PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE **180**, 191–195 (1985)

Blood Parameters and Body Composition in Fetuses from Reciprocal Crosses of Genetically Lean and Obese Swine[1] (42163)

R. T. STONE,*,[2] D. R. CAMPION,† J. KLINDT,* AND R. J. MARTIN‡

Roman L. Hruska U.S. Meat Animal Research Center, Agricultural Research Service, U.S. Department of Agriculture, Clay Center, Nebraska 68933; †Richard B. Russell Agricultural Research Center, College Station Road, Athens, Georgia 30613; and ‡College of Home Economics, Department of Foods and Nutrition, University of Georgia, Athens, Georgia 30602

Abstract. Lines of swine previously selected for either high backfat (obese) or low backfat (lean) were investigated to determine the effect of maternal obesity and the relationship between serum parameters and body composition. Fetal weight, percentage body protein, fat, fat-free organic matter and ash, and serum concentrations of albumin, growth hormone, triiodothyronine, and cortisol were compared in fetuses from straight line and reciprocal crosses at 110 days of gestation. Fetuses from the obese line weighed less but had a greater percentage body protein, fat, and fat-free organic matter than did fetuses from the lean line. Serum concentrations of albumin and triiodothyronine were less whereas those of growth hormone were greater in fetuses from the lean line compared to fetuses from the obese line. Values for these parameters in fetuses from the reciprocal crosses were generally intermediate to those of fetuses from the lean and obese lines. Comparisons of fetuses from the reciprocal and line crosses by linear contrast showed that the observed differences were mainly due to the average genetic effect of individual fetal genotypes and not due to maternal effects. Correlations computed from the residual variance showed a positive relationship between percentage body protein, serum albumin, and triiodothyronine while percentage body fat was not correlated with any of the other traits. Serum growth hormone was negatively correlated with fetal weight. We conclude that there is no apparent maternal effect of obesity or relationship of fetal fat content with any of the other variables measured in these lines of swine at the stage of fetal development at which these determinations were made.

The developmental aspects of obesity and the influence of maternal obesity on fetal and neonatal development are difficult to evaluate in many animal models for a variety of reasons. Reproductive capacity is often impaired in genetically obese inbred strains of rodents (1) and reduced fertility and cannibalism are often observed in dietary-induced models for obesity (2). Also, several models display metabolic abnormalities which influence fetal development (e.g., hyperinsulinemia) (1). Thus, despite the potential importance of understanding metabolic events associated with the development of obesity and the implications of maternal obesity affecting neonatal growth and development (3), limited information is available on the developmental aspects of obesity.

Selection in Yorkshire and Duroc swine for 16 or 18 generations, respectively, for high (obese) and low backfat (lean) resulted in lines within each breed that differed in conformation, growth, and carcass characteristics (4). At 100 kg body wt, the obese lines exceeded the lean lines in backfat thickness and total body fat by approximately 135 and 90%, respectively (5, 6). Subsequent to these studies the Yorkshire and Duroc breeds were crossed within lines to produce composite lines of lean and obese swine. Obesity in these swine is not apparently associated with hyperinsulinemia since only subtle differences in plasma glucose, insulin, and triglycerides have been observed between these lines (7). Previous comparisons of fetuses from these obese swine or from obese feral (Ossabaw) swine to fetuses from either lean or contemporary breeds of swine have shown differences in body composition and weight, and concentrations of serum growth hormone, albumin, triiodothyronine (T_3), and cortisol (8–10).

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[2] To whom all correspondence should be addressed.

0037-9727/85 $1.50

Since deliberate selection for obesity in domestic swine and natural selection in the feral swine have resulted in similar changes in serum parameters and body composition, it seems possible that these parameters are genetically correlated traits associated with the development of obesity. The purpose of this study was to determine the relationship between body composition and serum parameters and to evaluate average genetic effects and maternal effects of obesity on fetal development in these lines of swine by comparing fetuses from straight line and reciprocal crosses.

Materials and Methods. *Animals.* Yorkshire and Duroc breeds of swine were selected for 16 or 18 generations, respectively, for either high or low backfat thickness (11). Subsequently, the breeds were crossed within lines and have been maintained without selection for about 11 generations. Gilts from these lines were randomly assigned to mating groups and estrus was synchronized (12). For each mating group (sire listed first), the number of litters, and the mean number of fetuses per litter were: lean × lean = 6, 9.0; lean × obese = 6, 9.7; obese × lean = 8, 9.0; obese × obese = 7, 8.0. Gilts were maintained on a standard gestation ration and, at 110 days of gestation (full term = 114 days), fetuses were taken by cesarean section (13). Blood from the umbilical vein and body weights were obtained for all fetuses. The intestinal contents were removed from three randomly selected fetuses in each litter and the whole fetuses were frozen for body composition analysis.

Analytical determinations. Serum concentrations of growth hormone, T_3, and cortisol were determined in all fetuses by radioimmunoassay (8, 14). Inhibition of iodinated growth hormone binding by dilutions of adult serum, fetal serum, or porcine pituitary extract was parallel to purified growth hormone (U.S.D.A., pGH-B1). The sensitivity was 0.1 ng/assay tube and the intraassay and interassay coefficients (mean ± SE) of variations were 6.4 ± 2.5 and 18.7 ± 3.8%, respectively. Binding was not inhibited by the addition of porcine LH, FSH, or prolactin up to 100 ng/tube. Cortisol concentrations were determined in a single assay and the coefficient of variation was 1.8%. A kit (Cambridge Medical Diagnostics) was used to determine T_3 concentrations. High and low controls provided by the manufacturer reportedly contained 1.7 ± .5 and 4.7 ± 1 ng/ml and the values obtained in this single assay were 1.5 and 4.1 ng/ml, respectively. Serum albumin concentrations were determined by radial immunodiffusion (15). Frozen fetuses were ground separately and total body protein was estimated from Kjeldahl nitrogen. Total body lipids were determined gravimetrically after chloroform:methanol extraction (16, 17). The fat-free organic matter was calculated by subtracting the fat and ash content of the samples from the dry weight before dividing by the sample weight.

Statistical analysis. The analyses of variance were performed on the litter mean values of each parameter as litters were considered the experimental unit. The model contained the effect of mating group with the number of fetuses per litter included in the model as a covariate to adjust for the effects of litter size on the parameters evaluated. Linear contrasts of mating group means were used to estimate maternal and average genetic (direct) effects (18). Correlations among dependent variables were computed from residual variances and covariances.

Results. Serum albumin concentrations in fetuses from the obese line were greater ($P < 0.05$) than those in fetuses from either the lean line or the reciprocal crosses (Table I). Growth hormone concentration was greater ($P < 0.05$) and T_3 was less ($P < 0.05$) in fetuses from the lean line compared to the obese line. Fetuses from reciprocal crosses did not differ from each other or from fetuses from either of the parental lines in growth hormone or T_3 concentration. Body weight was less ($P < 0.05$) in fetuses from the obese line compared to those from the lean line and those from neither parental line differed significantly from the reciprocal crosses (Table II). The percentages of body protein and fat-free organic matter were greater ($P < 0.05$) in fetuses from the obese line than from either the lean line or the reciprocal crosses. The percentage body fat in fetuses from the obese line exceeded ($P < 0.05$) that in fetuses from the reciprocal crosses and that in fetuses from the lean line by about 0.17 and 0.23%, respectively. Percentage of body ash or serum

TABLE I. FETAL SERUM PARAMETERS AT 110 DAYS OF GESTATION IN STRAIGHT LINE AND RECIPROCAL CROSSES OF LEAN AND OBESE SWINE (LEAST SQUARES MEAN OF MATING GROUPS ± SE)

Group[c]	Albumin (μg/ml)	Growth hormone (ng/ml)	Triiodothyronine (T_3; ng/ml)	Cortisol (ng/ml)
Lean × lean	726 ± 115[a]	68.7 ± 9.8[a]	13.7 ± 4.0[a]	145 ± 18[a]
Lean × obese	1043 ± 132[a]	50.2 ± 11.4[a,b]	22.7 ± 4.7[a,b]	116 ± 21[a]
Obese × lean	999 ± 99[a]	58.8 ± 8.5[a,b]	23.7 ± 3.5[a,b]	117 ± 16[a]
Obese × obese	1459 ± 110[b]	38.0 ± 9.5[b]	29.3 ± 3.9[b]	163 ± 17[a]

[a,b] Values within columns with different superscripts are different ($P < 0.05$).
[c] Sire listed first.

cortisol concentration did not differ between any of the mating groups. Values for the parameters evaluated in fetuses from the reciprocal crosses were generally intermediate to those in fetuses from the parental lines. Comparisons of these parameters from the different mating groups by linear contrast showed no heterotic or maternal effects. Average genetic effects of the individual fetal genotypes had the greatest influence on these parameters.

Residual correlations among the traits measured are listed in Table III. Fetal weight was positively correlated with albumin concentration ($P < 0.01$) and negatively correlated with growth hormone ($P < 0.05$). Percentage body protein was significantly correlated with the albumin, T_3, and percentage of fat-free organic matter and ash. Percentage body fat was not significantly correlated with any other parameter measured. The relevance of the correlation of cortisol with fat-free organic matter and T_3 is questionable.

Discussion. We have compared several serum and body composition parameters in fetuses at 110 days of gestation from straight line and reciprocal crosses between lean and obese lines of swine. Of the serum parameters evaluated, albumin and T_3 concentrations were greater and growth hormone concentration was less in fetuses for the obese line compared to those from the lean line. As expected from previous studies, the residual correlation between fetal weight and the concentrations of albumin and growth hormone were positive and negative, respectively, (13, 19, 20). Growth hormone concentration tended to be negatively correlated with the other parameters evaluated, however, the relative importance is not clear since growth hormone has no defined role in the control of fetal growth (21). The greater concentration of T_3 and percentage body protein in fetuses from the obese line compared to the lean line, and the positive correlation between T_3 and percentage body protein provide indirect evidence for an effect of T_3 on protein deposition in fetal pigs. Because cortisol concentrations in fetal pig serum are highly variable as they increase rapidly late in ges-

TABLE II. FETAL PARAMETERS IN STRAIGHT LINE AND RECIPROCAL CROSSES OF LEAN AND OBESE SWINE: BODY COMPOSITION AT 100 DAYS OF GESTATION (LEAST SQUARES MEAN OF MATING GROUPS ± SE)

Group[c]	Body weight (g)	Protein (%)	Fat (%)	FFOM[d] (%)	Ash (%)
Lean × lean	1124 ± 68[a]	10.3 ± 0.17[a]	1.55 ± 0.17[a]	12.7 ± 0.20[a]	3.5 ± 0.1[a]
Lean × obese	1039 ± 78[a,b]	10.5 ± 0.19[a]	1.61 ± 0.03[a]	13.0 ± 0.23[a]	3.3 ± 0.1[a]
Obese × lean	940 ± 59[a,b]	10.2 ± 0.16[a]	1.60 ± 0.02[a]	12.8 ± 0.12[a]	3.5 ± 0.1[a]
Obese × obese	836 ± 65[b]	11.2 ± 0.16[b]	1.77 ± 0.03[b]	13.7 ± 0.19[b]	3.5 ± 0.1[a]

[a,b] Values within columns with different superscripts are different ($P < 0.05$).
[c] Sire listed first.
[d] FFOM—fat-free organic matter.

TABLE III. CORRELATIONS AMONG BLOOD AND BODY COMPOSITION PARAMETERS[a]

	Trait							
Traits	Protein	Fat	FFOM[b]	Ash	Albumin	GH	T_3	Cortisol
Weight	0.28	0.02	0.26	0.28	0.66**	−0.47*	0.03	−0.07
Protein		0.32	0.50*	0.74**	0.43*	−0.19	0.47*	0.23
Fat			0.14	0.41	0.37	0.01	0.22	−0.08
FFOM				0.56**	0.29	−0.11	0.25	0.54*
Ash					0.40	−0.14	0.22	0.24
Albumin						−0.37	0.42	0.03
GH							0.19	0.25
T_3								0.53*

[a] Correlations were computed from residual variances and covariances. Residual degrees of freedom = 20.
[b] FFOM—fat-free organic matter.
* $P < 0.05$, ** $P < 0.01$.

tation (22), it is difficult to interpret correlations as not being due to chance. However, as observed in this study, a positive correlation between T_3 and cortisol has been reported in newborn sheep (23). Reported relationships of fetal endocrine parameters to other fetal parameters have been largely confined to overall fetal growth or age, thus, data relating fetal body composition to endocrine parameters are not available for comparison.

Fetuses from the lean line were heavier but had less body fat and protein than did those from the obese line. The difference in the absolute value between the percentage fat is small (0.2%), but may be an important contribution to the increased neonatal survival in obese swine compared to lean lines, since energy stores are limited in newborn swine (9, 10, 24). Hoffman *et al.* (9) reported similar data comparing fetuses from obese feral swine to those from a contemporary breed. Also, they report a higher percentage dry matter in the obese feral fetuses which is consistent with the higher percentages fat-free organic matter, protein, and fat in fetuses from the obese line compared to those from the lean line observed in this study. The lower percentage of body protein in the fetuses from the lean line compared to those from the obese line is the reverse of what has been reported for these lines of swine at 4 weeks of age and older (5, 25). These data emphasize that the genetic potential for increased fat deposition relative to protein deposition in these swine is not overtly expressed until postnatal development.

Artificial selection for backfat thickness in contemporary swine breeds and natural selection (for survival) in feral swine has resulted in genetic lines that differ similarly from contemporary breeds in several metabolic parameters and in body composition. It would seem possible that at least some of these parameters are associated with the development of obesity or that they are due to additive genetic effects of maternal obesity. However, the percentage body fat was not significantly correlated with any other parameter measured in this study. Further, values for the parameters measured were generally intermediate for fetuses from the reciprocal crosses compared to fetuses from straight line crosses and comparisons of the mating groups by linear contrast did not suggest any maternal or heterotic effects. It has been reported that maternal effects (26) and heterotic (27) effects are more pronounced during postnatal development. Mice selected for high and low body weight at 5 weeks of age were found not to differ in fat content until 10 weeks of age (28). Thus, the present results do not preclude maternal effects being expressed postnatally which could be partially responsible for the rather pronounced differences in body fat and protein that are characteristic of these lines of swine at a few weeks of age.

Neonatal survival is about 20% higher in both the obese line and the feral obese swine compared to contemporary breeds of swine which suggests that they are more metabolically mature at birth (8, 10). It is unlikely that this difference in survival can be totally accounted for by the smaller litter sizes in the obese and fetal swine. Thus, it can be argued that the observed differences between obese swine and contemporary or lean swine may reflect metabolic changes associated with increased neonatal survival rather than changes associated with the developmental or maternal aspects of obesity. This would suggest that these lines of swine might be a better model for studying the metabolic aspects of neonatal survival than for the development of obesity.

We acknowledge the technical assistance of Misi Robinson, Benny Barrett, and Mary Hart and the clerical assistance of Debbie Brown. We are also grateful to Roussel-UCLAF, Paris, France, and Dr. S. K. Webel, McHenry, Ill., for providing Altrenogest for the synchronization of estrus, Dr. D. N. Marple for the gift of the porcine growth hormone antiserum, and the U.S.D.A. Hormone Program, and Dr. D. J. Bolt for the purified porcine growth hormone.

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Received December 21, 1984. P.S.E.B.M. 1985, Vol. 180.
Accepted May 16, 1985.