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Vaccines for respiratory disease in cattle

Respiratory disease is one of the most serious disease complexes affecting beef cattle production. For example, it is claimed to cost the UK industry about £70 million per year. It is usually associated with young cattle and can occur in a variety of situations. It is a good example of multifactorial disease in that its aetiology involves, in addition to a variety of microorganisms, a number of environmental factors. Several distinct syndromes occur and a number of microorganisms are thought to be important, including the bacteria Pasteurella haemolytica type A1, P. multocida, Haemophilus somnus, Corynebacterium pyogenes, Mycoplasma bovis and M. dispar. Of the viruses, bovine herpes virus 1 (BHV1) and respiratory syncytial virus (RSV) are known to be important, the former also causing the specific syndrome, infectious bovine rhinotracheitis (IBR) in addition to its involvement in the pneumonia complex. Other viruses of possible importance include para-influenza 3 (Pi3), adeno-viruses, bovine viral diarrhoea (BVD) virus, coronavirus and rhinovirus.

In the USA shipping fever is the most common respiratory syndrome in cattle and is thought to be a pneumonia pasteurellosis. This is analogous to a condition in housed suckled calves in the UK which in many instances may be a primary pasteurellosis. However enzootic pneumonia of artificially reared dairy-bred calves is also very common in the UK and its microbiology appears to be much less consistent and more complex.

Vaccines have been available for a considerable period but in view of the complex aetiology, their efficacy is equivocal in many cases. A pentavalent inactivated viral vaccine has been available for some years comprising BVD, Pi3, adenovirus, IBR and reovirus type 1, but this was found to be poorly immunogenic with the exception of the adenovirus and IBR components. Modified live vaccines against Pi3, RSV and IBR are also commercially available but field results on the efficacy of the former two are somewhat equivocal. For example in one study, although the modified live Pi3 vaccine produced an immune response which protected against experimental challenge, there was no corresponding reduction in the prevalence of respiratory disease. The temperature sensitive IBR vaccines have now been used for some time in the field and appear to give good protection against this clinical entity. Furthermore it has been claimed that these vaccines are effective when used in the face of an outbreak of IBR. One problem with IBR vaccines is that the antibody response is indistinguishable serologically from that produced by the wild virus and thus difficulties can occur in terms of diagnosis particularly when certification is required, e.g. for export purposes.

A new quadivalent vaccine containing inactivated antigens of RSV, Pi3, M. bovis and M. dispar has been developed in the UK and tested over the last five years. It appears to have given good protection against disease where the vaccine components have been associated with the aetiology of disease. However it is clear that disease still occurs due to other agents not covered by this vaccine since it did not give complete protection. The inclusion of Pasteurella haemolytica type A1 would be a useful improvement to this vaccine.

As stated above Pasteurella is considered to be the major organism associated with shipping fever. Unfortunately there is doubt about the efficacy of Pasteurella bacteria in cattle although these appear to be effective in sheep. Work in the USA suggests that an immunogenic cytotoxin of P. haemolytica may provide a more effective antigen in cattle.

Vaccines are available in the USA for the prevention of BVD but none is currently licensed in the UK. Good published efficacy data on these vaccines are limited.

What of the future? To date most commercial vaccines have been produced with little precise knowledge of the relevant aetiological agents, virulence mechanisms and important host defence mechanisms. Consequently more basic research is required in these areas so that more appropriate vaccines can be developed. Recombinant technology is a potentially potent tool for the development of safe and effective subunit vaccines (see review). However it may be some time before such vaccines can replace existing vaccines due mainly to the relative simplicity and often low production costs of the latter.

A further problem regarding the commercial development of cattle pneumonia vaccines lies in the size of the potential market. Whilst in the USA the vaccine market is quite large, approximately $25 million, it is very much smaller in Canada ($2 million) and in Europe. For example the total UK market is estimated at £2.4 million and includes lungworm vaccine. Therefore there may not be great commercial incentive for some pharmaceutical companies to develop such products. Of course it might be argued that the market is related to vaccine efficacy. Therefore if good vaccines are produced then the potential market will be much greater.

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References
1 Morzaria, S.P., Richards, M.S., Harkness, J.W. and Maund, B.A. Vet. Rec. 1979, 105, 410
2 Stott, E.J., Thomas, L.H., Collins, A.P., Crouch, S., Jebbett, J., Smith, G.S., Luther, P.D. and Casswell, R. J. Hyg. 1980, 85, 257
3 Gentry, M.J., Confer, A.W. and Panciera, R.J. Vet. Immunol. Immunopathol. 1985, 9, 239
4 Wilkie, B.N. Humoral and cell mediated resistance mechanisms in cattle. In: Bovine Respiratory Disease (Ed. R.W. Loon) 1984, Texas A&M University Press, College Station, 1984, p. 102
5 Bachrach, H.L. Recombinant DNA technology for the preparation of subunit vaccines. J. Am. Vet. Med. Assoc. 1982, 181, 992