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Steroid immunisation of ewes to increase lambing

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Immunisation of ewes against steroids: A review

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ABSTRACT

In the 10 years since it was observed that immunisation of ewes against steroid hormones resulted in an increased ovulation rate, research has provided some understanding of the mechanism of immunoneutralisation and of the factors which influence or modify the immunological and physiological response of ewes. It has also led to the development of a commercial vaccine.

The mechanism of action is still uncertain although several changes in the endocrine balance of the ewe may be involved. Active immunisation against a number of steroids has been shown to increase ovulation rate and with passive immunisation, a mixture of steroid antibodies produced the best result.

One possible mechanism via a reduced negative feedback on the pituitary and increased gonadotrophin release has been recorded. Effects at the ovarian level influencing follicular atresia must be also considered.

The initial attempts at the practical application of this technology were unsuccessful. Although ovulation rates were increased, fewer lambs were born per ewe joined due to problems of anoestrus and anovulation. From these data the relationship between antibody titre and response was established and alterations to the composition of the antigen and treatment schedule were developed to modify the antibody response.

Factors such as ewe age, level of nutrition and breed had little effect on the response. The response to changes in nutrition and live weight appear to be additive to those of immunisation, as is the response to exogenous gonadotrophins (PMSG). The timing of treatment relative to mating appears to have some effect, with intervals of less than 21 days reducing the lambing response through a high proportion of barren ewes. However there has been considerable variation in the final response indicating a major effect of early embryonic mortality. Lamb birth rank distribution has been within the predicted range and been seen mainly as an increase in twins with some higher order multiples. The mortality of lambs from treated ewes has been similar to that of lambs of the same birth rank from untreated ewes. The growth and reproductive performance of the progeny from treated ewes has been unaffected.

INTRODUCTION

The recent commercial application of immunisation of ewes against androstenedione to increase lambing had its basis in a chance discovery in Edinburgh in 1974 (Scaramuzzi, 1976; Scaramuzzi, Davidson and Van Look, 1977). These workers recorded an unexpected increase in ovulation rate in ewes which had been actively immunised against either oestradiol or androstenedione. Similar findings were reported by Australian scientists (Cox, Wilson and Mattner, 1976).

This stimulated a number of investigations to see whether these relatively simple procedures would lead to an increase in litter size and lambing performance of ewes. Initial attempts were only partially successful. Although increases in ovulation rate were confirmed by a number of workers (Van Look *et al.*, 1978; Martin *et al.*, 1978, 1979; Gibb, 1979; Smith, 1980; Gibb, Thurley and McNatty, 1981) they were often accompanied by increased incidence of anoestrus and of barren ewes through reduced conception rates and no increase in lambs born per ewe joined (LB/EJ) was reported. However some studies found that immunised ewes that lambed produced more lambs per ewe lambing (LB/EL) than did untreated ewes. Unequivocal evidence of a substantial increase in lambs born per ewe joined following steroid immunisation was first published by Smith *et al.* (1981a). Subsequently this was confirmed by others (Cox *et al.*, 1981, 1982; Scaramuzzi, Cox and Hoskinson, 1982; Gibb *et al.*, 1982). The first commercial preparation of androstenedione — 7HSA in a DEAE dextran adjuvant (Fecundin®) was released in October 1983.

IMMUNOGENS

Steroids are low molecular weight substances which under normal conditions are unable to invoke an immune response. However if the steroid is conjugated to a heterologous protein this relatively high molecular weight material is able to stimulate the immune system in sheep.

The choice of steroid does not seem to be critical for this purpose. Increased ovulation rates have been reported following the immunisation of ewes against oestradiol-17β (Scaramuzzi, 1976), oestrone (Cox *et al.*, 1976), androstenedione (Scaramuzzi, Davidson and Van Look, 1977), testosterone (Scaramuzzi, 1979) and progesterone (Hoskinson *et al.*, 1982).

The actual linkage used to conjugate the steroid and protein does not seem important and several protein carriers have proved satisfactory (Hoskinson *et al.*, 1981).

However, analyses of the early immunisation data showed that the immune response to treatment (measured as the steroid antibody titre) was extremely variable from ewe to ewe. Those ewes which gave antibody responses at the extreme upper end of the range had a greater tendency to be anoestrous and barren at lambing (Gibb, Thurley and McNatty, 1981; Martin *et al.*, 1979; Smith *et al.*, 1981a) whilst increases in ovulation rate and lambing occurred over a range of more moderate levels of antibody titre.

Most of the early work with steroid immunisation involved the use of Freund's complete adjuvant to stimulate the immune response. The subsequent introduction of DEAE dextran as an alternative adjuvant (Cox and Wilson, 1976) produced a shorter duration antibody response which generally enabled a response within the desired titre range to be obtained (Cox *et al.*, 1981). In addition to the choice of adjuvant, the titre response obtained can be influenced by the interval between the primary and secondary injections and by the simultaneous administration of other antigens at the time of treatment (Smith *et al.*, 1983a; Cox, 1984; Webb *et al.*, 1984). These considerations have been incorporated into the instruction schedule for the use of Fecundin® .

PASSIVE IMMUNISATION

The administration to a recipient ewe of serum containing antibodies (in this case raised against a steroid-protein conjugate in an actively immunised animal) enables much more precise control over the anitbody titre at the time of mating. Land *et al.* (1982) have reported an increase in ovulation rate and lambing performance in ewes treated with a number of steroid antibodies including androstenedione. Of particular interest in their results was the attainment of the highest increase in lambing with a mixture of antisera to 4 steroids namely oestradiol-17β , oestrone, androstenedione and testosterone. However the commercial adoption of a passive immunisation technique will require the large scale production of high-titre sheep antibodies. Such production procedures are not yet available.

ANTIBODY SPECIFICITY

Initial reports on the specific steroid antibodies obtained after vaccination with Freund's adjuvant indicated that these antibodies were specific to the steroid used (Scaramuzzi, Davidson and Van Look, 1977; Scaramuzzi *et al.*, 1977). However, more recent reports have indicated that many immunised animals contained antibodies which bound several steroids. For example Scaramuzzi *et al.* (1980) and Gibb *et al.* (1982) both report that several animals immunised against androstenedione contained antibodies which bound oestrone as well as androstenedione. These findings suggest that active immunisation may often lead to the production of antibodies with variable specificity.

MECHANISM OF ACTION

The immunisation of ewes against a particular steroid leads to the formation of antibodies with the capacity to bind that steroid. This in turn leads to a decreased metabolic clearance rate (Wickings, Becher and Nieschlag, 1976) and also results in elevated concentrations of biologically inactive steroid in the plasma (Fairclough, Smith and Peterson, 1976). These high levels of steroid are thought to be biologically inactive because the steroid is bound to the antibody. However the extent of the biological inactivity will depend on the relative avidity or affinity of the antibody compared to that of the receptors for the steroid in the various target tissues.

The relationships between the reduced biological activity of a steroid and the increase in ovulation rate is obscure. A major obstacle to determining the mode of action of the steroid immunisation procedure is the lack of information on the mechanisms which influence the number of follicles that will be ovulated.

Hormone Levels

Immunisation against both androgens and oestrogens has been shown to increase plasma luteinising hormone (LH) concentrations by increasing the frequency of its release from the pituitary (Martensz *et al.*, 1976; Martensz, Scaramuzzi and Van Look, 1979; Martensz and Scaramuzzi, 1979; Scaramuzzi, Martensz and Van Look, 1980). However, the exogenous administration of LH at high frequency did not result in an increased ovulation rate (Scaramuzzi and Radford, 1983) while the administration of human chorionic gonadotrophin increased ovulation rate (Radford, Averell and Szell, 1984). Differences in LH pulse frequency were reported between ewes having 1 or 2 ovulations (Thomas, Oldham and Martin, 1984). In contrast, the administration of follicle stimulating hormone (FSH) at a frequency of 1 injection per hour increases ovulation rate (McNatty *et al.*, pers. comm.). Elevations of plasma FSH levels were recorded in ewes immunised against oestrogens but not in those immunised against androgens (Martensz, Scaramuzzi and Van Look, 1979; Martensz and Scaramuzzi, 1979; Plant, Dobson and Ward, 1978; Scaramuzzi, Martensz and Van Look, 1980). However, these findings are somewhat equivocal as they were obtained from animals with abnormally high antibody titre levels, in fact high enough to induce anoestrus. More recent data (Webb *et al.*, 1984; Pathiraja *et al.*, 1984) obtained on passively immunised ewes with relatively low titre levels confirmed the general trends if not the magnitude of the increases in gonadotrophin levels.

Thus while a postulated decrease in the negative feedback of gonadal steroids on pituitary-hypothalamic function because of a reduced biological activity of oestrogen increasing FSH could explain the action of the oestrogen antigens, there is no direct evidence for this mechanism in the androgen immunised ewe.

The understanding of the mechanism of action becomes even more clouded when it is found that immunisation against oestrone and oestradiol increased the ovarian vein concentration of androstenedione (Scaramuzzi, Martensz and Van Look, 1980) and immunisation against both androstenedione and testosterone increased the jugular plasma concentrations of oestrone and oestradiol (Scaramuzzi *et al.*, 1980; Scaramuzzi *et al.*, 1981a). This is in addition to the increased levels of antibody-bound steroid that was immunised against. These responses are consistent with gonadotrophin stimulation of the ovary but raise some doubts as to the specificity of the negative feedback mechanisms for gonadotrophin release from the pituitary.

Ovary

Increases in ovarian size and weight of non-luteal ovarian tissue have been reported following immunisation against oestrone (Scaramuzzi, Martensz and Van Look, 1980) and androstenedione (Scaramuzzi *et al.*, 1980) which is consistent with increased gonadotrophic stiumulation. The hypothesis that steroid immunisation results in ovaries becoming more sensitive to gonadotrophins has been partly negated by the finding of similar dose-response relationships to exogenous pregnant mares serum gonadotrophin (PMSG) in oestrone-immunised and control ewes (Hoskinson, Hinks and Scaramuzzi, 1982; Smith *et al.*, 1983b). Evidence for a similar type of PMSG response in androstenedione immunised ewes is not yet available. Recently, Scaramuzzi (1984) and Scaramuzzi and Hoskinson (1984) have reported that the rate of follicle growth, the number of follicles and the size distribution of ovarian follicles did not differ between control and androstenedione immunised ewes despite a marked increase in ovulation rate. However they noted an increase in the number of large non-atretic follicles and concluded that the increased availability of these follicles was the immediate cause of the elevated ovulation rate in androstenedione immunised ewes. This enhanced survival of large follicles of follicle classes 11 and 12 may be mediated by a reduction in the rate of androgen induced atresia by the presence of androgen binding antibodies in the follicular fluid of androstenedione immunised ewes.

Other Parameters

Scaramuzzi *et al.* (1982) have reported on the effects of immunisation on the time relationshps of events in the periovulating period. They showed that immunisation against oestrone did not influence the time intervals from (1) luteal regression (plasma progesterone < 1 ng/ml) to onset of oestrus, (2) onset of oestrus to start of the LH surge, (3) start of the LH surge to ovulation, (4) onset of oestrus to ovulation. Immunisation against androstenedione reduced the interval from luteal regression to onset of oestrus but did not alter the other relationships. The workers reported no effect of immunisation against oestrone on egg recovery rate but a reduced level of fertilisation (– 20%). Smith *et al.* (1983b) confirmed the lack of effect on egg recovery rate but also reported no effect on fertilisation rate. However Boland *et al.* (1984) have reported a reduction in both parameters in ewes immunised against androstenedione.

RELATIONSHIP BETWEEN ANTIBODY TITRE AND OVULATION RATE

Van Look *et al.* (1978) reported a higher antibody titre in ewes with 3 or more ovulations compared to those with 1 or 2 ovulations. This suggested a relationship between titre and ovulation rate. Subsequently Martin *et al.* (1979) were unable to confirm this finding except at the extremes of antibody response, with low ovulation rates at very low titres and anovulation as a result of very high titres. This curvilinear type response was confirmed by Smith *et al.* (1983c) for actively immunised ewes and by Webb *et al.* (1984) following passive immunisation of ewes. It is apparent that there is a very wide range of titres over which moderate increases in ovulation rate may occur and also that some ewes remain as single ovulators regardless of antibody titre level.

Of particular interest are the reports of prolonged elevation of response for up to 16 weeks following the booster injection (Smith, 1983a) notwithstanding the sharp decline in antibody titres over this period (Cox, Wilson and Wong, 1984). It would appear that once the system has been perturbed by immunisation the ovulation rate response in maintained for long periods.

FACTORS INFLUENCING THE RESPONSE

The response to steroid immunisation has been measured both in terms of ovulation rate (the direct end-point) and in terms of lambs born per ewe joined (the indirect end-point). While most research-orientated studies have measured both end-points many field trials provide details on lamb numbers only.

Apart from the previously mentioned problems of anoestrus and barrenness which can negate any gains in ovulation rate, another major problem is the variable discrepancy between the recorded number of ovulations and the number of lambs born i.e. the partial failure of multiple ovulations (PFMO) which has contributed markedly to the variation in the ratio lambs born to ewes joined (LB/EJ) in treated flocks (Smith, 1984).

In general there have only been a few instances where a significant increase in ovulation rate has not been obtained using the immunisation technique and consequently the failure to obtain additional lambs has been due to factors which influence the level of PFMO and barrenness.

Spacing Between the Primary and Secondary Injection

Smith *et al.* (1981a) showed no difference in the ovulation rate or LB/EJ when the interval between injections was 15 or 30 days. The lack of any effect on lambing has been confirmed in recent field trials (Scaramuzzi *et al.*, 1983; Geldard, 1984).

Interval Between Booster Injection and Joining

A booster-to-joining interval of 14 days reduced both the number of ewes exhibiting oestrus and its duration compared to ewes joined 30 days after booster treatment (Smith *et al.*, 1981b, 1983c, d). A slight delay (4 days) in oestrus onset was noticed in ewes joined 21 days after booster when compared to untreated ewes (Smith, 1983b). There was no effect of the booster-to-joining interval on ovulation rate (Smith *et al.*, 1982b, c, 1983c, d). Field trials have indicated little increase in LB/EJ if the booster-to-joining interval was less than 9 to 10 days. This was associated with low conception rates and increased barrenness (Scaramuzzi *et al.*, 1983; Geldard, Dow, Kieran, 1984; Geldard 1984). Those workers report an increase in LB/EJ and a reduction in barrenness as the booster-to-joining interval increased to 14 days beyond which no major differences were recorded. However Croker *et al.* (1984) have shown improved results as the interval was increased from 2 to 4 weeks.

For optimum results a minimum of 3 weeks between injection and joining is clearly needed.

Ewe Breed or Genotype

With 2 notable exceptions there appears to be little difference in ovulation response over a very wide range of breeds: Welsh Mountain ewes (Scaramuzzi, Davidson and Van Look, 1977), Merinos (Martin *et al.*, 1979; Cox *et al.*, 1982), Romneys and Coopworths (Smith *et al.*, 1981a), Perendale (Smith and Cox, 1981), Waihora Romney (Smith *et al.*, 1982a), Marshal Romney (Knight *et al.*, 1983), Galway (Quirke and Gosling, 1980), Dorset Horn (Scaramuzzi, Cox and Hoskinson, 1982), Border Leicester x Merino (Cox *et al.*, 1983), Scottish Blackface (Quirke *et al.*, 1983), Border Leicester x Romney and Corriedale (Scaramuzzi *et al.*, 1983), Borderdale (Geldard, Scaramuzzi and Wilkins, 1984), British Romney, Scottish ½ breed, Welsh ½ breed, Suffolk x breed, Kerry and Welsh Hill Speckle Face (Harding, Joby and Hardy, 1984) and Booroola x Romney (Kyle and Smith, 1984).

Important exceptions are ewes carrying the Booroola high fecundity gene (Kyle and Smith, 1984) and Finnish Landrace (Quirke and Gosling, 1980), both of these genotypes showing an excessive ovulation rate response to androstenedione immunisation. Apart from these, the response of different genotypes to immunisation has been similar and additive to those differences due to gentoype (Smith *et al.*, 1982a). However the results from field trials indicate a lower response (LB/EJ) from Merino ewes than from the cross breeds and New Zealand breeds (Geldard, 1984). These observations are confounded with differences in live weight, nutrition, management and location and need to be more critically evaluated.

Age of Ewe

Similar increases in ovulation rate have been recorded in treated ewes ranging from 6 months to 7 years and no effects of age on the number of extra lambs born have been recorded in the field trials where ages ranged from 18 months to 7 years (Geldard, 1984).

Season of Joining

Increases in ovulation rate were similar for Coopworth ewes treated out of season in December and joined in January (2 months early) and for ewes treated in March and joined in April (Smith *et al.*, 1983d). Increases in lambs born per 100 ewes joined were reported for both Merino and Border Leicester x Merino ewes treated and joined in spring and early summer and those treated and joined in late summer or autumn (Geldard, 1984). Immunisation did not influence the effectiveness of the 'ram effect' in inducing out of season breeding (Scaramuzzi *et al.*, 1981b; Smith *et al.*, 1983d).

Plane of Nutrition About Joining

Smith *et al.* (1981a) showed that both immunisation and flushing (increased level of nutrition in the prejoining period) increased ovulation rate and the effects were additive in both Coopworth and Romney ewes. This effect was confirmed with the same ewes in the following year (Smith and Cox, 1981; Smith *et al.*, 1982a; Smith, 1983a). Moreover this increase in ovulation rate was generally reflected in increases in LB/EJ. Increases in ovulation rate from immunisation were also shown to be additive to those due to increases in the level of dietary protein intake (Smith, 1982, 1983a). A similar response to improved nutrition in Merino ewes was reported by Croker *et al.* (1983) and in Corriedale ewes by Cummins *et al.* (1984). In some of the trials of Smith *et al.* (1981c) immunised ewes in the low nutrition groups showed good increases in ovulation rate despite a marked loss in live weight over the prejoining period. This may indicate that the immunisation and nutrition effects are independent at this level of response.

Ewe Live Weight at Joining

Field trials (Scaramuzzi *et al.*, 1983; Geldard, Scaramuzzi and Wilkins, 1984; Geldard, Dow and Kieran, 1984; Geldard, 1984) have shown an increasing response (LB/EJ) to immunisation as ewe live weight at joining increased. In these experiments, the live weight effect was confounded with that of breed, level of nutrition (both prior to and at joining), season of year, age, management procedures and location. Thus there is a critical need to examine the ewe live-weight effect under more controlled conditions, particularly as the ovulation rate data of Smith *et al.* (1982a) does not support such an effect. The effect of increased live weight at joining may be to influence the survival rate of the additional embryos through to lambing.

Dietary Phyto-oestrogens

The effects of phyto-oestrogens, particularly coumestrol, in reducing ovulation rate and LB/EJ are well documented (Smith *et al.*, 1979). The effects of high dietary levels of coumestrol (from fungus-infected lucerne) on the response to immunisation with both oestrone and androstenedione antigens reported by Smith *et al.* (1981d, 1982b, 1982c) Smith and Cox (1981) and Smith (1983a) indicate smaller increases in both ovulation rate and LB/EJ with both immunogens from ewes grazing lucerne containing coumestrol. The suppressive effect of coumestrol on both OR and LB/EJ was evident in both immunised and non-immunised ewes. This again suggests some independence in the mechanism of effect, but it does enable the use of immunisation to overcome in part the problem of dietary coumestrol intake at joining.

The effect of immunisation in the presence of other phyto-oestrogens (e.g. formononetin) is quite different. Both androstenedione and oestrone immunisation exacerbated the deleterious effect of the isoflavone (Little *et al.*, 1984).

Variation in Lambing Response

Because of the influence of the factors indicated above and of possible as yet unidentified interactions between these factors and the additional complication of a variable level of embryonic mortality it is not surprising that a wide range of lambing results has been reported for flocks treated with steroid immunogens. The results of New Zealand trials up to and including 1983 (using a dextran adjuvant with the androstenedione immunogen) have been summarised by Smith (1984), Smith, McGowan and Maclean (1985) while the Australian field trials have been summarised by Geldard, Dow and Kieran (1984).

Figure 1 shows the overall pattern of response (LB/EJ) of all trials in which a dextran adjuvant was used with a steroid antigen. These included the results of Smith, McGowan and Maclean (1985), Geldard, Dow and Kieran (1984), Cox *et al.* (1982), Scaramuzzi, Cox amd Hoskinson (1982), Geldard, Scaramuzzi and Wilkins (1984), Cox *et al.* (1983), Croker *et al.* (1982) and the unpublished results of trials conducted in New Zealand in 1984 (J.F. Smith, unpublished; C.M. Kelly, Glaxo NZ Ltd., personal communication), a total of 113 flocks.

They show a range of responses from − 2 to + 53 lambs born per 100 ewes joined with an overall mean increase of 22.2 (± 11.8 SD) for immunised ewes. A similar spread of results with increases from 10 to 36 lambs born per 100 ewes immunised has recently been reported in the UK (Harding, Joby and Hardy, 1984).

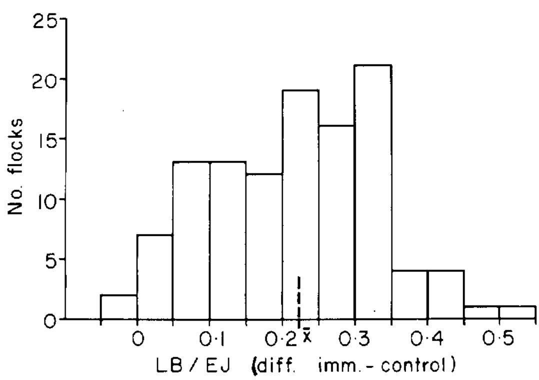

FIG. 1 Response in LB/EJ produced by immunisation in Australian and New Zealand trials.

EFFECT OF REPEATED TREATMENT IN SUCCESSIVE YEARS

In terms of antibody titres and ovulation rates collective experience thus far suggests that the response obtained in the first year sets the response for subsequent years (Cox *et al.*, 1982). However reproducibility has not always been the case with respect to LB/EJ. Several trials have shown increased LB/EJ following repeated treatment of ewes in successive years (Cox *et al.*, 1982) but others have shown the response in the second year to be lower (Smith *et al.*, 1982a). The reduced response may be due to a relatively lower live weights of the immunised ewes compared to the control ewes at the second joining following a greater weight loss over the lactation period as a result of the higher litter size (Smith, 1984).

EFFECT OF IMMUNISATION ON THE DISTRIBUTION OF LAMB BIRTH RANK

The change of distribution in lamb birth rank with increasing level of flock fecundity has been documented for non-immunised ewes (Davis *et al.*, 1983). Examination of the distribution of birth rank from immunised flocks shows that it is identical to that expected in an untreated flock with the same level of lambs born per ewe lambing (Smith, 1983a, 1984). This is important when considering the effect the application of immunisation will have on farm management. The use of immunisation in flocks with a base level of fecundity of 1.5 LB/EL will result in an increase in the proportion of triplets and quads as well as an increase in twins. This statement differs somewhat from that of Geldard (1984) "These extra lambs will be mainly twins....", the majority of whose data was obtained from flocks with low basal levels of fecundity. However, in New Zealand trials with flocks whose average fecundity was 1.38 (LB/EJ) and which showed an increase in LB/EL after immunisation of 0.26, the proportion of ewes having twins increased from 48.3% to 56.3% but those having triplets or quads also increased from 4.4% to 16.1% (Smith, 1983a).

LAMB MORTALITY

Because the practical end-point of any system to increase fecundity of flocks is the number of lambs weaned per ewe joined, the effects of immunisation on lamb mortality need to be examined closely. Most reports indicate a greater overall mortality in lambs from immunised ewes (Smith, 1983a, b), largely because of increasing mortality as birth rank increases rather than because of any differences in mortality rate of lambs of the same birth rank (Smith 1983a). Geldard, Dow, Kieran (1984) reported a 4.5% higher mortality among lambs from immunised ewes. In general however, there is a serious lack of detailed information on lamb losses in field trial.

PERFORMANCE OF PROGENY FROM IMMUNISED EWES

The growth rates and reproductive performance of female progeny from immunised ewes have been studied in detail in both Australia (Wilson *et al.*, 1983) and New Zealand (Smith, 1983a, Smith *et al.*, 1984). No discernible effects on growth rates, wool production, or reproductive performance have been reported. Wilson *et al.* (1983) have reported no difference in the response of progeny from immunised ewes to subsequent immunisation.

In contrast to the situation for female progeny the published data on the performance of male progeny varies between the 2 countries. Smith (1983a) reported no effect of immunisation of the dam on growth rate, testes size, semen quality and libido of the male offspring up to the 2-tooth stage in New Zealand whereas the Australians report a reduced libido at 18 months of age in the ram progeny of ewes immunised with androstenedione (Mattner *et al.*, 1984).

No transfer of antibody from ewe to foetus was observed *in utero* (Mattner *et al.*, 1984) but some transfer of antibody from ewe to the lamb has been recorded via the colostrum shortly after birth (Wilson, Cox and Wastie, 1984). However the use of passive immunisation against androstenedione in ram lambs shortly after birth failed to influence subsequent libido (Mattner *et al.*, 1984) and has led to the conclusion that any effect must be *in utero* and may be due to loss of androstenedione across the placental barrier.

Any adverse effect of immunisation on performance of ram progeny will have serious implications on the use of the technique in stud breeding flocks. Resolution of these discrepant results is therefore important.

PRODUCTIVITY OF EWES SUBJECTED TO STEROID IMMUNISATION

Despite considerable data on the effects of immunisation on the reproductive performance of ewes in a wide range of environments there are almost no reports on the effect of immunisation on overall productivity of flocks maintained under similar management systems.

Immunisation against both oestrone and androstenedione has substantially increased the productivity of Coopworth ewes stocked at 22 ewes per ha by an increase in the production of meat per ha (Smith, Maclean and McGowan, 1983) and despite a small decrease in wool production/ha. The increased lamb production is accompanied by an older age at slaughter and thus greater lamb feed requirements. Moreover this has contributed to the lower ewe live weights at subsequent joinings (Smith 1984).

CONCLUSION

The administration of a steroid-protein conjugate to ewes stimulates the production of steroid antibodies. This leads to alterations in the secretory patterns of the gonadotrophins and steroids and perturbations to the hypothalamic-pituitary-ovarian axis. In some as yet unknown way, these changes result in an increased ovulation rate which under most circumstances leads to extra lambs. The extent and effectiveness of the technique in producing extra lambs is modified by many factors including the treatment schedule, the type of ewe and her management. Thus while the details of how the technique works still require elucidation it seems that it offers a most practical means of increasing ewe fecundity and production.