Responses to divergent selection for plasma insulin-like growth factor-1 (IGF-1) in sheep

P.C.H. MOREL, H.T. BLAIR, S.N. McCUTCHEON, B.H. BREIER[1] AND P.D. GLUCKMAN[1]

Department of Animal Science, Massey University, Palmerston North, New Zealand.

ABSTRACT

A divergent selection experiment with Romney sheep, using plasma concentration of IGF-1 measured 4 weeks after weaning as the selection criterion, was initiated in 1986. From 111 ram lambs born and reared as twins, 4 with the highest level of IGF-1, 4 with the lowest level and 4 selected at random were used to create three lines (high, low and control). Each ram was randomly mated with 25 ewes. Data from 1986 (number of lambs=111), and two F1 generations (1988, n=241 and 1989, n=151) are presented here. Analysis of variance showed that date of birth, age of dam, rearing rank, and sex significantly contributed to variation in plasma levels of IGF-1. Expression of variation in plasma IGF-1 between years appeared to be influenced by variation in pasture supply. Residual correlations between IGF-1 levels and production traits were positive but of variable magnitude (weaning weight, 0.14 to 0.43; post-weaning growth rate, -0.07 to 0.24; fleeceweight, 0.27). Based on the selection differential generated by initial screening of rams and the average divergence between the high and low lines, realized heritabilities of 0.22 and 0.27 were obtained for plasma IGF-1 concentration in 1988 and 1989, respectively.

Keywords Sheep, selection responses, Insulin-like Growth Factor-1.

INTRODUCTION

Plasma concentration of insulin-like growth factor-1 (IGF-1) has potential as a selection criterion in animal improvement programmes. Divergent selection on the basis of plasma IGF-1 in mice has been shown to influence liveweight (Blair *et al.*, 1989; Baker *et al.*, 1991), organ growth (R.A. Siddiqui *et al.*, unpublished data), reproductive performance and mammary gland weight (Kroonsberg *et al.*, 1989). There is also evidence of a genetic association between circulating IGF-1 levels and lactational performance in dairy cattle (Ahlborn-Breier *et al.*, 1987).

A divergent selection experiment with Romney sheep, using plasma concentration of IGF-1 four weeks after weaning as the selection criterion, was therefore initiated at Massey University in 1986 to test responses to selection.

This paper reports on the degree of variation in plasma concentrations of IGF-1 in sheep, and examines the importance of some non-genetic effects controlling this variation. The degree of covariation between plasma concentrations of IGF-1, weaning weight, liveweight, daily gain, fleeceweight and a selection index are also examined. The direct responses to selection for plasma concentration of IGF-1 four weeks after weaning are presented for the first generation.

MATERIALS AND METHODS

F0 Generation

Date-of-birth (23 August to 28 September 1986), birth rank and pedigree of lambs in a commercial Romney flock were recorded. At weaning, 111 ram lambs sired by three different rams and reared as twins were chosen for this study. Animals were weighed at : weaning (8 December 1986), blood sampling (5 and 16 January 1987, 4 months) and about 9 months of age (15 May). A fleece weight was also obtained at 9 months of age. This represented an equal period of wool growth for all animals since they were previously shorn at 4 months of age. A selection index comprising breeding values for weaning weight, fleeceweight, dam's number of lambs born and liveweight at 9 months of age was produced for each individual by the Sheeplan animal recording

[1] Department of Paediatrics, University of Auckland Medical School, Auckland, New Zealand.

TABLE 1 Means and standard deviations (SD) of the various traits recorded in 1986, 1988 and 1989.

Trait	1986 Mean	1986 SD	1988 Mean	1988 SD	1989 Mean	1989 SD
n	111		241		151	
Age at weaning (d)	96.2	5.2	81.4	10.6	73.1	10.5
IGF-1 (ng/ml)	303	74	423	122	534	122
Weaning wgt (kg)	21.5	3.2	20.1	3.7	21.4	4.4
4 mth wgt (kg)	24.4	4.2	22.6	4.0	-	-
5 mth wgt (kg)	-	-	23.4	4.1	-	-
6 mth wgt (kg)	-	-	-	-	32.0	5.1
9 mth wgt (kg)	40.9[1]	4.7	-	-	-	-
ADG1 (g/day)	90	70	97	70	-	-
ADG2 (g/day)	70[1]	100	26	26	-	-
9 month fleece (kg)	2.0[1]	0.3	-	-	-	-
Selection index (cents)	17.5[1]	24.7	-	-	-	-

[1] n=90

scheme (Clarke and Rae, 1977). Average daily gains were calculated between weaning and blood sampling (ADG1) and subsequent to blood sampling (ADG2).

At the end of January 1987, 4 rams with the highest level of IGF-1, 4 with the lowest level and 4 selected at random were used to create three lines (high (H), low (L) and control (C) respectively). Each ram was randomly mated with 25 Romney ewes of unknown IGF-1 levels in 1988 and 1989.

F1 Generations

Lambs of the F1 generation were born from 14 August to 3 October 1988 and from 14 August to 30 September 1989. Pedigree, date-of-birth, sex and rearing rank were recorded. In 1988, 241 lambs were weighed at weaning (25 November), at 4 months of age (21 December) and at 5 months of age (20 January). In 1989, 151 lambs were weighed at weaning (15 November) and at 6 months of age (20 February). Average daily gains were calculated between weaning and blood sampling (ADG1) and subsequent to blood sampling (ADG2) in 1988. All lambs were blood sampled about 4 weeks after weaning (27 December 1988 and 18 December 1989).

Blood Sampling

Blood samples were obtained by jugular venipuncture (into vacutainers using EDTA as the anticoagulant) and plasma stored at -20 °C until analysis of IGF-1 concentrations. Prior to analysis, the two plasma samples from each animal of generation F0 were bulked volumetrically. IGF-1 concentrations were measured by radioimmunoassay following acid-ethanol extraction using the procedure of Gluckman *et al.* (1983). Intra- and inter-assay coefficients of variation were 5.0% and 9.8% respectively. Plasma concentrations are expressed with respect to recombinant human-met-IGF-1 (rh-met-IGF-1, batch #742-44; Dr B.D. Burleigh, International Minerals and Chemicals, Pitman-Moore, Northbrook, IL, USA).

Statistical Analysis

In order to examine the effects of date-of-birth (DOB), dam age (DA; 2,3 or 4 + years), rearing rank (RR; single or twin), sex (S; male or female) and line (LI; High,

TABLE 2 Effect of date-of-birth, dam age, rearing rank and sex on plasma IGF-1 concentrations (ng/ml). Values are expressed as a regression coefficient (B) ± standard error (se) of the coefficient for date-of-birth and as least squares means ± pooled standard error (se) for other effects. Means with different superscripts within effects and years are significantly different (P < 0.05)

Year	Date of Birth			Dam Age				Rearing Rank			Sex		
	B	se		2	3	4+	se	1	2	se	f	m	se
1986	0.8	1.4	NS	351[a]	259[a]	259[a]	35	-	-	-	-	-	-
1988	-3.2	0.7	***	393[a]	427[ab]	441[b]	13	440[a]	401[b]	11	421[a]	419[a]	11
1989	-2.4	0.9	**	540[a]	525[a]	499[a]	18	551[a]	492[b]	15	502[a]	541[b]	15

NS p > 0.05; ** = p < 0.01; *** = p < 0.001

Control or Low) on variation in the traits being examined, a linear model was fitted using the statistical package REG (Gilmour, 1985). Only significant interactions between fixed effects were fitted for the 1988 data. No interactions were fitted for the 1989 data because of the small number of observations in some sub-cells. Correlations between the various traits were obtained by correlating the residuals after fitting the linear models.

RESULTS AND DISCUSSION

Means and standard deviations for the various traits examined in 1986, 1988 and 1989 are shown in Table 1. The contribution of date of birth, dam age, rearing rank and sex to the variation observed in IGF-1 concentrations and the least squares means for these factors are given in Table 2.

Nutritional Conditions

Figure 1 shows the monthly pasture cover (kg dry matter per hectare) in 1986, 1988 and 1989 on the farms where the selection flocks were maintained. Pasture cover was assessed by rising plate meter (Earle and McGowan, 1989). The quantity of pasture available for grazing could be characterised as good in 1989, poor in 1986 and very poor in 1988. Since poor nutrition leads to a depression in plasma IGF-1 concentration (Elsasser *et al.*, 1989), this could explain the lower IGF-1 concentrations found in 1986 and 1988 in comparison to 1989.

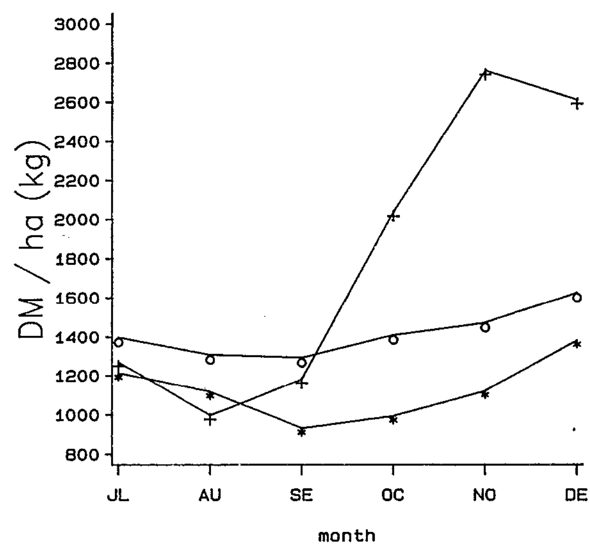

FIG 1 Monthly pasture cover (kg dry matter per hectare) assessed by rising plate meter in 1986 (o), 1988 (*) and 1989 (+).

Non-Genetic Factors

The impact of age (date-of-birth), dam age, rearing rank and sex on liveweights, ADGs and fleeceweight was consistent with other reports (Baker *et al.*, 1979; Newmann *et al.*, 1983).

IGF-1 level increased with the age at blood sampling (date of birth effect) in 1988 and 1989 (Table

TABLE 3 Residual correlations between traits observed in 1986 (below diagonal) and in 1988 and 1989 (above diagonal).

	IGF-1	weight at weaning	4 m.	5 m.	6 m.	9 m.
IGF-1	-	0.14 0.41	0.22	0.26	0.30	-
Wng wgt	0.43	-	0.82	0.79	0.61	-
4 m.wgt	0.51	0.85	-	0.92	-	-
9 m.wgt	0.37	0.66	0.71	-	-	-
FW	0.27	0.31	0.37	-	-	0.57
Index	0.43	0.43	0.74	-	-	0.90

All correlations $p < 0.05$

2). Similar results have been reported in sheep (Roberts *et al.*, 1990) and cattle (Breier *et al.*, 1988). In 1986, the smaller variation in age at weaning (coefficient of variation = 5 % in comparison to 13-14 % in 1988-89) and poor grazing conditions (Fig. 1) could have masked the relationship between IGF-1 level and age.

The effect of dam age on IGF-1 concentration was significant only in 1988. Since it is known that young ewes rear lambs of lighter weight it might be expected that as further data are obtained dam age will be confirmed as having a significant impact on lamb IGF-1 levels. However, there is also the possibility that, by the time of blood-sampling, lambs born to young ewes may be exhibiting compensatory growth, thereby increasing IGF-1 levels. Thus, there is a need to collect more information to assess the impact of dam age on IGF-1 levels.

In 1988 and 1989 twin lambs had significantly lower IGF-1 concentrations than single lambs. Similar results have been reported in sheep (Roberts *et al.*, 1990).

No difference between the sexes was found in 1988. In 1989 males had higher IGF-1 concentration than females. Roberts *et al.* (1990) examined the ontogeny of circulating IGF-1 in sheep and also found higher concentrations for males. However, they did not observe a divergence between the sexes in IGF-1 levels until about 6 months of age. An interaction between sex and rearing rank was found for IGF-1 concentration in 1988. In single-reared lambs, but not in twin-reared lambs, males had higher IGF-1 concentrations than females.

Residual Correlations

Correlations between the various traits, after adjustment for date of birth, dam age, rearing rank and sex, are shown in Table 3.

The IGF-1 concentration was moderately positively correlated with liveweights at weaning and subsequently, but the magnitude of this relationship varied between years. As the preweaning period is critical for the development of the mature IGF-1 system (Sara *et al.*, 1986), different nutritional conditions between years could be responsible for the differences observed in magnitude of this relationship. The lower correlations were found in 1988 when the pasture cover (kg dry matter per hectare) and the weaning weights were lower. The correlations between IGF-1 concentration and liveweight calculated in sheep by Roberts *et al.* (unpublished data) were higher (0.4 to 0.6). Positive correlations between IGF-1 concentration and liveweight or liveweight gain have also been reported in other species (for example mice : Baker *et al.*, 1991; and cattle: Bishop *et al.*, 1989).

Although IGF-1 concentrations were moderately correlated with ADG1 (0.18 and 0.24), the correlation with ADG2 was negligible (-0.07 to 0.12). This would suggest that IGF-1 concentrations reflected differences in growth rate prior to blood-sampling, but were not useful in predicting the rate of growth subsequent to blood sampling.

The relationship found between IGF-1 and fleeceweight and the index was probably caused by the positive correlation existing between IGF-1 and

TABLE 4 Least squares-means ± pooled standard errors (se) for IGF-1 concentration and weaning weight in High (H), Control (C) and Low (L) lines in 1988 and 1989. Means with different superscripts within years are significantly different (P< 0.05)

Year	IGF-1 concentration (ng/ml)				Weaning weight (kg)			
	H	C	L	se	H	C	L	se
1988	446^{a}	403^{b}	414^{ab}	13	19.6^{ab}	19.3^{a}	20.4^{b}	0.3
1989	515^{a}	508^{a}	476^{a}	20	21.1^{a}	20.5^{a}	20.2^{a}	0.5

liveweight.

Genetic Factors

After correction for date-of-birth, dam age, rearing rank and sex, a line effect was fitted for plasma IGF-1 concentration and weaning weight, the least-square means and pooled standard errors being shown in Table 4. In both years High line lambs had higher IGF-1 concentration than Low line lambs, but these differences were not significant. No difference in weaning weight between the High and Low line lambs was observed.

The selection differential generated between the High and the Low line rams in 1986 was 293 ng/ml. Assuming a random contribution from the ewes, the line difference of 32 ng/ml in 1988 and 36 ng/ml in 1989 in the first generation progeny correspond to realized heritabilties of 0.22 and 0.27 respectively. Blair *et al.* (1989) found a realized heritability of 0.15 after 7 generations of divergent selection on IGF-1 concentration in mice. In their selection experiment Baker *et al.* (1991) found a realized heritability of 0.10 after 5 generations. Thus a similar degree of genetic variation seems to be expressed in mice and sheep. While these heritabilities estimates are only low to moderate, the large degree of variation in IGF-1 levels (coefficient of variation of about 25 %) would enable moderate rates of genetic progress to be achieved.

CONCLUSION

In sheep, IGF-1 concentration shows considerable variation, a low to moderate heritability and positive phenotypic correlation with production traits. When selecting on IGF-1 concentration correction for rearing rank and nutritional conditions (if different) should be undertaken. Before making a decision on the potential use of IGF-1 as a selection criterion, further generations of selection are needed to measure the correlated responses in production traits such as reproduction rates, weaning weight, fleeceweight and carcass composition.

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