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THE INFECTION AND TREATMENT METHOD OF VACCINATION AGAINST HEARTWATER

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ABSTRACT

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The history of vaccination techniques against heartwater and the development of the infection and treatment method are reviewed briefly. Present techniques and their shortcomings are defined and possible areas of improvement discussed.

EARLY ATTEMPTS AT VACCINATION

Numerous attempts at vaccination against heartwater were made prior to 1926 when Cowdry demonstrated the causative relationship between *Cowdria ruminantium* and the disease. These procedures were well documented by Alexander (1931) and included the inoculation of bile, the use of hyperimmune serum, various attempts at the attenuation of the heartwater agent, repeated inoculations of sub-lethal doses, repeated subcutaneous inoculation and inactivation with formalin.

All these attempts failed. The organisms either remained unaltered and retained their virulence, or were inactivated to such an extent that they failed to stimulate an immunity. Where the sub-cutaneous route of inoculation was used the erratic results led to dubious conclusions.

The first practical and effective method of immunization was introduced by Neitz & Alexander (1941, 1945), who utilized the innate age resistance of calves to vaccinate them. This method, which is in fact merely an ingenious form of controlled exposure, involved the intravenous inoculation of calves under 1 month of age with virulent *C. ruminantium*-infected sheep blood.

This is a practicable method of immunization but by no means without shortcomings (Uilenberg, 1984). Its use is limited to very young calves and the method can therefore not be used to immunize, without risk, older susceptible animals introduced into endemic areas, or in endemically marginal areas, where prolonged droughts have led to an enzootically unstable situation.

Furthermore, losses due to natural tick-transmitted heartwater of cattle immunized as calves are reported from time to time. A recent study in which the resistance to artificial challenge of cattle vaccinated as calves and subsequently exposed to ticks was compared with that of cattle also vaccinated as calves but not exposed to ticks, questioned the value of calf vaccination (Du Plessis, Bezuidenhout & Lüdemann, 1984).

It is also uncertain whether calves born from susceptible dams possess the same innate resistance. All 311 calves born from susceptible cows that were recently immunized, were treated without delay when either an early morning temperature of 39,5 °C or an evening temperature of 40 °C was recorded. The severity of the reactions could not be determined, since no calves were left untreated as controls because of their considerable value (Lente van der Merwe, unpublished data, 1986). Since these calves were treated on the day judged to be the first day of the febrile reaction, it must be emphasized that the percentage of animals that would have reacted could not be determined and many of them were probably treated unnecessarily.

Reports on the innate resistance of lambs and goat kids are contradictory, but it appears to be less pronounced than in calves and seldom exceeds 2 weeks (Thomas & Mansvelt, 1957). Six out of 32 lambs under 3 weeks of age recently inoculated with infected sheep blood died without their temperature being monitored and all 26 that survived showed febrile reactions and recovered after treatment (Lente van der Merwe, unpublished data, 1986). Contrary to this finding, however, improved Boergoat kids appeared to be more resistant. In a recent trial in which 67 2- to 12-day-old kids born under heartwater endemic conditions were vaccinated and their temperatures monitored, only 4 of them (6 %) showed a febrile reaction. They were treated and made an uneventful recovery (C. J. F. Lüdemann, unpublished data, 1987).

As drugs capable of controlling the heartwater reaction such as Uleron (Neitz, 1940), became available, the vaccination of older ruminants without severe losses became feasible. Neitz & Alexander (1945) first advised the use of a drug (Uleron) to control the reaction to the artificial immunization of cattle and thus originated the so-called "conventional method" of vaccination practised to this day. Also referred to as the "infection and treatment" method (Uilenberg, 1983, 1984), it entails the close monitoring of vaccinated animals and the application of treatment as soon as the febrile reaction commences. The method, as summarized by Uilenberg (1984) is advocated by the Food and Agricultural Organization of the United Nations.

The procedure of treating well in advance of the commencement of the febrile reaction was practised as a modification of this method (Neitz & Alexander, 1945; Fick & Schuss, 1952; Poole, 1962) and became known as the "block method"; it is discussed elsewhere in these proceedings (Du Plessis & Malan, 1987).

PRESENT DAY TECHNIQUES

Antigen production

Over the years the blood of sheep, infected with field-isolated strains of the heartwater agent, served as source of antigen. At the Veterinary Research Institute, Onderstepoort, the immunization procedure was eventually standardized by establishing a uniform procedure of production of sheep blood infected with a strain of *C. ruminantium*, subsequently referred to as the Ball 3 strain. This method of vaccine production is more fully dealt with elsewhere in these proceedings (Oberem & Bezuidenhout, 1987).

A trial vaccine consisting of a filtrate of *C. ruminantium*-infected *Amblyomma* nymphae (Bezuidenhout, 1981) was used in 43 bulls, 180 calves, 52 adult sheep and goats, 235 lambs and 58 goat kids. Temperatures recorded showed that the incubation period after vaccination with the nymph suspension was 2–4 days shorter than that usually recorded after vaccination with the blood vaccine. Cattle reacted from Day 8 post-inoculation and sheep a little earlier, from Day 6.

While the immunity elicited with the tick vaccine was similar to that stimulated by the blood vaccine (Bezui-

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denhout & Spickett, 1985), a shortcoming of the former proved to be the allergic shock that sometimes occurred after intravenous administration of the vaccine. While only 2,7 % of the 5 000 ruminants inoculated with the blood vaccine showed slight shock and only 29 calves (0,48 %) required antihistamine treatment, the picture was different when the tick suspension was used. Thirty-seven out of 253 lambs (15,7 %) and 31 out of 58 goat kids (53 %) developed severe symptoms including oedema and hyperaemia of the ears, eyelids, lips and other woolless areas, urination, defaecation, constant bleating and dyspnoea. All required intensive treatment with antihistamines. None of the adult cattle, sheep and goats showed these symptoms.

Handling of the vaccine

It is important, for the sake of completeness, to note that the vaccine must be stored and transported in liquid nitrogen or in dry ice. It must not be allowed to thaw in transit and must be injected within ½ h of thawing. Recently it has been shown that vaccine stored in liquid nitrogen and thawed slowly at 4 °C will retain its infectivity at this temperature for 24 h (J. A. Olivier, unpublished data, 1987). Vaccine stored in liquid nitrogen can therefore be readily transported, kept in a thawed state in an icebag and injected during the next 24 h without the loss of infectivity.

Route of inoculation

The most commonly used route is via the *vena jugularis* in both cattle and sheep. However, the ear vein *(vena auricularis)* was found convenient by Arnold & Asselberg (1981) in Brahman cattle. The *vena cephalica* in the foreleg is the most convenient route in long-woolled sheep.

Temperature monitoring

It is general practice in South Africa to temperature the animals once daily during the early morning. The author prefers also to record the evening temperature. Temperatures above those given in Table 1 are regarded as the first sign of a heartwater reaction.

TABLE 1 Temperatures above which animals are considered to be reacting to heartwater inoculation

Species	Temperature (°C)	
	a.m.	p.m.
Cattle	39,5	40,0
Goats	39,5	40,0
Sheep	40,0	40,5

Treatment

There are two schools of thought in this regard, one of which advises treatment of the vaccinated animals on the first sign of a temperature rise. In accordance with the opinion that the immunity of animals treated too early may be inadequate (Du Plessis & Malan, 1987), other workers treat only on the 2nd or even the 3rd day of the febrile reaction. Unless the temperature has fallen to normal by the next day, treatment is repeated after 24 h. Some workers repeat the treatment the next day irrespective of whether the temperature is down or not. If it persists beyond 48 h after the last treatment, it is regarded as a persistent temperature reaction (Van der Merwe, 1979) and a further dose is given, preferably intravenously. Sulphadimidine has been found to give good results in severe reactions that persisted in spite of repeated oxytetracycline treatments (Van der Merwe, 1979). Bloodsmears should be examined to eliminate the possibility of concurrent infections.

Dosage rates used vary but generally the tetracyclines are recommended at 10 mg/kg, or less in the case of doxycycline given either intramuscularly or intravenously (Immelman & Dreyer, 1982). Long-acting formulations of oxytetracyclines are given at 20 mg/kg only along the intramuscular route. Although this practice has been discouraged as a result of the severe necrosis observed at the injection site (Petzer, Giesecke & Van Staden, 1984), long-acting formulations are widely used in breeding animals not destined for slaughtering. Treatment with these remedies does not interfere with the establishment of immunity (Simpson & Wiley, 1951), unless given too early.

FUTURE PROSPECTS

The infection and treatment method of immunization against heartwater is effective but by no means ideal. The main shortcomings requiring further research are the virulence and the fragility of the causal agent in the vaccine and the fact that it must be administered intravenously to be effective.

At the moment indications are that the heartwater agent has to be alive and pathogenic to be immunogenic. Unless an innovative method of attenuation or inactivation of the agent that at the same time preserves its immunogenicity can be found, this obstacle will remain insurmountable.

The fact that the infectious agent in the vaccine remains viable for extended periods at temperatures of −80 °C and lower only, places it out of the convenient reach of the farmer or most private practitioners. The investigations of Birnie, Endris & Logan (1986) on the use of various diluents capable of prolonging the survival of the agent and the finding that freeze-dried mouse tissue infected with the Kümm strain of *C. ruminantium* and subsequently stored at 4 °C, will retain its infectivity for 42 days (J. L. du Plessis, unpublished data, 1986), have begun to address this problem.

Although the intravenous route is easy in practised hands, many farmers have to rely on professional help, making the vaccination of their animals a time-consuming and expensive exercise. This problem is dealt with elsewhere in the proceeding (Bezuidenhout, Olivier, Gruss & Badenhorst, 1987).

Attention to these problems it is hoped, will result in greater effectiveness and safety of the vaccine. Provided the causal agent can be inactivated without loss of immunogenicity, the vaccine would also be safe to use in countries such as the USA where the disease does not as yet occur, but where potential vectors that could become infected, do exist.

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