THE DEVELOPMENT OF VACCINES USING MIXTURES OF ANDROGEN- AND OESTROGEN-IMMUNOGENS SUITABLE FOR INCREASING FECUNDITY IN SHEEP

R.I. COX,* PATRICIA A. WILSON* and M.S.F. WONG*

Immunization of sheep against the steroids, androstenedione (A), testosterone (T) or oestrone (E) results in an increase in ovulation rate and a subsequent gain in lambing percentage, provided the antibody response is controlled (Cox et al. 1982). For Merino ewes, lambing percentages have been improved by actively immunizing against several steroids simultaneously (Wilson et al. 1988). Where several steroids are involved there are marked interactions affecting individual steroid antibody responses. A study of these interactions formed the basis of the present work aimed at developing new vaccines.

Experiments were carried out to test the effect on individual steroid antibody titres of (a) immunogen mixtures of A, T and E conjugated to differing proteins (human or bovine serum albumins, HSA or BSA); (b) varying immunogen components in the primary and booster immunizations; (c) varying proportions of two immunogens; (d) having two different steroid substituents on the one protein carrier molecule.

Steroid-protein immunogens were dissolved or suspended in 5% DEAE-dextran/0.45% saline. Sheep were immunized with a standard subcutaneous dose of 1.2 mg protein equivalent in 2 ml adjuvant and a booster treatment was given 3 weeks later. Blood was collected 1 week after the boost. Specific antibody titres were determined as the dilution of serum showing 50% of maximal binding of tritium labelled steroids, and are referred to as arithmetic averages for 5-7 sheep.

With mixtures of immunogens, antibody levels tended to be depressed for all the steroids involved. Thus, titres were 1:4900 (A.HSA) and 1:4500 (E.HSA) when immunogens were not mixed and 1:800 and 1:3050 respectively when administered together. One immunogen containing a single steroid in a booster treatment could maintain the responses for all steroids used in the primary treatment. Thus, for an A.HSA, T.HSA and E.BSA combination, the titres in the first year were 1:900, 1:1600 and 1:250 respectively and, on boosting a year later with A.HSA alone were 1:1400, 1:1500 and 1:300 respectively. Useful E titres were still obtained at proportions as low as 1 in 50 of E.HSA to A.HSA and 1 in 200 of E.BSA to A.HSA. An immunogen containing relatively low E content together with a standard A content gave the required responses to both components. Thus, an immunogen with 3 moles E and 26 moles A/mole HSA gave acceptable titres of 1:1700 and 1:6900 respectively.

These data formed the basis of vaccine systems to provide moderate titres for A, T and E in the range of 1:200 - 1:3000 and in particular to keep the E titre from rising above these levels to obtain optimal fecundity. The application of some of these systems has led to improved fecundity in Merino sheep (Wilson et al. 1988). Further development of new mixtures of immunogens is expected to give more practical vaccines.


* CSIRO, Division of Animal Production, P.O. Box 239, Blacktown, N.S.W. 2148.