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I M M U N O L O G I C A L   F A C T O R S   A S S O C I A T E D  
W I T H   F O O T - R O T   I N   S H E E P

A thesis presented in partial fulfilment of the requirements for  
the degree of Doctor of Philosophy at Massey University

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## P R E F A C E

Foot-rot in sheep has troubled farmers for many years not because of any spectacular epidemics associated with high mortality but because the chronic lameness associated with foot infection, and its consequences, frequently interfere with farm husbandry. Methods of control and eradication have been known since 1940 but as they generally involve many hours of strenuous work, the development of more efficient methods of foot-rot control has been the aim of different research groups.

Two findings which suggested that foot-rot organisms might be accessible to blood-borne inhibitors helped change the attitude of researchers involved with this problem. The first was the successful use of parenterally administered antibiotics against foot-rot infection and the second was the demonstration that serum globulins were able to make contact with Fusiformis nodosus<sup>1</sup> in situ. The results of these experiments carried out at the McMaster Institute, Sydney led to a reappraisal of existing research projects and the formation of a new policy leading towards the development of experimental vaccines.

By 1970 when the writer's course of study began, it had been shown that bench scale vaccines conferred some protection against foot-rot infection and that vaccination was effective in stimulating resistance even after infection had become established. There were no methods available other than direct sheep challenge experiments for evaluating different types of vaccine and although the existence of anti-F. nodosus bactericidal antibody was known, there was still considerable doubt about the immune mechanisms involved in protection. There had been no investigation of the antigenic potential of F. nodosus products of growth or indeed of the bacterial cells themselves and as a consequence the influence of media components on the immunogenicity of the resulting culture had received little attention.

Before the foot-rot vaccines could be applied under New Zealand field conditions, two major problems had to be overcome. Firstly a large scale method of culture had to be developed that would produce economic yields of F. nodosus while retaining those antigens important for pro-

<sup>1</sup> Fusiformis nodosus was shown to be the primarily important and transmitting organism of sheep foot-rot.

tection of sheep. Secondly, an adjuvant system had to be chosen that would be effective in stimulating an adequate antigenic response but would cause minimal damage to the carcass.

To obtain the essential information upon which large scale modifications might be based, a series of experiments were designed to improve understanding of some basic aspects of foot-rot vaccine effectiveness. As a starting point for the investigation different methods of bacterial culture were used and the resulting F. nodosus cells were compared for gross morphology and ultrastructure as well as for their degree of immunogenicity after incorporation into various vaccine formulations. The serological response by the sheep to vaccination administered before and during F. nodosus infection was investigated to find a laboratory test system that would reflect the immune status of the animals. Experiments were also carried out to test the possibility of a humoral protective system, and the other contributor to specific resistance, cell mediated immunity, was investigated in normal and naturally infected sheep.

This programme of research produced results, that with the conclusions that were drawn from them, form the major part of the following thesis.