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Insulin-like growth factor 1, growth and body composition in red deer stags

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Abstract

Insulin-like growth factor 1 (IGF1) correlates with antler growth and body growth in penned red deer stags. The present study aimed to investigate the relationships among plasma concentration of IGF1, body growth and carcass composition in grazing stags. Twenty-eight 10-month-old stags were kept at pasture from September to February. They were bled, weighed and their antlers measured fortnightly. Plasma was analysed for total IGF1. All stags were slaughtered in February (aged 15 months); organ weights were recorded and the carcasses were analysed chemically for water, fat and ash. The stags began the study weighing 60·7 (s.e. 1·4) kg and were 96·3 (s.e. 2·0) kg at the end. They grew rapidly in spring and early summer but growth rate slowed in mid summer before increasing again in late summer.

Total plasma IGF1 for each stag throughout the study correlated positively with antler length ($P < 0.001$), total live-weight gain ($P < 0.001$), hot carcass weight ($P < 0.01$), fat-free carcass weight ($P < 0.01$), carcass fat weight ($P > 0.05$) and carcass fat percentage ($P > 0.05$). Thus IGF1 correlated significantly with all measures of body weight except fat. IGF1 correlated positively with antler growth rate ($P < 0.001$) calculated individually for each stag during each fortnight. IGF1 correlated positively with the spring phase of live-weight gain calculated as above ($P < 0.001$) but negatively ($P < 0.01$) with live-weight gain during the late summer growth phase. The relationships between IGF1 and growth in penned stags also pertain in grazing animals, and in addition IGF1 is closely associated with carcass lean mainly via an overall effect on body size.

Keywords: *body measurements, carcass composition, IGF1, red deer.*

Introduction

Insulin-like growth factor 1 (IGF1) is believed to mediate the growth promoting effect of growth hormone on cartilage and bone (the somatomedin hypothesis) (Salmon and Daughaday, 1957), although the precise mechanism is unclear (D'Ercole, Stiles and Underwood, 1984). The annual spring-summer elevation of plasma IGF1 correlates strongly and positively with antler growth (Suttie, Gluckman, Butler, Fennessy, Corson and Laas, 1985; Suttie, Fennessy, Gluckman and Corson, 1988) and body growth (Suttie, Fennessy, Corson, Laas, Crosbie, Butler and Gluckman, 1989) in red deer stags. Young red deer stags fed *ad libitum* have a very marked seasonal pattern of live-weight gain with relatively low growth rates during winter and high rates of gain in spring-summer (Suttie, Goodall, Pennie and Kay, 1983). It has been suggested that IGF1 is stimulatory for antler and body growth in red deer, but the rôle of IGF1 in determining body composition of deer is not known. IGF1 is related to composition (fat or lean) of live-weight gain in beef bulls (Anderson, Bergen, Merkel, Enright, Zinn, Refsal and Hawkins, 1988). Therefore, it was decided to measure plasma IGF1 in red stags during the spring-summer and determine whether differences in body composition at slaughter in autumn correlated with IGF1. An additional goal was to determine whether IGF1 increased seasonally in pasture-fed deer in the same way as it does in deer kept indoors (Suttie *et al.*, 1985). A preliminary account of this work has been published previously (Suttie, Fennessy, Corson and Gluckman, 1987).

Material and methods

Animal management and slaughter

Twenty-eight red deer stag calves aged 10 months at the start of the study were kept on pasture at Invermay Agricultural Centre, Mosgiel, New Zealand. At 2-week intervals for 26 weeks from

September to February (southern hemisphere summer), they were weighed, their antler status (i.e. whether pedicle, antler velvet or antler clean of velvet) and antler length and testis diameter were measured and a blood sample was withdrawn into a pre-heparinized evacuated tube.

The antlers were removed when they were cleaned of velvet at the close of the study and were then weighed and measured. At the close of the study all of the stags were humanely slaughtered in a research abattoir. The carcass, liver, spleen, pancreas, combined testes, fat associated with the kidney and kidneys and the femur was dissected, weighed and measured from the proximal tip of the greater trochanter to the distal tip of the medial condyle. The length of the carcass was measured. The *semimembranosus* muscle was dissected and weighed. One-half of the carcass was ground through a 4-mm screen and aliquots of the resultant homogenized mince were analysed for fat, ash, water and protein using methods described by Lord, Fennessy and Littlejohn (1988).

IGF1 analysis

Plasma IGF1 was measured by radioimmunoassay after acid ethanol extraction using the method of Gluckman and Butler (1983) as validated for deer by Suttie *et al.* (1985) with the following modifications. The acid ethanol extraction has been further validated for post natal ruminant plasma in that values obtained using the acid-ethanol extraction show a high correlation ($r = 0{\cdot}92$, slope = 0·97, no. = 12, $P < 0{\cdot}001$) with values obtained following extraction on Sephadex G75 chromatography in formic acid (1 mol/l). Values are expressed in terms of recombinant met-hIGF1 batch number 742-44 (Dr Burleigh, International Minerals Corporation, Pitman Moore, Terre Haute, Indiana). The inter- and intra-assay variations were 0·115 and 0·05 respectively. The minimum detectable level of IGF1 was 0·05 ng per tube.

Biometric analysis

The body compsition measures were correlated with the mean IGF1 concentration over the study for each stag by linear regression analysis. The mean IGF1 concentration was the arithmetic mean of all 13 IGF1 values obtained during the study for each stag. In addition the 2-weekly IGF1 levels (mean of plasma concentrations at the beginning and end of each period) were correlated with live-weight gain and change in antler length over each 2-week period individually for all stags by linear regression analysis. Multiple regression analysis of measured variables was carried out using final live weight as a covariate followed by mean IGF1 using the GENSTAT statistical package (Lawes Agricultural Trust, 1984).

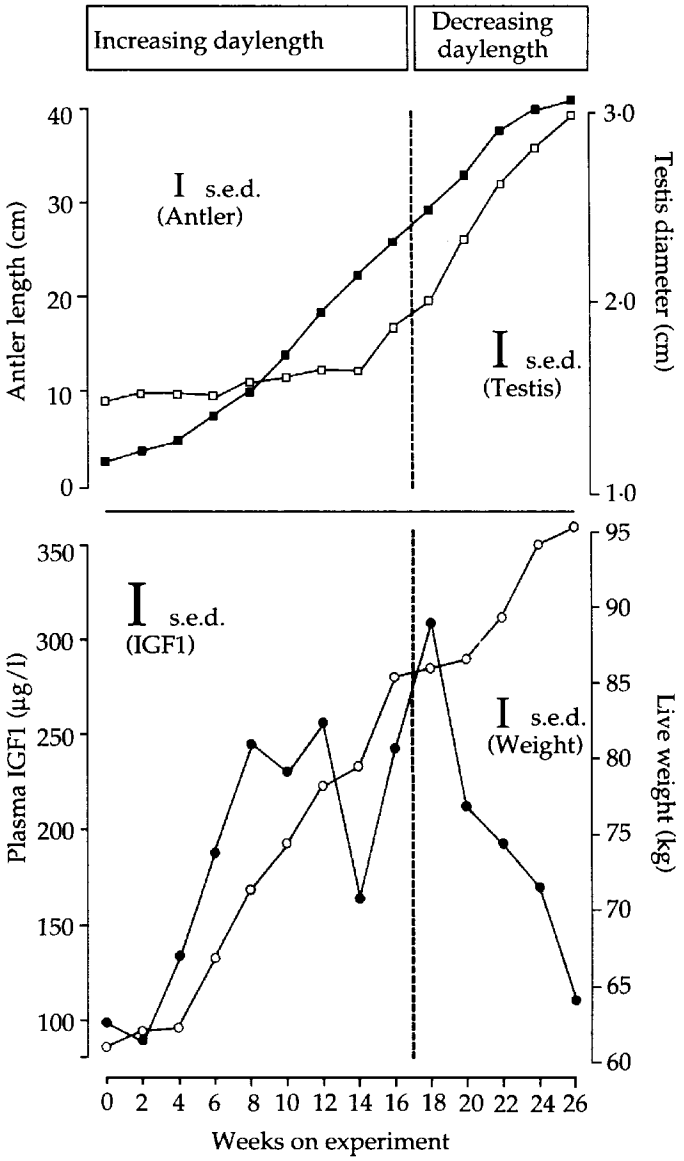

Figure 1 Mean testis diameter (❑), antler length (■), live weight (○) and plasma IGF1 (●) of 28 stags for 26 weeks.

Results

Plasma IGF1 levels rose during the spring, decreased slightly in mid summer then rose again before falling sharply in late summer towards the end of the study (Figure 1). Mean live weight increased from 60·7 (s.e. 1·4) kg at the start to 96·3 (s.e. 2·0) kg at the close of the trial. Although live-weight gain slowed slightly from 16 to 20 weeks, it was almost continuous throughout the study (Figure 1). Antler length increased throughout the study and was complete at the end as all the stags had cleaned their antlers of velvet (Figure 1). Testis size did not increase from the start of the study until week 14 when an abrupt increase in testis diameter took place (Figure 1). Testis diameter was highest in February at the close of the study.

Table 1 *Mean values for antler dimensions total live-weight gain and body composition data at slaughter and correlation coefficients for the relationship with mean IGF1 for stags*

	Mean	s.e.	*r*
Antler			
Hard antler			
length (cm)	41·9	2·3	0·550**
weight (g)	172·3	15·1	0·401*
Total live-weight gain (kg)	35·6	0·9	0·592***
Carcass components			
Hot carcass			
length (cm)	111·0	0·9	0·546**
weight (kg)	55·8	1·3	0·521**
Femur			
length (cm)	28·8	0·2	0·363
weight (g)	463·0	10·1	0·466*
Organs			
liver (g)	1524·0	27·3	0·419*
pancreas (g)	87·9	3·4	0·490*
spleen (g)	240·0	8·8	0·148
kidneys (g)	223·0	6·1	0·438*
testes (g)	80·0	2·9	0·407*
M. semimembranosus (g)	1141·0	64·2	0·464*
Kidney fat (g)	138·0	12·1	0·279
Weight of fat (kg)	5·1	0·1	0·236
Water (kg)	35·9	0·4	0·549**
Ash (kg)	3·3	0·1	0·254
Protein (kg)	11·5	0·2	0·464*
Fat-free (kg)	50·7	0·6	0·528**
Proportions†			
Fat	9·0	0·4	0·059
Water	64·6	0·3	0·130
Ash	5·7	0·1	–0·342
Protein	20·7	0·2	–0·105
Fat-free	91·0	0·5	–0·059

† Proportions for carcass components are of hot carcass weight.

The summary data for body dimensions at slaughter and body composition are shown in Table 1. Mean IGF1 correlated significantly and positively with antler length and weight, and carcass, organ, bone and muscle weight but not femur length (Table 1). The relationship between plasma IGF1 and total live-weight gain (kg) and the weight of the *semimembranosus* muscle is shown graphically in Figures 2 and 3 respectively. IGF1 did not correlate significantly with carcass component proportions but did correlate significantly and positively with body water and body protein content but not fat content (Figure 4; Table 1).

Using individual data throughout the study IGF1 correlated significantly and positively with changes in antler length (Table 2). Although overall the concentration of IGF1 correlated positively with individual live-weight gain, the correlation between IGF1 and live-weight gain before the summer solstice was very highly significant ($P < 0·001$) and positive,

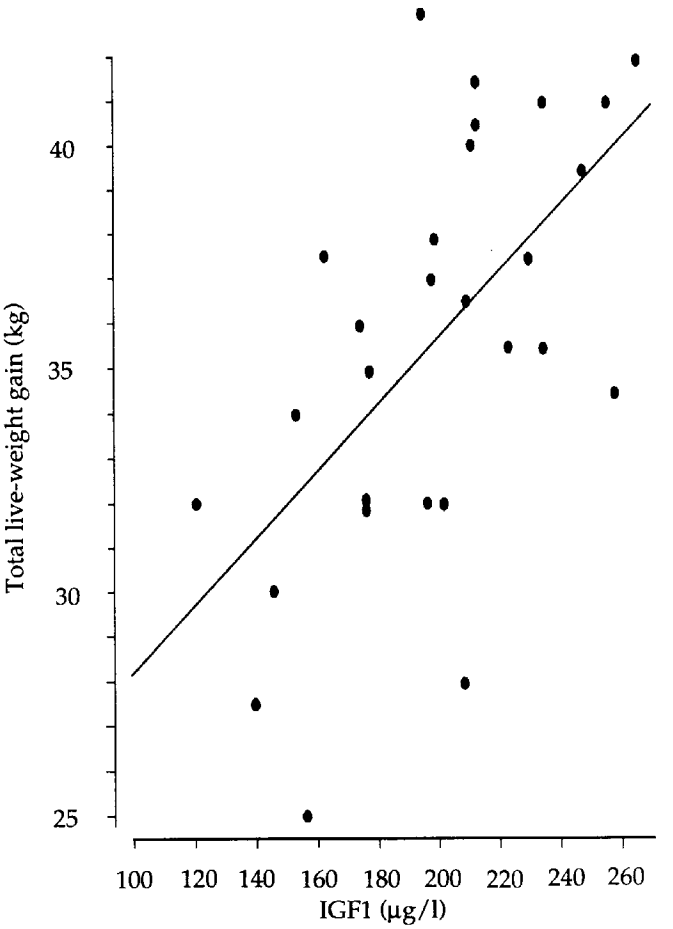

Figure 2 Total live-weight gain throughout the study of 26 weeks and mean plasma IGF1 for 28 stags. The linear regression equation is $y = 0·0741\ x + 20·7971$.

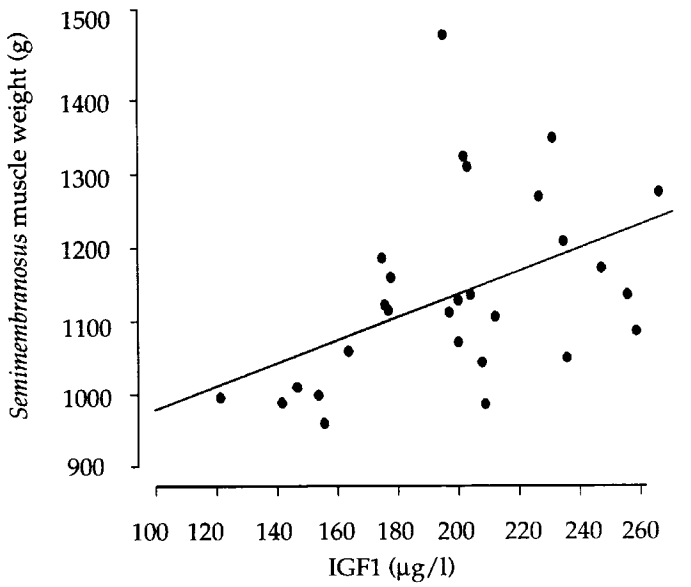

Figure 3 *Semimembranosus* muscle weight and mean plasma IGF1 for 28 stags. The linear regression equation is $y = 1·584x + 824·4587$.

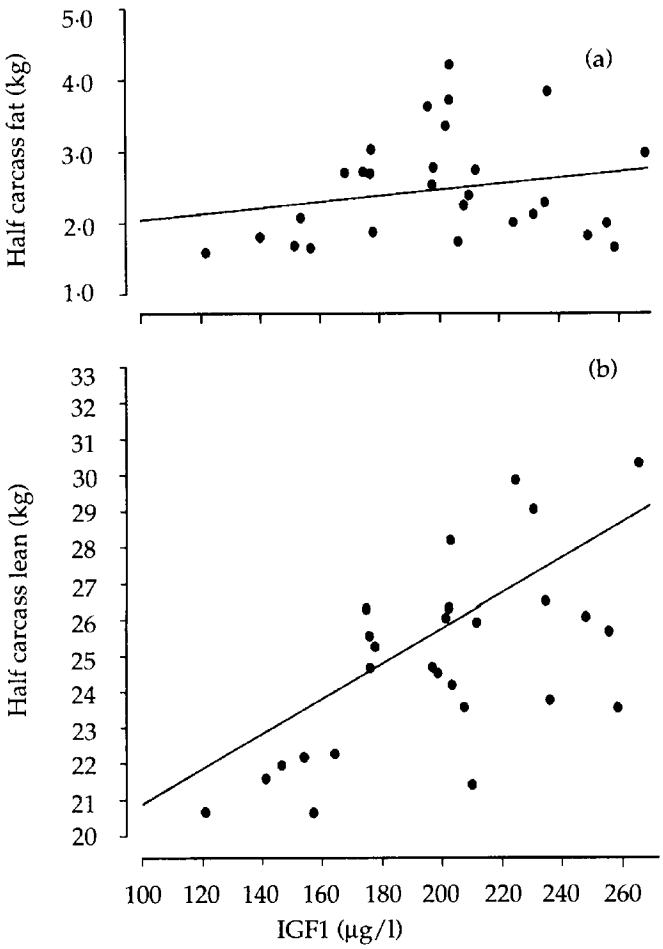

Figure 4 Half carcass (a) chemical fat and (b) lean (water protein and ash) weight and mean plasma IGF1 for 28 stags. The linear regression equations are (a) $y = 0{\cdot}0047\ x + 1{\cdot}5812$ and (b) $y = 0{\cdot}0429\ x + 16{\cdot}622$ respectively.

Table 2 *Correlation between total plasma IGF1 for each stag over each 2-week period (mean of plasma concentration of the beginning and end of each period) and antler growth rate and live-weight gain. Each animal is treated individually for each time period (no. = 336)*

Antler growth rate	0·338***
Live-weight gain (overall)	0·117*
Live-weight gain (before summer solstice)	0·418***
Live-weight gain (after summer solstice)	–0·273**

while that after the summer solstice was highly significant and negative ($P < 0{\cdot}01$) (Table 2). The correlation between pre- and post-summer solstice live-weight gain for individual animals was not significant ($r = 0{\cdot}078$, $P < 0{\cdot}05$).

Multiple regression of measured parameters on a final live weight covariate followed by mean IGF1 showed that, in as much as measures in Table 1 were related to IGF1, this was mediated by body size. However, significant relationships were found between IGF1 and antler measurements and pancreas weight which were independent of body size.

Discussion

Live-weight gain and antler growth followed the normal seasonal pattern at Invermay, and body and antler size fell within the expected range for yearling stags on pasture in New Zealand (Moore, Littlejohn and Cowie, 1988). Body composition was very similar to that reported by Suttie *et al.* (1983) for yearling Scottish red deer stags. Thus, the stags can be considered normal representatives of their species and the frequent blood sampling and handling did not adversely influence growth and development.

Plasma IGF1 concentrations of stags at pasture were increased during the summer compared with spring and autumn in agreement with studies of stags kept indoors (Suttie *et al.*, 1985 and 1989). There was, however, a conspicuous difference in the present study from the previous studies in that plasma IGF1 levels were increased during late summer; in stags reared indoors plasma IGF1 levels had decreased by this time. In addition the peak of IGF1 occurred earlier in the spring in the indoor studies compared with the present study. Because nutrition is known to play a rôle in determining the plasma concentrations of IGF1, in that undernutrition lowers IGF1 (Breier, Bass, Butler and Gluckman, 1986), the difference in the timing of the seasonal peak in IGF1 may be due to dietary insufficiencies in early spring prior to the flush of pasture growth; likewise the decrease in IGF1 in mid summer may be due to a summer decrease in pasture quality. Whether the seasonal increase in IGF1 is under photoperiodic control or is merely a consequence of the seasonal body and antler growth pattern remains to be elucidated.

There were significant positive correlations between IGF1 live-weight gain and antler growth rate confirming an earlier study in deer (Suttie *et al.*, 1985). In addition, the correlations between IGF1 and body growth parameters have been extended to include body composition. The precise mechanisms underlying correlations between IGF1 and growth are unclear. Although it has been shown that IGF1 can restore growth to hypophysectomized rats (Schoenle, Zapf, Humbel and Froesch, 1982) and increase growth in entire rats (Hizuka, Takano, Shizume, Asakawa, Miyakawa, Tanaka and Horikawa, 1986), Skottner, Clark, Robinson and Fryklund (1987) could not confirm this effect in a large scale study in hypophysectomized rats. For several reasons it has been suggested that IGF1 may induce growth solely by acting locally in its tissue of origin (paracrine) rather than being transported from a secretory organ to a target organ in the blood (endocrine) (D'Ercole *et al.*, 1984). First, IGF1 in the plasma is bound to multiple binding proteins which appear to limit its bioactivity and clearance from

plasma (Hodgkinson, Davis, Burleigh, Henderson and Gluckman, 1987). Secondly, the precise source of plasma IGF1 is unclear; although many tissues can secrete IGF1 it is believed that most is released by the liver (Bourguignon, 1988) under GH control (Froesch, Schmid, Schwarder and Zapf, 1985).

Recently however, growth enhancement has been shown in transgenic mice expressing human IGF1 (hIGF1) (Matthews, Hammer, Behringer, D'Ercole, Bell, Brinster and Palmiter, 1988) and the authors concluded the results confirmed a growth regulatory rôle for IGF1 and suggested that both endocrine and paracrine processes were involved in IGF1-mediated growth. Perhaps this is the best context in which to discuss the present data; they do not lend themselves to a discussion of endocrine *v.* paracrine effects, but rather the appearance of greater amounts of IGF1 in the plasma appears to occur in individual animals with certain patterns of body composition and organ size. Stags with larger bodies had higher mean levels of IGF1 than those which were smaller. It is known that articular cartilage has receptors for IGF1 (McQuillan, Handley, Campbell, Bolis, Milway and Herington, 1986) and that local production of IGF1 by fibroblasts occurs (Adams, Nissley, Handwerger and Rechler, 1983) so it seems very likely that bone development is under IGF1 control. However, muscle development may also come under IGF1 control because there are IGF1 receptors in skeletal muscle (Zapf, Froesch and Humbel, 1981). The carcass size of transgenic mice expressing IGF1 was greater than controls (Matthews *et al.*, 1988) indicating that IGF1 probably does control body size. Matthews *et al.* (1988) also found transgenic hIGF1-expressing mice had enlarged spleens, pancreas and kidneys compared with controls. In the present study, IGF1 correlated significantly with pancreas and kidney weight but not spleen weight. The spleens from the stags were weighed after the animal had been bled out, but those from the mice were frozen immediately after death and were thus weighed full of blood. Matthews *et al.* (1988) consider that the enlarged kindeys and pancreas in the transgenic hIGF1 mice were due to an endocrine effect of IGF1 rather than to a paracrine effect because the size increases were proportional to circulating IGF1 and because only the exocrine cells of the pancreas expressed IGF1. Hizuka *et al.* (1986) found that IGF1 administration increased kidney, liver and testis weight in entire rats; all three organs correlated significantly with IGF1 in stags. The kidney fat weight did not correlate significantly with IGF1, however, probably due to the fact that adipocyte glucose transport is not IGF1 dependent (Schoenle, Zapf and Froesch, 1983).

IGF1 correlated significantly and positively with total carcass lean (protein, ash and water) weight but not fat weight nor proportion of any carcass component. This agrees well with Anderson *et al.* (1988) who found IGF1 correlated positively with carcass lean but not carcass fat in beef bulls. This relationship is of some interest because, as larger animals tend also to be fatter, it could be considered that the correlation between fat and IGF1 should be significant.

IGF1 was related most closely to body size, and using body size (final live weight) as a covariate did not improve the relationships between many carcass measures and IGF1. This means that these measures are correlated with IGF1 probably via body size. Conspicuous exceptions were pancreas weight and antler weight and length. Therefore, IGF1 may have an effect on pancreas and antler over and above its effect on body size. This supports a notion that IGF1 is a trophic hormone for antler growth (Suttie *et al.* 1985 and 1988). The pancreas itself did not correlate with body size ($r = 0{\cdot}130$, $P > 0{\cdot}05$) so there appears to be a direct trophic effect of IGF1 on the pancreas. The relevance for aspects of growth and development are not known.

After the summer solstice the IGF1 correlation with growth was significantly negative, although this did not affect the overall correlation between IGF1 and live-weight gain in the study. Tissue deposition in stags occurs in a seasonal sequence of lean followed by fat (Drew and Suttie, 1982). The lean portion occurs early in the season which would correspond to the high correlation between IGF1 and live-weight gain and the fat portion later in accord with the timing of the low correlation between IGF1 and live-weight gain. This may present further evidence for a relationship between IGF1 and lean gain rather than fat gain. The fact that the two phases of the relationship between IGF1 and growth correspond with clear phases of testicular development (presumably an indicator of steroid production) points to possible involvement of the gonad in determining the growth response to IGF1. Body composition data throughout the summer period would be needed to test this hypothesis adequately.

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References

Adams, S. O., Nissley, S. P., Handwerger, S. and Rechler, M. M. 1983. Developmental patterns of insulin-like growth factor – I and II synthesis and regulation in rat fibroblasts. *Nature, London* **302:** 150-152.

Anderson, P. T., Bergen, W. G., Merkel, R. A., Enright, W. J., Zinn, S. A., Refsal, K. R. and Hawkins, J. 1988. The relationship between composition of gain and circulating hormones in growing beef bulls fed three dietary crude protein levels. *Journal of Animal Science* **66:** 3059-3067.

Bourguignon, J-P. 1988. Linear growth as a function of age at onset of puberty and sex steroid dosage: therapeutic implications. *Endocrine Reviews* **9:** 467-488.

Breier, B. H., Bass, J. J., Butler, J. H. and Gluckman, P. D. 1986. The somatotrophic axis in young steers: influence of nutritional status on pulsatile release of growth hormone and circulating concentrations of insulin like growth factor 1. *Journal of Endocrinology* **111:** 209-215.

D'Ercole, D., Stiles, A. J. and Underwood, L. E. 1984. Tissue concentration of somatomedin C: further evidence for multiple sites of synthesis and paracrine or autocrine mechanisms of action. *Proceedings of the National Academy of Sciences USA* **81:** 935-941.

Drew, K. R. and Suttie, J. M. 1982. Quality meat from farmed deer. *Proceedings of the New Zealand Deer Farmers Association Annual Conference* **7:** 39-47.

Froesch, E. R., Schmid, C., Schwarder, J. and Zapf, J. 1985. Actions of insulin like growth factors. *Annual Review of Physiology* **47:** 443-467.

Gluckman, P. D. and Butler, J. H. 1983. Parturition related changes in insulin-like growth factors I and II in the perinatal lamb. *Journal of Endocrinology* **99:** 223-232.

Hizuka, N., Takano, K., Shizume, K., Asakawa, K., Miyakawa, M., Tanaka, I. and Horikawa, R. 1986. Insulin-like growth factor 1 stimulates growth in normal growing rats. *European Journal of Pharmacology* **125:** 143-146.

Hodgkinson, S. C., Davis, S. R., Burleigh, B. D., Henderson, H. V. and Gluckman, P. D. 1987. Metabolic clearance rate of insulin like growth factor 1 in fed and starved sheep. *Journal of Endocrinology* **115:** 233-240.

Lawes Agricultural Trust. 1984. *GENSTAT V Mark 404B.* Rothamstead Experimental Station, Harpenden, Hertfordshire.

Lord, E. A., Fennessy, P. F. and Littlejohn, R. P. 1988. Comparison of genotype and nutritional effects on body and carcass characteristics of lambs. *New Zealand Journal of Agricultural Research.* **31:** 13-19.

McQuillan, D. J., Handley, C. J., Campbell, M. A., Bolis, S., Milway, V. E. and Herington, A. C. 1986. Stimulation of proteoglycan biosynthesis by serum and insulin-like growth factor — I is cultured bovine articular cartilage. *Biochemical Journal* **240:** 423-430.

Matthews, L. S., Hammer, R. E., Behringer, R. R., D'Ercole, A. J., Bell, I. G., Brinster, R. L. and Palmiter, R. D. 1988. Growth enhancement of transgenic mice expressing human insulin-like growth factor 1. *Endocrinology* **123:** 2827-2833.

Moore, G. H., Littlejohn, R. P. and Cowie, G. M. 1988. Liveweights, growth rates and antler measurements of farmed red deer stags and their usefulness as predictors of performance. *New Zealand Journal of Agricultural Research* **31:** 285-291.

Salmon, W. D. and Daughaday, W. H. 1957. A hormonally controlled serum factor which stimulates sulphate incorporation by cartilage in vitro. *Journal of Laboratoy and Clinical Medicine* **49:** 825-836.

Schoenle, E., Zapf, J. and Froesch, E. R. 1983. Regulation of rat adipocyte glucose transport by growth hormone: no mediation by insulin-like growth factors. *Endocrinology* **112:** 384-386.

Schoenle, E., Zapf, J., Humbel, R. E. and Froesch, E. R. 1982. Insulin-like growth factor 1 stimulates growth in hypophysectomized rats. *Nature, London* **296:** 252-253.

Skottner, A., Clark, R. G., Robinson, I. C. A. F. and Fryklund, L. 1987. Recombinant human insulin like growth factor: testing the somatomedin hypothesis in hypophysectomised rats. *Journal of Endocrinology* **112:** 123-132.

Suttie, J. M., Fennessy, P. F., Corson, I. D. and Gluckman, P. D. 1987. Insulin-like growth factor 1 and body size in red deer stags. *Proceedings of the Endocrine Society of Australia* **30:** P 38.

Suttie, J. M., Fennessy, P. F., Corson, I. D., Laas, F. J., Crosbie, S. F., Butler, J. H. and Gluckman, P. D. 1989. Pulsatile growth hormone, insulin-like growth factors and antler development in red deer (*Cervus elaphus scoticus*). *Journal of Endocrinology* **121:** 351-360.

Suttie, J. M., Fennessy, P. F., Gluckman, P. D. and Corson, I. D. 1988. Elevated IGF1 levels in stags prevented from growing antlers. *Endocrinology* **122:** 3005-3007.

Suttie, J. M., Gluckman, P. D., Butler, J. M., Fennessy P. F., Corson, I. D. and Laas, F. J. 1985. Insulin-like growth factor 1: antler stimulating hormone? *Endocrinology* **116:** 846-848.

Suttie, J. M., Goodall, E. D., Pennie, K. and Kay, R. N. B. 1983. Winter food restriction and summer compensation in red deer stags (*Cervus elaphus*). *British Journal of Nutrition* **50:** 737-747.

Zapf, J., Froesch, E. R. and Humbel, R. E. 1981. The insulin-like growth factors (IGF) of human serum: chemical and biological characterization and aspects of their possible physiological role. *Current Topics in Cellular Regulation* **19:** 257-309.

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