle from infected to non-infected areas, can help to reduce the spread of the disease. After the epidemic, there may be problems such as immune recessive infection and continuous detoxification, and it is necessary to further clarify and standardize the treatment of the same herd of cattle.

## Compliance with ethical standards

*Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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