Lumpy skin disease in southern Africa: a review of the disease and aspects of control

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ABSTRACT

This article reviews some of the important aspects of lumpy skin disease (LSD) that may impact on its successful control. A resurgence of the disease in the last decade has highlighted some constraints of the Neethling strain vaccine, but there is no evidence of vaccine breakdowns owing to the presence of heterologous field strains. More research is needed on epidemiology and transmission of LSD in South Africa to formulate control measures.

Key words: capripox, control, immunity, lumpy skin disease virus, transmission, vaccine.

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INTRODUCTION

In 1929 a new disease of cattle was reported from Zambia (then Northern Rhodesia)[18] that manifested itself by the appearance of skin nodules. Initially these were thought to be caused by insect bites, and the condition was referred to as 'Pseudo urticaria'.

Fourteen years later, a more severe form of the same disease was described in cattle in Botswana and was given the name 'Ngamiland Cattle Disease'[23]. By this time there was evidence to suggest that the condition was being caused by an infectious agent[22,23].

The disease continued to spread and resulted in a panzootic that lasted for a number of years, and affected cattle in most southern African countries.

By 1944 it had spread to South Africa. The first cases were reported in the Marico District of the Western Transvaal (now North West Province)[22] where it was known as 'knopvelsiekte' (Afrikaans for lumpy skin disease (LSD)). There was speculation that the transport of cattle promoted the spread of the disease agent, but once watercourses were reached it spread rapidly along low-lying areas, probably by insect vectors. Lumpy skin disease then spread to the former Orange Free State, Natal, Western Cape and Transkei[13]. During this period it is estimated that 8 million cattle were affected[11]. Cases then abated, probably owing to the development of widespread immunity, but a severe outbreak occurred in the Eastern Transvaal in 1953–1954. Epizootics of the disease continued to be reported until 1962. Veterinary researchers identified the aetiological agent as a poxvirus and a vaccine was then developed by attenuation of a field isolate, which helped to control further outbreaks[25]. For the following 30 years the incidence of LSD was very low. Vaccine use dropped to low levels[4]: as illustrated in Fig. 1, there has not been sustained use of LSD vaccine. Annual sales have seldom risen above 2 million doses over the 1984–1999 period (Onderstepoort Biological Products sales figures, 1999), a coverage of roughly 20% of the average cattle population of South Africa.

During the last decade, higher rainfall and a low level of overall immunity are probably indirectly responsible for a resurgence of the disease, with cases being reported in the Eastern and Western Cape, where it was last observed in the 1950s.

Disease quiescence is probably due to unfavourable climatic conditions that reduce vector prevalence, with a concomitant reduction of the host immunity that later results in extensive outbreaks. However, this aspect of the disease has not been investigated.

AETIOLOGY

Early attempts to isolate and characterise the aetiological agent of LSD indicated that a virus was the causative agent[22]. However, more than 1 virus was isolated from skin lesions on a number of occasions, and these were divided into 3 groups: Group I, represented by an orphan virus (bovine herpesvirus-4); Group II, consisting of Allerton virus (bovine herpes mammilitis, or bovine herpesvirus-2); and Group III, containing a virus that resembled vaccinia virus[19,25]. The orphan virus was found to be non-pathogenic and in most cases resulted from mixed infections with the Group III

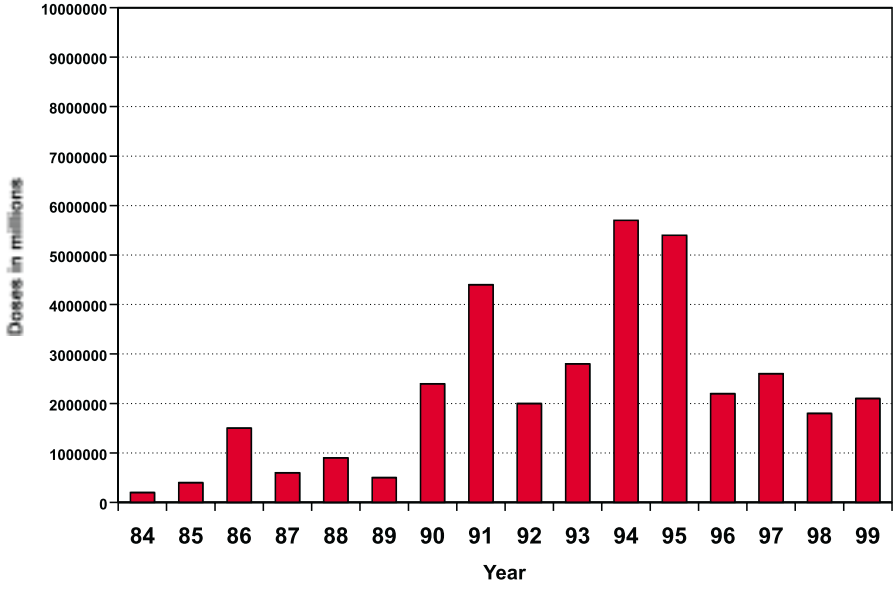

Fig 1: **The use of LSD vaccine during the period 1984–1999.**

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Table 1: **Cross-neutralisation of South African LSDV field isolates with the vaccine strain Neethling T61E19.**

Antigen[b]	Antisera					
	Neethling T61E19	220/90	50/97	248/93	103/91	58/93
Neethling T61E19	120[a]	40	80	40	20	60
220/90[c]	120	120	80	40	80	80
103/91[c]	120	40	40	80	160	160
248/93[c]	80	80	120	160	160	120
58/93[c]	160	20	160	40	120	240
50/97[c]	30	120	160	60	160	60

[a]Dilutions expressed as reciprocal of titre.
[b]Neutralisation performed using 100 $TCID_{50}$.
[c]LSDV field isolates.

virus. Allerton virus was found to be widespread in cattle throughout South Africa and its clinical signs were often confused with those of true LSD as described by Thomas and Mare in 1945[22]. Experimental inoculation of cattle with purified Group III virus proved that this virus was the true agent of LSD in cattle as described in Botswana in 1943[23] and in South Africa in 1945[22].

One of the first purified Group III virus isolates was a South African isolate named the Neethling-isolate. The virus became officially known throughout Africa as lumpy skin disease virus (type Neethling)[1,25], or more simply lumpy skin disease virus (LSDV).

LSDV belongs to the family Poxviridae and shares the genus Capripoxvirus with sheep pox (type member) and goat pox viruses. All 3 members of the genus Capripoxvirus are antigenically similar, sharing a common precipitating antigen, which permits the use of heterologous virus for protection. For example, in Kenya a sheep pox virus isolate is used for controlling LSD in cattle[7]. Capripoxvirus isolates collected from Africa over a 30-year period appear to be genetically stable on the basis of restriction endonuclease digestion analysis of their DNA[16]. A similar comparative study of LSDV (SA-Neethling) field isolates collected between 1945 and 1959 with the South African vaccine strain supported their results[24]. Only minor differences in the highly variable terminal regions of the genomes were observed. There is furthermore no evidence of antigenic variation of LSDV field isolates[9]. A recent study showed that the Neethling vaccine strain cross-neutralised with LSD field strains (P Hunter and I Louw, unpubl. data, 2000) (See Table 1).

EPIDEMIOLOGY

Transmission

Field evidence has indicated the involvement of insect vectors as the main mode of transmission and the virus was isolated from 2 species of biting flies, *Stomoxys calcitrans* and *Musca confiscata,* in the 1960s[26]. Experimental transmission of the disease was first achieved using the stable fly *S. calcitrans* in 1987[17]. Since the stable fly is associated with intensive farming and is the mechanical transmitter of the protozoal diseases *Anaplasma maginale* and *Besnoitia besnotii*[20] in South Africa, it is highly likely that it transmits LSDV in the field. Other biting insects may be involved but no recent research has been done on this aspect of the disease in South Africa.

Climate

Extensive epizootics of LSD have been associated with periods of high rainfall and concomitant high levels of insect activity[22]. The disease is reported to occur throughout mild winters into the following summers, with a peak of activity during late summer/autumn. These observations are consistent with the ideal requirements for the rapid increase of the putative insect vector populations.

Southern Africa is subject to the climatological phenomenon known as El Niño-Southern Oscillation (ENSO), which results in the alternation of periods of unusually high rainfall with periods of drought. Abnormally high rainfall periods have been shown to accompany an increased incidence of African horsesickness[5], but the relationship of this disease to LSD has never been analysed.

Natural host reservoirs

Game animals have been proposed as natural reservoirs of LSDV, but experimental infection of impala and giraffe[28] caused severe clinical disease resulting in death, indicating that these species are not natural, long-term maintenance hosts and may be at risk from the disease under favourable conditions. However, in the same study, young buffalo and adult wildebeest (gnu) were also experimentally infected, and failed to react clinically or show a rise in subsequent antibody titres. Antibodies to LSDV have been detected in wild-caught buffalo, although, the incidence was low[10]. In some reports, low serological prevalence of antibodies to the virus has been taken as an indication that game are not maintenance hosts of the disease[14]. As free-living game are generally subject to a high degree of selection pressure from both predation and disease, it has been difficult to elucidate their exact role in the epidemiology of LSD.

It is also not known whether small livestock play any role in the epidemiology of the disease in southern Africa.

CLINICAL DISEASE

Natural cases of LSD are manifested initially by lachrymation, fever, loss of appetite, and disinclination to move. The skin nodules appear later at roughly 10 days after the initial temperature reaction, distributed all over the body and accompanied by swelling of the lymph nodes. Soft yellow-grey nodules and ulcers also occur in the mucous membranes of the mouth, nose, respiratory tract and the reproductive organs, and subcutaneous swellings on the legs are often seen[4,22] (Fig. 2). Seven to 10 days after their first appearance, the nodules start to break away and form scabs, which ultimately fall off. Secondary bacterial infection can lead to suppurating ulcers and abscesses. In extreme cases lesions in the respiratory tract may lead to suffocation, or secondary infections may ultimately lead to the death of the animal.

LSD should be differentiated from Allerton (herpes) virus infection, which also causes skin nodules, so-called false, or pseudo lumpy skin disease. Pseudo lumpy skin disease is characterised by a less prominent, flat skin lesion, which resolves rapidly and is accompanied by a mild transient fever[3] (Fig. 2).

Experimental infection can be invoked by the subcutaneous, intradermal or intravenous route. The different routes give rise to varying rates of infection, generalisation of infection being seen more frequently with intravenous infections[8].

In field and experimental cases, 10–50% of animals fail to develop generalised disease[6,8,21]. This is attributed to genetic resistance determined by major histocompatibility complexes (MHC) found on the cell surfaces of individual animals[2]. In cattle, these cell surface antigens have been shown to be associated with resistance to a number of diseases. This may also play a role in the response to vaccination (see Vaccination and Immunity).

Resistance to LSD in cattle does not appear to be related to breed since both

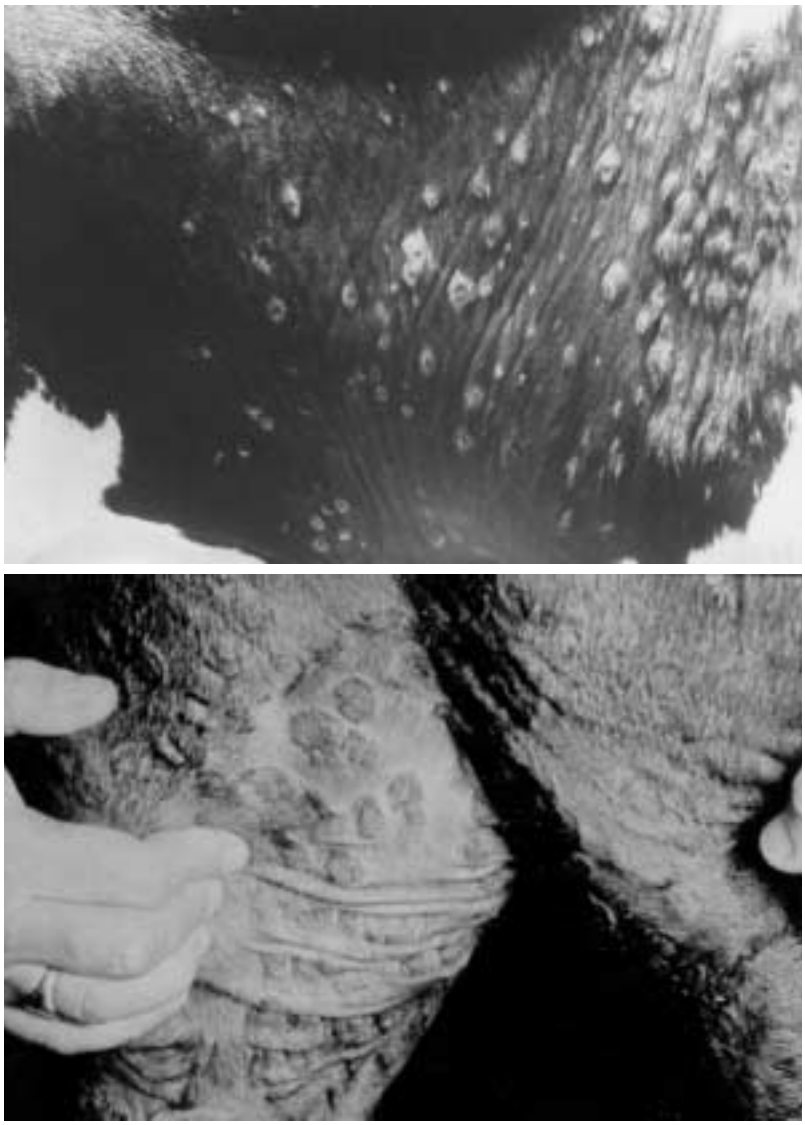

Fig. 2: **Comparison of skin lesions caused by lumpy skin disease** (top) **and Allerton** (bottom) **viruses. Note that skin lesions caused by Allerton virus are more flattened than those caused by LSDV, which tend to be more nodular.**

Bos taurus and *B. indicus* cattle can exhibit either severe or mild clinical signs of the disease. Speculation that the severity of the disease is related to different strains of LSDV has been discounted by researchers, who suggest that the route of vector feeding is a more likely determinant, since experimental intravenous infection causes a higher percentage of generalised infections[8].

Reports of field outbreaks indicate that very young calves, lactating and malnourished animals develop the most severe infections, probably due to impaired cellular immunity.

ECONOMIC IMPACT

Although the mortality rate caused by LSD is usually low, the disease is of major economic importance owing to production losses[27]. Dairy cattle are severely affected, experiencing a 50% drop in milk production, secondary mastitis originating from the development of lesions on the teats and loss of some quarters of the udders. Cows may abort in the course of the disease. General debilitation, loss of fertility of bulls and severe damage to hides are other serious sequelae of the disease[12].

VACCINATION AND IMMUNITY

In LSD-endemic areas such as South Africa, vaccination is the only viable means of control. The South African vaccine was developed by attenuation of a field isolate in tissue culture and on the chorioallantoic membranes of embryonated hen's eggs[26]. Immunity to LSD is chiefly cell-mediated, but antibodies are a useful measure of response to vaccination[15]. Antibodies appear 10 days post-vaccination and reaches a peak 30 days later. A local response to the vaccine is usually correlated with good antibody production. As with infection with virulent wild-type virus, some bovines are refractory to LSD vaccination, failing to develop a local reaction or detectable levels of antibodies. These animals are nevertheless immune when challenged[26]. A field investigation into the responsiveness of cattle to successive vaccinations revealed that 3/30 cows fail to seroconvert. One of these cows produced a calf that died of LSD at 2 weeks of age, apparently owing to lack of colostral antibody secretion (H. Aitchison, unpubl. data, 1997). This may account for some reports of vaccine failure in young calves of vaccinated dams.

The attenuated South African vaccine strain has been shown to protect against clinical disease[26] but experiences during the outbreaks in 1990/91 have challenged the assertion that immunity to LSD is life-long, and more frequent vaccination is now recommended[15].

'Vaccine breakdowns' investigated by one of the authors in the last few years are discussed below:

- *Vaccination of animals already incubating the disease*: this is a common occurrence since farmers only become aware of the presence of the disease once skin nodules appear in some animals. By this time, much of the herd may already be incubating the disease. Vaccination is then too late to protect these animals. Inadequate needle hygiene can in fact spread the disease during the vaccination process, resulting in the disease appearing to occur almost simultaneously in a large number of animals.
- *Confusion with 'pseudo lumpy skin' disease caused by Allerton virus*: this herpes virus is also vector transmitted and is prevalent at the same time of the year as LSD. The shape of the lesions, severity of the disease and the isolation of virus from skin biopsy samples can distinguish between the 2 conditions.
- *LSD in calves*: vaccinated cows that develop an antibody response will confer maternal immunity to LSD by means of colostrum and this lasts for roughly 6 months[26]. Calves may develop LSD at this age if they are not vaccinated timeously. However, there is evidence that cows that do not mount a humoral response will not be able to protect susceptible calves.

Other cases of vaccine failure seen have been due to the mishandling of the vaccine through exposure to sunlight and high temperatures or storage after reconstitution.

DISCUSSION

After an absence of the disease during the 1960s–1990s, there has been a resurgence of LSD and it has become as widespread as it was when it initially reached epidemic proportions in the 1950s. Since

the disease is probably spread by biting flies, which are unlikely to serve as long-term maintenance hosts, it is unknown how the disease is maintained during interepedemic periods. Certain species of game animals might maintain the virus, but as yet not enough evidence is available to confirm their involvement in the epidemiology of the disease. It is also unknown what possible role small livestock might play. In South Africa, LSDV has never been isolated in the field from goats or sheep, although, under laboratory conditions, the virus is able to grow to high titres in lamb cells.

LSD has spread extensively in South Africa in recent years. Favourable climatic factors for the reproduction and spread of probable insect vectors has been implicated. The low level of vaccination during the period before the outbreak in 1990/91 and in subsequent years was insufficient to prevent spread of the disease, although the transport of infected animals almost certainly exacerbated the situation. More extensive, sustained and timeous use of vaccine is required to reduce the prevalence and spread of the disease.

Recent South African field isolates tested in cross-neutralisations with the Neethling vaccine strain indicate that there is no lack of protection between field and vaccine strains. Most 'vaccine failures' investigated were caused by infrequent or improper use of the vaccine. The failure/inability of some cattle to mount a humoral response to LSDV may cause deaths in young calves due to lack of colostral antibody production.

Research into vectors and epidemiology of LSD in South Africa is essential for better disease control in the country and the subregion. The excellent molecular research tools available for detection of LSDV in possible vectors and potential carrier hosts will facilitate this type of research. Recent work on the biology of pox viruses may allow the creation of more effective LSD vaccine strains which could overcome host immune strategies and maternal antibody interference, which are constraints at present. LSDV is also a useful vector for the genes of other organisms such as bovine ephemeral fever, and this approach may give rise to a new vaccine within the next decade.

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REFERENCES

1. Alexander R A, Plowright W, Haig D A 1957 Cytopathogenic agents associated with lumpy-skin disease of cattle. *Bulletin Epizootic Diseases of Africa* 5: 489–492
2. Amills M, Raiya V, Norimine J, Lewin H A 1998 The major histocompatibility complex of ruminants. *Revue Science et Techniques* 17(1): 108–120
3. Barnard B J H 1994 Pseudo lumpy skin disease/bovine herpes mammilitis. In Coetzer J A W, Thomson G R, Tustin R C (eds) *Infectious diseases of livestock with special reference to southern Africa.* Oxford University Press, Cape Town: 942–945
4. Barnard B J H, Munz E, Dumbell K, Prozesky L 1994 Lumpy skin disease. In Coetzer J A W, Thomson G R, Tustin R C (eds) *Infectious diseases of livestock with special reference to southern Africa.* Oxford University Press, Cape Town: 604–612
5. Baylis M, Mellor P S, Meiswinkel R 1999 Horse sickness and ENSO in South Africa. *Nature* 397: 574
6. Capstick P B 1959 Lumpy skin disease – experimental infection. *Bulletin of Epizootic Diseases of Africa* 7: 51–62
7. Carn V M 1993 Control of capripox infection. *Vaccine* 11(31): 1275–1279
8. Carn V M and Kitching R P 1995 The clinical response of cattle experimentally infected with lumpy skin disease (Neethling) virus. *Archives of Virology* 140: 503–513
9. Davies F G, Otema C 1981 Relationships of capripox viruses found in Kenya with two Middle Eastern strains and some orthopox viruses. *Research in Veterinary Science* 31: 253–255
10. Davies, F G, 1991 Lumpy skin disease, an African Capripoxvirus disease of cattle. *British Veterinary Journal* 147: 489–503
11. Diesel A M 1949 The epizootiology of lumpy skin disease in South Africa. *Proceedings 14th International Veterinary Congress, London* 2: 492–500
12. Green H F 1959 Lumpy skin disease – its effect on hides and leather and a comparison in this respect with some other skin diseases. *Bulletin Epizootic Diseases of Africa* 7: 63–74
13. Haig D A 1957 Lumpy skin disease. *Bulletin Epizootic Diseases of Africa* 5: 421–430
14. Hedger R S, Hamblin C 1983 Neutralizing antibodies to lumpy skin disease virus in African wildlife. *Comparative Immunology and Microbiology of Infectious Diseases* 6(3): 209–213
15. Kitching R P 1996 Lumpy skin disease. In *Manual of standards for diagnostic tests and vaccines* (3rd edn). Office International des Épizooties, Paris, France
16. Kitching R P, Bhat P P and Black D N 1989 The characterization of African strains of Capripoxvirus. *Epidemiology and Infection* 102: 335–343
17. Mellor P M, Kitching R P, Wilkinson P J 1987 Mechanical transmission of Capripox virus and African swine fever virus by *Stomoxys calcitrans. Research in Veterinary Science* 43: 109–112.
18. Morris J P A 1931 Pseudourticaria. Department Animal Health Report, Northern Rhodesia
19. Munz E K, Owen N C 1966 Electron microscopic studies on lumpy skin disease virus type 'Neethling'. *Onderstepoort Journal of Veterinary Research* 33: 3–8
20. Nevill E M 1997 Vectors: Muscidae. In Coetzer J A W, Thomson G R, Tustin R C (eds) *Infectious diseases of livestock with special reference to southern Africa.* Oxford University Press, Cape Town: 53–61.
21. Perlman L J 1993 Molecular characterization of the lumpy skin disease virus genome. MSc thesis. University of Cape Town
22. Thomas A D, Mare C v E 1945 Knopvelsiekte. *Journal of South African Veterinary Medical Association* 16: 36–43
23. Von Backstrom U 1945 Ngamiland cattle disease: preliminary report on a new disease, the etiological agent being probably of an infectious nature. *Journal of South African Veterinary Medical Association* 16: 29–35
24. Wallace D B 1994 Genomic characterization of southern African isolates of Capripox and Avipox viruses. MSc thesis, University of Cape Town
25. Weiss K E 1963 Lumpy skin disease. In *Emerging Diseases of Animals, FAO Agricultural Studies* 61: 179–201
26. Weiss K E 1968 Lumpy skin disease. *Virology Monographs* 3: 112–282.
27. Woods J A 1988 Lumpy skin disease – a review. T*ropical Animal Health and Production* 20: 11–17
28. Young E, Basson P A, Weiss K E 1970 Experimental infection of giraffe, impala, and Cape buffalo with lumpy skin disease virus. *Onderstepoort Journal of Veterinary Research* 37: 79–88