SELECTION FOR PLACENTAL EFFICIENCY IN SWINE

A Dissertation

presented to

the Faculty of the Graduate School

University of Missouri-Columbia

In Partial Fulfillment

of the Requirements for the Degree

Doctor of Philosophy

---

by

HENRY MESA ECHEVERRI

Dr. William R. Lamberson, Dissertation Supervisor

DECEMBER 2004

The undersigned, appointed by the Dean of the Graduate School, have examined the dissertation entitled.

SELECTION FOR PLACENTAL EFFICIENCY IN SWINE

Presented by Henry Mesa Echeverri

a candidate for the degree of Doctor of Philosophy

and hereby certify that in their opinion it is worthy of acceptance

Dr. William R. Lamberson

Dr. Jiangdo Sun

Dr. Timothy J. Safranski

Dr. Jonathan A. Green

Dr. Eric Antoniou

Dr. Randall S. Prather

ACKNOWLEDGEMENTS

I believe that the best teachers are those that help their students learn how to learn. I want to thank Dr. William Lamberson for guiding me during this 'learning to learn' process and providing me with a role model of a balanced academic life. I am also grateful to Dr. Tim Safranski, who has always pushed me to understand the practical implications of the theory and results of my work, and to Dr. Jonathan Green, for his help and advice with the physiological aspects of the project. I would also like to thank Drs. Randall Prather, Eric Antoniou, and Jianguo (Tony) Sun for serving on my committee.

Many graduate students and technicians were involved with this project over the years. I want to thank them for their invaluable help. I want to thank the many friends I made during my program. Particularly, Kathleen Baska, Kristi Cammack, and Kyle Lovercamp provided a friendly environment (most of the time) that made work seem easier during my 'tenure' at MU.

I also want to thank my mother and my brother for their support. Finally, I want to thank my wife Catalina for all her sacrifices to make this possible.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

SELECTION FOR PLACENTAL EFFICIENCY IN SWINE

Henry Mesa Echeverri

Dr. William R. Lamberson, Dissertation Supervisor

ABSTRACT

With the overall goal of increasing profitability by increasing litter size at birth, two lines of pigs were divergently selected for four generations on an index of reproductive traits. The selection index **(SI)** included total born **(TB)**, birth weight **(BW)** and placental weight **(PW)** and was designed to increase **(H** line) or decrease (**L** line) the efficiency of the placental function **(PE)**, defined as the ratio BW:PW. (Co)variance components were estimated for direct and maternal additive effects by using an animal model with MTDFREML procedures. Estimated breeding values (**EBV**) were calculated by using records on individual BW (n = 2,111), PW (n = 2,006), PE (n = 1,677), and SI (n = 1,677). Litter traits were evaluated using records on 193 litters. Direct heritability estimates from single-trait models were 0.03, 0.25, 0.18, 0.11 and 0.08 for BW, PW, PE, SI, and TB, respectively. Genetic divergence was 20.7 ± 2.7 g, 0.24 ± 0.03, 0.11 ± 0.02, and 0.07 ± 0.02 per generation for PW, PE, SI, and TB, respectively ($P < 0.01$), but not significant for BW. At generation four, direct EBV was higher in L than H for PW ($P < 0.01$), was higher in H than L for PE ($P < 0.01$), and were not different for BW, SI or TB. These results indicate that placental weight and efficiency are susceptible to change by

genetic selection. However, the correlated response in litter size was an unexpected genetic trend towards a higher litter size in the L line

In a second phase of the experiment, the objective was to evaluate correlated responses in conceptus development and traits physiologically relevant for placental function in the selected lines. Fifty generation-3 second parity females from lines H and L were mated within line to produce generation-four litters for evaluation at d 30, 50, 70, 90, and 110 of gestation. Fetal weight was not significantly different between lines from d 30 to 90, but was lower in H than L at d 110 ($P = 0.02$). Crown-rump length was not significantly different between lines from d 30 to 70, but tended to be longer in H than L at d 90 ($P = 0.09$) and was shorter in H than L at d 110 ($P = 0.04$). Placental weight increased in both lines from d 30 to 50, at which point it remained relatively unchanged through the rest of pregnancy, except in L that showed a second increase from d 90 to 110. As a result, placental weight was not significantly different between lines from d 30 to 90, but was lower in H than L at d 110 ($P < 0.01$). Line differences in placental efficiency were not significant at any gestational age. These results suggest that in western breeds, a reduction in placental weight through selection is not accompanied by physiological changes to increase placental function and may result in decreased prenatal survival.

In the third phase of this experiment, the data obtained were used to determine factors influencing survival at farrowing and at weaning in swine. Farrowing survival (**FS)** and weaning survival (**WS**) were considered traits of the piglet and were scored as 1 if the individual was alive at those time points or as 0 if it died. Estimates of direct heritability were 0.16 and 0.18 for FS and WS, respectively. Estimates of maternal heritability were 0.14 and 0.10 for FS and WS, respectively. Variables associated with FS and WS were determined by using logistic regression procedures. Birth weight, placental weight, their interaction, and total born can be used as predictors of survival at weaning and farrowing. In the presence of birth weight information, placental efficiency does not improve the prediction of survival probability. Results from this experiment suggest that it is possible to select for increased survival at farrowing and at weaning. Information on a piglet's birth weight, placental weight, its litter average birth weight, and the individual's deviation from that average can be used to produce piglets with high survival probability.

CHAPTER I

INTRODUCTION

Background

The number of piglets alive at birth and at weaning represent the two major sources of variation in the profitability of the swine industry (Legault, 1983; Tess et al., 1983). According to a survey of commercial farms in the U.S, the average number of piglets born is 10.9. In each litter, an average of 8.3% are stillborn, and of those piglets born alive, 11% die before weaning (USDA, 2002). The National Swine Improvement Federation estimates the value of each additional piglet alive at birth and at weaning to be $13.5 and $6.00, respectively (NSIF, 1996). Even though in absolute terms a weaned piglet is more valuable than a newborn, the expenses of rearing an extra piglet to weaning subtract from its initial value and result in a lower marginal profit at weaning. Genetic and management strategies that increase the number of live piglets at these two critical periods would therefore be of great value to the swine industry.

Between 30% and 40% of the embryos produced at fertilization are lost before birth, and even though 75% of the losses occur by day 30 (Pope, 1994), the number of embryos present at this point still exceeds the capacity of the uterus to support them through pregnancy (Bazer et al., 1969; Pope et al., 1972; Bennett and Leymaster, 1989).

The high prolificacy of the Meishan pig can be explained in part by a reduced fetal weight and the ability of the placenta to sustain more grams of piglet per gram of placenta (Ford, 1997; Biensen et al., 1998). At the physiological level, the ability of the Meishan placenta to supply nutrients to the fast growing fetus in the last third of pregnancy is associated with an increase in placental vascularity without an increase in placental size (Biensen et al., 1999).

A correlated response to selection for increased litter size has been a reduction in birth weight (Johnson et al., 1999; Mesa et al., 2003). Such a response is undesirable since low birth weight adversely influences piglet survival and lifetime performance (Rydhmer, 2000). It has been suggested that selection for an increased ratio of piglet weight to its placenta weight (placental efficiency) could dramatically increase litter size (Wilson et al., 1999), but a positive association between litter size and placental efficiency was not detected in two prolific lines selected for either uterine capacity or an index of litter size and ovulation rate (Vallet et al., 2001; Mesa et al., 2003).

Objectives

The overall goal of this research is to identify methods of selection that can be applied by producers in an industry setting to increase litter size in swine. The specific objectives of this study are: 1) to evaluate the response to selection for a linear index designed to modify litter size through changes in placental efficiency; 2) to estimate genetic parameters for traits of interest; 3) to evaluate correlated responses in conceptus development and traits physiologically relevant for placental function through gestation; and 4) to determine factors influencing survival at farrowing and at weaning in swine.

CHAPTER II

LITERATURE REVIEW

Selection for Litter Size

Reproductive traits commonly have low heritability, prompting past skepticism regarding the feasibility of improving litter size through selection (Boylan et al., 1961). Despite limited results in earlier stages of a selection experiment for increased litter size (Ollivier, 1973; Ollivier and Bolet, 1981; Bolet et al., 1989), a combination of direct selection and migration from hyperprolific lines increased litter size by 1.4 piglets over 17 generations (Bolet et al., 2001).

Selection for ovulation rate at second estrus increased this trait by 3.7 ova over nine generations, and the correlated response in litter size was 0.06 ± 0.07 per generation. Reduced embryo survival in the selected line accounted for the small correlated response in litter size (Cunningham et al., 1979; Johnson et al., 1984). In a subsequent analyses of the data from the ovulation rate selection experiment, it was found that after accounting for population means at generation -1 and a second measurement of generation 9, the

actual correlated response in litter size was 0.089 ± 0.058 piglets per generation for a total estimated line difference of 0.8 piglets (Lamberson et al., 1991). Nine generations of direct selection for increased litter size in a line derived from the high ovulation rate line yielded an additional increase of 1.06 piglets relative to its control line, for a total response of 1.86 piglets, and suggested that selection for only ovulation rate is not an efficient way to increase prolificacy (Lamberson et al., 1991).

Selection for an index of ovulation rate and prenatal survival was expected to increase litter size 2.5 times faster than direct selection for litter size due to higher selection intensity and optimum weight on the component traits (Johnson et al., 1984), but other authors were skeptical towards the added value of selecting for components of litter size when compared to direct selection (Pérez-Enciso and Bidanel, 1997).

In the first five generations of selection for an index of ovulation rate and embryo survival at d 50, a response of 0.19 piglets at birth per generation was obtained (Neal et al., 1989). This response was 65% of that predicted by using a deterministic model, but still 1.5 times greater than the expected response to direct selection on litter size under similar conditions (Johnson et al., 1984). Using the actual population parameters for litter size and its components after 11 generations of selection, it was concluded that there was little difference in the efficiency of index selection and direct selection for litter size. However, that study left open the possibility that a more refined index that includes other components of litter size can be more efficient than direct selection (Johnson et al., 1999).

At generation 11 of selection for an index of ovulation rate and embryo survival the difference between lines was 1.3 piglets at birth, and after three generations of direct selection for litter size in the index line the total response increased to three piglets at birth relative to its control line (Johnson et al., 1999). During the same period that the difference between the index and control lines increased to 3.0 piglets, predicted uterine capacity in the selected line increased 1.1 piglets, suggesting that a combination of ovulation rate and uterine capacity was responsible for the response in prolificacy.

Two-stage selection, first for litter size at birth and then for ovulation rate, in a line previously selected for an index of ovulation rate and embryo survival (**IOL**) and a line derived from its unselected control (**COL**), produced a response over eight generations of 0.35 and 0.29 piglets per generation, respectively (Ruíz-Flores and Johnson, 2001). At the beginning of the experiment IOL had 1.06 more piglets at birth than COL, and the authors of that study concluded that the similar rate of improvement in both lines indicates that response to selection is not dependent on the mean genetic level of the lines. A two-stage selection strategy that puts emphasis on components of litter size such as uterine capacity and ovulation rate is therefore an efficient approach to increase prolificacy.

Correlated responses to increased litter size in the index line described by Johnson et al. (1999) are reductions in individual birth weight, piglet viability, and number of weaned piglets. In order to counteract these effects, selection in generations 15 and 16 was practiced on number of live piglets first, then followed by within family selection of heaviest boars and gilts as replacements (Petry and Johnson, 2004). Subsequently, crossbreeding of the selected index line with its control line and commercial Landrace

and Duroc lines was performed from generations 17 to 19; the estimated differences between the index and control lines were 3.53 piglets born, 2.53 piglets born alive, and 2.14 kg litter birth weight (Petry and Johnson, 2004). These results indicate that adjusting selection criteria to the characteristics of the population under study can produce dramatic effects by emphasizing the component trait of litter size that is more limiting at the moment. Secondly, crossbreeding proved to be an effective strategy to use prolific lines and in this way compensate for undesired characteristics in maternal ability and piglet survival at birth and at weaning.

Possibly the best example of the value to the swine industry of academic research into selection strategies to increase litter size has been provided by the index selection experiment discussed previously, what is now commonly known as the Nebraska Index Line. In a comparison of six maternal lines commercially available in the U.S., one of the evaluated lines was derived from a cross of 12 Index Line boars from generation 16 mated to commercial F1 females. In that study, the Index line-derived population farrowed and weaned the largest number of pigs, however, litter weaning weight was the lowest (Moeller et al., 2004).

Other selection experiments have focused on different components of litter size. It was proposed that selection for an increased ratio of piglet birth weight to its placental weight (placental efficiency, **PE**) would result in a correlated increase in uterine capacity and thus litter size; after one generation of divergent selection, a difference in PE of only 0.3 was reported to produce a difference of 2.9 piglets at birth (Wilson et al., 1999). Although the extraordinary response would support the validity of the approach, the base population of the experiment was composed of only eight litters, and each of the

divergent lines consisted of only six gilts and two boars (Wilson et al., 1999). The small size and the short duration of the experiment leave open the possibility that the response was due to genetic drift; a larger multigenerational experiment would be necessary to test the concept of increasing litter size through selection for placental efficiency.

Selection for either litter size after unilateral hysterectomy (an estimate of uterine capacity, **UC**) or ovulation rate (**OR)** for 11 generations increased these traits by 1.1 pigs per horn and 3.2 ova, respectively, relative to the control line (Leymaster and Christenson, 2000). There was no correlated response in ovulation rate in the UC line and, likewise, there was no correlated response in uterine capacity in the OR line, suggesting that that these two traits are genetically independent (Leymaster and Christenson, 2000). Differences in litter size and litter birth weight were not significant between the control and OR lines, but the UC line had 0.9 piglets and 0.8 kg litter birth weight more than the control line (Christenson and Leymaster, 2000). The authors concluded that both OR and UC must be increased simultaneously in order to increase litter size at birth (Christenson and Leymaster, 2000). Placental efficiency was lower in the UC than the OR and control lines; on the other hand, neonatal hematocrit increased as a correlated response in the UC line (Vallet et al., 2001). The authors of that study concluded that direct selection for neonatal hematocrit may not be feasible due to its low heritability (0.03), and that other methods of indirect selection for increased uterine capacity need to be evaluated (Vallet et al., 2001).

Conceptus Development

Attachment and Placentation

Given that fertilization rate in swine is generally 95% or higher (Perry and Rowlands, 1962), ovulation rate sets the upper limit to litter size (Bennett and Leymaster, 1989). Little embryonic mortality occurs before d 12 of pregnancy (d 0 = onset of estrus), while the majority of it occurs between d 12 and 30 (Pope, 1994). Since there are enough embryos at d 30 to provide improvement in litter size at farrowing, the challenge is to maximize fetal survival to term (Geisert and Schmitt, 2002). However, in order to improve fetal survival from d 30 until term, it is necessary to understand the factors influencing conceptus development from d 12 to 30, the period critical for attachment and placental development in the pig.

Porcine embryos are generally in the four-cell stage 4 d after estrus onset (around 48 h after ovulation) when they arrive at the uterus and are in the form of morula at d 5. The blastocyst may contain 150 cells or more before hatching from the zona pellucida by d 6 to 8 (Anderson, 1993). At d 8, the blastocyst has an outer layer of polarized trophectoderm, an embryonic disc, and an inner layer of endodermal cells (Stroband and Van der Lende, 1990). At d 9 and 10, spherical and ovoid blastocysts have a diameter of 0.5 to 1.0 mm. By d 11 some blastocysts are a filament > 5 cm long, and by d 12 half of the blastocysts are filaments 12 to 80 cm long and 0.2 to 0.4 mm in diameter (Anderson, 1978). The elongation rate from 10 to 150 mm is of 30 to 45 mm per h (Geisert et al., 1982a). At d 12 the embryos stop migrating, and at the same time they continue to elongate they release estrogen, the signal for pregnancy recognition (Dziuk, 1985). The process of elongation is accomplished by cellular reorganization (Anderson, 1978;

Geisert et al., 1982b), and any failure in this process may compromise placental development (Perry and Rowlands, 1962; Knight et al., 1977). By the end of the elongation period around d 16, the embryo is 1 m long but is folded in a space of 10 to 20 cm (King, 1993). Elongation stops when there is contact with the placenta of an adjacent littermate (Perry, 1981).

Attachment of the embryo to the endometrium starts at d 12 after estrus in the region adjacent to the embryonic disc, and it involves the interdigitation of microvilli from the conceptus with uterine epithelial cells (King, 1993). During d 12 to 14, the wall of the conceptus rises and folds over the embryonic disc to form the amniochorionic fold, which is composed of an amniotic wall facing the embryo and a chorionic wall facing the endometrium (Marrable, 1971). From d 12 to 18 the yolk sac develops from the endoderm, and within the walls of the yolk sac the first batches of embryonic erythrocytes are differentiated before going into the circulation (Marrable, 1971).

Around d 14, the allantois grows as an extension of the hindgut and by d 18 it is twice the size of the embryo. At d 19 the allantois and the chorion fuse to form the chorioallantois, and by d 30 this structure is completely vascularized with vessels of allantoic origin (Friess et al., 1980). The process of attachment is completed by d 24, and by d 30 the placenta is completely formed (Amoroso, 1952).

The areolae, structures specialized in the absorption of nutrients in the form of uterine secretions or histotrophe, first appear on d 30 of pregnancy and are formed by a corrugation of the chorioallantoic membrane over the uterine gland mouths (Friess et al., 1982). Although in early pregnancy each areola corresponds to a uterine gland, later in gestation they increase in size and number, and some fuse to cover multiple gland

openings (King, 1993). Embryonic membranes grow rapidly from 20 to 60 d of pregnancy, but their rate of growth declines thereafter to the point that at d 70 the placenta and embryo are equivalent in weight; from d 70 the placenta stabilizes its growth, but the fetus continues growing until birth (Marrable, 1971).

The process of placentation includes the establishment of blood vessels in the maternal and fetal tissues (Reynolds and Redmer, 2001). Around d 15 post estrus, the maternal endometrial vasculature network becomes distended and denser, and by d 32 the vasculature has developed a combination of countercurrent and crosscurrent feto-maternal circulation (Leiser and Dantzer, 1988; Dantzer and Winther, 2001). Angiogenesis is the development of new capillaries from existing vessels and occurs on the endometrium; in contrast, vasculogenesis occurs only in the conceptus and involves differentiation of mesenchymal cells into angioblasts (Sherer and Abulafia, 2001). The primary promoters of angiogenesis are vascular endothelial growth factor (VEGF), angiopoietin (ANG), acidic and basic fibroblast growth factors (FGF), and platelet-derived growth factors (PDGF); other promoters identified include transforming growth factors α and β (TGF-α and TGF- β), folliculostellate-derived growth factor, angiotropin, angiogenin and tumor necrosis factor α (TNF-α) (Breier, 2000; Sherer and Abulafia, 2001).

The VEGF family includes five members, placental growth factor (PlGF), and VEGF-A, -B, -C, and –D; this family exerts its functions through four receptors (neurophilin-1 and VEGFR-1, -2, and-3) (Korpelainen and Alitalo, 1998; Breier, 2000). The first one to be identified was VEGF-A which has at least five isoforms ($VEGF_{165}$ being the major one) derived from the same gene by alternative splicing (Breier, 2000).

The ANG system includes four angiopoietins (Ang-1, -2, -3, and -4) and two receptors (Tie-1 and -2) (Breier, 2000).

Expression of the VEGF gene is upregulated by hypoxia, several cytokines including epidermal growth factor and TGF- β, and growth factors such as insulin-like growth factor I (IGF-1) (Ferrara and Davis-Smyth, 1997; Ferrara, 2000). In the sheep, VEGF is upregulated 3- to 10- fold after estrogen treatment (Reynolds and Redmer, 2001). Endothelial cell proliferation, migration, tube formation, and increased vascular permeability, all important processes in angiogenesis, are induced by VEGF (Gille et al., 2001).

In swine, VEGF and its receptors VEGFR-1 and VEGFR-2, have been localized in the trophoblast and uterine luminal epithelium through gestation (Winther et al., 1999). From d 70 to 90 of pregnancy, VEGF gene expression increased in association with increased blood vessel density in two groups of pigs reportedly selected for four generations for divergent placental efficiency, and although there were no line differences in the mRNA level of VEGF and VEFGR-1 at d 70, by d 90 placentas of the high line expressed higher levels of these two genes (Vonnahme and Ford, 2003). Similarly, at d 90 of pregnancy Meishan conceptuses have higher VEGF concentrations in fetal blood and allantoic fluid than Yorkshire conceptuses, and these levels remain higher in Meishan conceptuses in fetal blood but not allantoic fluid at d 110 (Vonnahme and Ford, 2004).

Placental factors influencing fetal growth

From a physiological perspective, the efficiency of the placenta can be described in terms of each of the functions of this organ. We could consider how efficiently the placenta produces hormones or serves as an exchange organ of gases, nutrients and metabolites.

Endocrine activity is represented by the synthesis and secretion of a number of hormones, growth factors, cytokines, and other bioactive molecules (Anthony et al., 1995). Estrogen is the major hormone produced by the porcine placenta. It is essential for establishment of pregnancy and increases the expression of angiogenic and growth factors necessary for development (Spencer and Bazer, 2004). Among these products, growth hormone and insulin-like growth factors are recognized by their positive effects on fetal growth (Owens, 1991; Sterle et al., 1995; Zumkeller, 2000). The concentration of IGF in the fetus is positively correlated to birth weight in several species. In swine, fetal plasma concentrations are ten times higher for IGF-II than IGF-I in prenatal life, but after birth the prevalence of these growth factors is shifted (Fowden, 2003).

Insulin-like growth factors I and II are both required for normal embryo development in the mouse (Allan et al., 2001). In mice the *Igf2* gene is imprinted and expressed only from the paternal allele in placental tissues. This imprinting is regulated by the *H19* gene, also imprinted and developmentally regulated (Fowden, 2003). A mouse model lacking a transcript of the *Igf2* gene in the labyrinthine trophoblast, the major site of feto-maternal exchange, suffers from reduced placental growth followed by fetal growth restriction. Active amino acid transport is initially upregulated to compensate for the decreased passive permeability to nutrients of the placenta, but the

compensation then fails causing fetal growth retardation (Constancia et al., 2002). Also as a compensatory mechanism, the size of the placenta is increased relative to the size of the fetus in these mutant mice; however, both fetus and placenta are lighter than in wild types indicating that IGF-II influences placental size and function (Fowden, 2003).

Intrauterine growth retardation (IUGR) in humans is a common obstetric disorder that has effects on postnatal growth and health in adulthood. Intrauterine growth retardation can be caused by maternal illness or malnutrition, but in a large proportion of cases is caused by uteroplacental insufficiency (Wang et al., 2003). Pregnancy-associated plasma protein-A (PAPP-A) acts as a protease on IGF binding proteins and increases the growth stimulation effects of IGF. Pregnancy-associated plasma protein-A levels at 8 to 12 wk of gestation were positively associated with birth weight at 38 to 41 wk of gestation (Smith et al., 2002).

Exchange properties:

Several factors influence the efficiency of placental transport: placental surface area, uterine and umbilical blood flow, permeability of the barrier, carrier system, placental metabolism, and transplacental gradient (Schneider, 1991).

Although barrier thickness and surface area influence diffusion of substances across the placenta, the feto:placental ratio is not correlated with the number of tissue layers separating the maternal and fetal blood (Leiser and Kauffmann, 1994). What this means is that those species with more layers separating fetal and maternal blood compensate for the lower transfer efficiency by increasing blood flow, the surface area, the intimacy of the contact (from folded to labyrinthine placentas), or all of these elements.

Knight et al. (1977) found that fetal weight in swine was highly dependent on placental traits such as placental length, surface area, total areolae surface, and weight (r = 0.64, 0.72, 0.65, and 0.74, respectively); whereas placental weight alone as a predictor of fetal weight was as good as any combination of the other placental variables measured. Placental surface area is positively correlated with placental weight (Biensen et al., 1998). When the chorioallantois is separated from the endometrium and its non-permanent folds are elongated, the length of the chorioallantois was found to be 4.2 times that of the corresponding endometrium at d 51, 4.5 times at d 63, and 2.7 times at d 100 (Dantzer, 1984).

Endometrial microvascular density increases three- to five-fold in the ewe from day 11 to 30 after mating and continues increasing through gestation (Reynolds and Redmer, 1995). In the pig, differences in endometrial vascularity are associated with breed differences in prolificacy (Biensen et al., 1999).

In the case of respiratory gases, glucose, and water, the blood flow rate and the nature of the membrane are the limiting factors (Schneider, 1991). The less efficient synepitheliochorial (ruminants) or epitheliochorial (pigs) placentas are compensated in their lower exchange ability by corresponding increases in uterine blood flow to supply each feto-placental unit (FPU). For example, uterine blood flow is 0.16 $L \cdot min^{-1} \cdot kg^{-1}$ of FPU in guinea pigs (hemochorial placenta), while it is 0.30 and 0.34 $L \cdot min^{-1} \cdot kg^{-1}$ in the pig and cow, respectively (Père and Etienne, 2000).

At mid-gestation in sheep and cows, the placenta is only half the weight of the fetus but consumes more than 80% of the oxygen and glucose taken by the uterus. In late gestation the fetus is about four times the weight of the placenta, but the latter still

consumes 40 to 60% of these substrates (Owens, 1991). Even though the placenta uses nutrients largely to support its function, at the time of fast fetal growth the placenta can compete with the fetus for nutrients such as amino acids (Owens, 1991).

In theory, the best estimate of placental efficiency should be an actual measurement of the rate at which a compound of interest is transported across the placenta. But considering that this organ will compensate deficiencies in one aspect of transport by improving others to ensure the survival of the fetus, the weight ratio of the fetus to its placenta has meaningful biological significance. In this sense, the weight ratio could be considered a biological index reflecting all elements involved in the exchange of substances. Using this ratio, comparisons can be made across and within species of relative placental efficiencies; this would indicate that the placental design of the rodents and lagomorphs (hemochorial, labyrinthine, countercurrent flow) is the most efficient design. This view is supported by the high fetal to placental weight ratios observed (up to 20:1) when compared to other species (Leiser and Kauffmann, 1994).

Uterine factors influencing fetal growth

The number of live fetuses is limited by uterine length as uterine horns reach their maximum capacity. Under crowded conditions, each surviving fetus at d 50 was associated with 36 cm of initial uterine length (Wu et al., 1987). Each additional centimeter occupied by a fetus at d 28 increased its probability to survive to d 100 by 1.5% (Lamberson and Eckardt, 1996). Space restrictions are made evident by the presence of mummified fetuses. The frequency of mummies is not different between litters with less than nine and with more than 10 piglets at wk 7, but during wk 7 and 15 of gestation, the frequency of mummies in the former group stays constant at 1%, while

in the latter increases linearly with time from 1 to 12% (Wu et al., 1988). The amount of uterus available at implantation determines survival in the fetal period because space vacated by dead fetuses is not occupied by surviving littermates (Dziuk, 1985; Lamberson and Eckardt, 1996) and the uterus cannot increase in length beyond 50% of its size at d 3 (Chen and Dziuk, 1993).

Uterine lymphocytes of the natural killer (NK) lineage are speculated to serve a role in vascularization and the communication between the trophoblast and the maternal immune system during early placental development (Engelhardt and King, 1996; Engelhardt et al., 2002). During d 10 to 20 of pregnancy in swine, large numbers of NK cells are recruited to the endometrium, but NK activity decreases again around d 30 (Whitelaw and Croy, 1996). This recruitment is highly specific and dependent on the presence of a conceptus. Leukocyte concentration is three-fold greater in endometrium in contact with a conceptus than in endometrium between attachment sites (Engelhardt et al., 2002).

In sheep and pigs, endometrial gland hyperplasia and hypertrophy occur during gestation to provide the histotrophic support to the fetus, and this development is dependent on ovarian steroids and pregnancy recognition signals (Gray et al., 2001).

Endometrial protein secretion has been proposed as a factor influencing fetal survival. Specifically, scarcity of the substrates required for fetal erythropoiesis, such as uteroferrin produced by the endometrium, may contribute to the deleterious effects of crowding on fetal survival (Vallet, 2000). This hypothesis is based on the fact that the two periods of major mortality in crowded environments coincide with significant

changes in fetal erythropoiesis, namely initiation of fetal erythropoiesis at d 25, and drastic reductions in plasma levels of transferrin and uteroferrin after d 85.

Nutrient uptake by fetuses in the gravid uterus is increased more by increasing uterine blood flow than by increasing extraction efficiency by the placenta (Reynolds et al., 1985). In swine, the pattern of uterine blood flow is similar in cycling and pregnant females up to d11, but increases three- to four-fold on d 12 and 13 in pregnant females only. By d 14, blood flow decreases to levels slightly higher than d 11, remains relatively constant up to d19 and then increases from 0.15 $L \cdot min^{-1}$ at d 19 to 0.5 $L \cdot min^{-1}$ at d 30 (Ford and Christenson, 1979).

Increased blood flow to the uterus, associated with increased placental vascularity, is one of the mechanisms that allows adequate exchange of nutrients and metabolites at the feto-maternal interface during late pregnancy (Reynolds and Redmer, 1995). In normal swine pregnancies, uterine blood flow increases 2.3-fold from d 44 (1.21 $L \cdot min^{-1}$) to d 111 (2.84 $L \cdot min^{-1}$) (Père and Etienne, 2000). Variation in uterine blood flow is more closely related to litter weight or weight of the placentas ($r = 0.76$, $P < 0.001$) than to litter size ($r = 0.56$, $P < 0.05$) at d 111 of pregnancy in swine. This suggests that the total mass of the feto-placental units that can be supported is relatively fixed and helps explain why piglets from large litters are lighter at birth (Père and Etienne, 2000).

Uterine position has been reported to influence fetal weight. Heavier fetuses are found at the ovarian end, intermediate at the cervical end, and lighter in the middle (Perry and Rowell, 1969). A possible explanation of this effect is the hemodynamic theory, which states that arterial blood is supplied at higher pressures at terminal than intermediate sites because of the architecture of the maternal vasculature (Wootton et al.,

1977). Other studies found that heavier piglets at d 70 and 104 are at the ovarian ends of the uterus, while lighter pigs tend to occupy the cervical ends (Wise et al., 1997). Additionally, lightweight pigs within a litter have lower blood concentration of IGF-I, which suggests that endocrine components may also play a role in the uterine position effect (Wise et al., 1997). However, by using a uniform scale of fetal position, other authors found that no particular position in the uterine horn is associated with advantages in fetal growth (Ashworth et al., 2001).

Another type of uterine position effect has also been detected; when fetuses at d 104 are between two fetuses of the opposite sex they are lighter than when between fetuses of the same sex. This difference is not detectable at d 70 and is not related to placental weight, but may be linked to immune differences or endocrine effects (Wise and Christenson, 1992).

Fetal factors influencing fetal growth

Uterine capacity is influenced by the absolute demand for nutrients and the ability of the fetus to direct an increase in the supply of these nutrients, especially during the last half of gestation. There are inherent sex differences in nutritional demands. When supplied adequate amounts of uterine space males tend to be heavier than females at d 41, but in crowded environments females are heavier, and there is a tendency for a reduced number of males (Chen and Dziuk, 1993). They hypothesized that both the reduced sex ratio and the weight differences indicate that male fetuses have a greater demand for nutrients.

Genotype has also been showed to have an effect on prenatal development. Meishan fetuses have a reduced growth rate relative to western breed fetuses at all stages

of gestation, and this is likely to decrease the nutrient demands of Meishan fetuses (Christenson, 1993; Wilson et al., 1998). In crossbreeding experiments between Meishan and western breeds, the maternal genotype accounted for > 70% of individual weight variation at d 30 and 20 to 25% at birth (Ashworth et al., 2001). However, other crossbreeding experiments with Meishan and western breeds have showed that although uterine factors determine conceptus size, the conceptus genotype controls placental efficiency via increased vascularization and therefore can influence its growth rate in the last third of pregnancy (Biensen et al., 1999).

As already mentioned, birth weight, the end result of the prenatal development process, has a direct genetic component and a maternal genetic component. The maternal effect (maternal heritability) is much higher (h^2 = 0.15 to 0.20) than the direct effect (h^2 = 0.04), and the genetic correlation between both effects is on average 0.33 (Grandinson et al., 2002; Knol et al., 2002). Even though piglet survival at farrowing and at weaning increase with increasing individual birth weights, litters with high genetic merit for survival tend to have a lower average birth weight (Leenhouwers et al., 2002b). Simultaneously, litters with high genetic merit for survival have higher serum cortisol levels, heavier adrenal glands, and higher levels of liver and muscle glycogen. Higher glycogen levels are completely due to the higher cortisol levels, implying that developmental maturity at birth results in piglets with a better ability to survive at farrowing and during the early postnatal period (Leenhouwers et al., 2002b).

CHAPTER III

SELECTION FOR PLACENTAL EFFICIENCY IN SWINE: GENETIC PARAMETERS AND TRENDS

ABSTRACT

Genetic trends and genetic parameters were estimated for individual and litter traits by using data from four generations of replicated divergent selection on an index of reproductive traits. The selection index **(SI)** included total born **(TB)**, birth weight **(BW)** and placental weight **(PW)** and was designed to increase **(H** line) or decrease (**L** line) the efficiency of the placental function **(PE)**, defined as the ratio BW:PW. (Co)variance components were estimated for direct and maternal additive effects by using an animal model with MTDFREML procedures. Estimated breeding values (**EBV**) were calculated by using records on individual BW (n = 2111), PW (n = 2006), PE (n = 1677), and SI (n = 1677). Litter traits were evaluated using records on 193 litters. The model included the fixed effects of contemporary group for all traits, with the addition of sex for individual traits and parity for litter traits. Litter was fitted as an uncorrelated random effect for all traits, and TB was used as a linear and quadratic covariate for BW, PW, and PE. Direct heritability estimates from single-trait models were 0.03, 0.25, 0.18, 0.11 and 0.08 for BW,

PW, PE, SI, and TB, respectively. Estimated breeding values were compared between lines by using a model including generation, line within generation, and replicate within line as the error term. Genetic divergence was 20.7 ± 2.7 g, 0.24 ± 0.03, 0.11 ± 0.02, and 0.07 ± 0.02 per generation for PW, PE, SI, and TB respectively ($P < 0.01$), but not significant for BW. At generation four, direct EBV was higher in L than H for PW (55.9 ± 8.7 g vs. -24.2 ± 9.5 g, respectively; $P < 0.01$), was higher in H than L for PE (0.58 ± 0.10 vs. -0.35 ± 0.09, respectively; $P < 0.01$), and were not different for BW, SI or TB. These results indicate that placental weight and efficiency are susceptible to change by genetic selection. However, the correlated response in litter size was an unexpected genetic trend towards a higher litter size in the L line of 0.05 ± 0.01 piglets per generation ($P < 0.01$).

Introduction

Uterine capacity, defined as the maximum number of fetuses a female can carry to term, may be a factor limiting litter size in many swine populations (Bennett and Leymaster, 1989). Studies of the reproductive physiology of the highly prolific Meishan breed suggest that increasing the ratio of piglet weight to its placenta weight (placental efficiency) could be an effective way of increasing uterine capacity, and therefore litter size, in commercial breeds. Divergent selection for placental efficiency resulted in an extraordinary response in litter size after one generation (Wilson et al., 1999), but the small size of the lines used in that study leaves open the possibility that the effect was the result of genetic drift and will not be reproducible in larger populations.

Selection for reproductive components has successfully increased the number of fully formed piglets, but the correlated reduction in piglet birth weight may be responsible for the smaller response in number born alive, the increased number of

stillborn piglets, and the higher preweaning mortality (Johnson et al., 1999). Placental weight and efficiency were subsequently evaluated in this population (Mesa et al., 2003). Placental weight also decreased as a correlated response to increased litter size and, unexpectedly, placental efficiency was higher in the control line. Thus litter size had increased in the selected line by mechanisms other than improved placental efficiency.

An index was chosen as the selection criterion because it has been shown that selection for a trait defined as a ratio of two positively correlated component traits puts unequal pressure on the components, while selection on a linear index places predetermined selection pressure on the component traits (Gunsett, 1984). The objective of the present study was to estimate the response to selection for a linear index designed to alter placental efficiency, and to evaluate the effect of placental efficiency on litter size in swine.

Materials and Methods

Divergent selection for an index of reproductive traits was applied to a population derived from the University of Missouri Duroc x Landrace-Yorkshire rotational crossbred herd. The base population was composed of litters from 20 sows (ranging in parity from two to nine) in each of two farrowing groups (replicates) separated by one month. Number of fully formed piglets **(TB)**, and individual birth **(BW)** and placental weight **(PW)** were recorded and this information used to construct a selection index **(SI)**. Within each replicate the 24 highest and lowest indexing female progeny and the seven highest and lowest indexing male progeny were chosen to create divergent lines with either high or low placental efficiency, respectively. This selection scheme was continued within replicate in the upward **(H)** and the downward **(L)** selected lines for high and low index

values, respectively. To facilitate data collection each farrowing group was limited to a seven-day period. Generation interval was one year, and females produced only one litter. Due to the limitation imposed on the breeding season, death losses, inexperienced and immature sires, and female infertility, line sizes were smaller than planned. Number of parents per line and generation are presented in Table 1.

At birth, to match each piglet to its placenta, the umbilical cord of each fully formed piglet was double tagged with identically numbered mouse ear tags (Gey Band & Tag Co. Norristown, PA). One tag was placed approximately 10 cm from the piglet and the umbilical cord severed so the first tag retracted into the birth canal with the cord stump. The second tag was placed on the piglet's umbilical cord stump approximately 5 cm from the abdomen. Piglets were weighed immediately after birth, before suckling began, and all placentas were collected and individually weighed at delivery.

All piglets were processed and ear notched within 24 hours of farrowing. Fostering was minimal. Piglets were weaned when the oldest litter was 21 d old and maintained in environmentally controlled nursery facilities. At five mo of age, pigs were transferred to a modified open front building (generation 0), pasture lots (generation 1), or dirt lots (generations 2 and 3) until a new breeding cycle began. Animals were fed a corn-soybean meal based diet formulated to meet or exceed the nutritional requirements at every stage (N.R.C., 1998). Management of animals at all stages was done in accordance with approved procedures at the University of Missouri South Farm Swine Pasture Unit (MUIACUC protocol # 3198).

For detection of estrus, beginning at 160 d of age gilts were exposed to direct contact with a mature, intact boar for 10 min daily. After at least 75% of gilts had

expressed their first estrus, a breeding period of 2 wk was initiated with the intention of synchronizing estrous cycles. Synchronization was accomplished with two i.m. injections of 10 mg of dinoprost (Lutalyse, Pharmacia and Upjohn Co., Kalamazoo, MI; 5 mg/mL), given 12 h apart to pregnant females 14 d after finalization of the breeding period.

After synchronization of estrus, detection of estrus was resumed once daily and females were inseminated with fresh diluted semen (3×10^9 cells per dose) from males in the same line and replicate, avoiding half- and full-sibling mating. Females were bred 12 and 24 h after the first signs of behavioral estrus. At 107 d of pregnancy, females were transferred to the Animal Sciences Research Center farrowing facility where parturition was supervised 24 h per day. In the morning of the fifth day of the seven-day farrowing period, parturition was induced in remaining females with the same protocol used for synchronization of estrus.

The selection index included the size of the litter in which the piglet was born, BW and PW adjusted for differences in litter size and gestation length, and parity number in the base population. The index was constructed using the information obtained from the first 20 litters in the base population. With the objective of giving each component equal weight, each trait was divided by its standard deviation to remove the effect of the units used and the inherent differences in variability. Litter size was further adjusted to take into account that its heritability was estimated to be half that of the other two traits and that individual selection for litter size using the dam's record halves the selection differential. The aim of the index was to obtain bigger litters, with heavier piglets sustained by smaller (i.e. more efficient) placentas in the H line and the opposite in the L line.

The selection index was calculated as:

$$\textbf{Index} = (0.25*TB)/\sigma_{TB} + BW/\sigma_{BW} - PW/\sigma_{PW}$$

The resulting index was:

$$\textbf{Index} = 0.073(TB) + 0.003(BW) - 0.012(PW).$$

The only selection criterion in generations 0 and 1 was the high or low selection index value. To avoid selection of runts in subsequent generations, piglets weighing less than one-third of their litter average and less than 1,000 g were culled. Four individuals from H and one from L were culled in generation 2, while seven from H and nine from L were culled in generation 3.

(Co)variance components were estimated for direct and maternal additive effects by using an animal model with MTDFREML procedures (Boldman et al., 1993). The pedigree file represented seven generations including 2,236 individuals. Estimated breeding values (**EBV**) were calculated for individual BW, PW, PE, and SI. Litter traits were considered a trait of the dam. The model included the fixed effects of contemporary group (all animals born within a week) for all traits, with the addition of sex for individual traits or parity for litter traits. Litter was fitted as an uncorrelated random effect for all traits, and TB was used as a linear and quadratic covariate for BW, PW, and PE.

Data were collected on piglets from 193 litters with the number of individual observations as follows: BW = 2111, PW = 2006, PE = 1677, and SI = 1677. Analyses were performed to identify line differences on litter traits including total number born (**TB**), number born alive **(NBA),** number of mummified fetuses **(NMF),** number weaned

(NW), number stillborn **(NSB)**, litter birth weight **(LBW)**, litter placental weight **(LPW)**, and preweaning survival **(SURV)** calculated as (NW/NBA)*100.

Statistical analyses were performed using the GLM procedure of SAS (SAS Inst. Inc., Cary, NC). The model used to test line effects for both the phenotypes and the breeding values included the effects of generation, line nested within generation, and replicate nested within line. Replicate within line was used as the error term. Genetic trends were estimated by regression of the line-generation least-squares mean EBV on generation number.

Results

Reported least-squares means are the combination of two replicates within each line. Inbreeding accumulated at a rate of 0.042 ± 0.005 per generation and was not significantly different between lines. Line least-squares phenotypic means are plotted by generation in Figure 1. Line differences were not significant at any generation for BW or SI. Similarly, line differences were not significant between lines at any generation for TB, NBA, NSB, NMF, NW, SURV, or LBW (11.0 ± 0.2, 10.6 ± 0.2, 0.6 ± 0.1, 0.8 ± 0.1, 9.7 ± 0.2, 90.5 ± 1.0 %, and 15.26 ± 0.27 kg, respectively).

At generation four, placental weight was lower in H than L (274.8 ± 9.2 vs. 333.1 ± 8.7 g, respectively; $P < 0.05$), placental efficiency tended to be higher in H than L (5.3 ± 0.2 vs. 4.7 ± 0.1, respectively; $P < 0.10$), and litter placental weight tended to be lower in H than L (2.13 ± 0.21 vs. 2.86 ± 0.20 kg, respectively; $P < 0.10$).

Variance component estimates from single-trait analyses are presented in Tables 2 and 3. Direct heritability estimates from single-trait models were 0.03, 0.25, 0.18, 0.11 and

0.08 for BW, PW, PE, SI, and TB, respectively. Maternal heritability estimates were 0.13, 0.09, 0.03, 0.00 and 0.07 for BW, PW, PE, SI, and TB, respectively.

Direct and maternal genetic correlation estimates from two-trait analyses are presented in Table 4. Two-trait analyses involving litter size represent the correlation between a dam's individual traits and the litter size it subsequently produced. The direct additive correlations of TB with BW, PE, and SI were -0.33, -0.63, and -0.18, respectively. Phenotypic correlations were 0.61 between BW and PW, 0.09 between BW and PE, and 0.29 between BW and SI ($P < 0.001$). Phenotypic correlations were -0.67 between PW and PE, and -0.56 between PW and SI ($P < 0.001$). The phenotypic correlation between PE and SI was 0.86 ($P < 0.001$). None of the phenotypic correlations between a sow's individual traits and the litter it produced were significantly different from zero.

Least-squares mean EBV by line for individual traits are plotted against generation in Figure 2. Genetic divergence trends were 20.7 ± 2.7 g, 0.24 ± 0.03, and 0.11 ± 0.02 per generation for PW, PE and SI, respectively ($P < 0.01$), but not significant for BW. Least-squares mean EBV by line for litter traits are plotted against generation in Figure 3. Among litter traits, genetic divergence was 24.0 ± 5.8 g, 16.7 ± 2.1 g, 0.07 ± 0.02, and 0.06 ± 0.02 per generation for LBW, LPW, TB and NBA, respectively ($P < 0.01$), but not significant for NSB, NMF, NW, or SURV. Regression coefficients of least-squares mean EBV on generation for each line are presented in Table 5.

At generation four, direct EBV was higher in L than H for PW (56.5 ± 8.2 g vs. -24.6 ± 8.8 g, respectively; $P < 0.01$), was higher in H than L for PE (0.57 ± 0.09 vs. -0.35 ± 0.08, respectively; $P < 0.01$), and was not different for BW, SI or TB.

Discussion

This study's direct heritability estimate for total born (0.08) agrees well with the value of 0.10 previously reported in the literature (Lamberson, 1990), but is somewhat lower than those ranging from 0.13 to 0.18 in other studies (Southwood and Kennedy, 1991; See et al., 1993; Johnson et al., 1999; Ruíz-Flores and Johnson, 2001). Similarly, the heritability estimate for number born alive (0.08) is similar to the 0.10 reported for U.S. breeds (Chen et al., 2003), but is lower than the 0.13 to 0.17 reported elsewhere (Southwood and Kennedy, 1991; See et al., 1993; Irgang et al., 1994; Johnson et al., 1999). Maternal heritability in this study for number born alive (0.08) is higher than the 0.03 to 0.05 reported for other populations, where the maternal effect is at most one-third of the direct effect (Southwood and Kennedy, 1991; See et al., 1993; Irgang et al., 1994). In contrast, in this study the heritability of the direct and maternal effects were of the same magnitude.

This study's direct and maternal heritability estimates for number of weaned piglets (0.03 and 0.02, respectively) are considerably smaller than the 0.09 to 0.12 and 0.04 to 0.08, respectively, obtained from Yorkshire and Landrace crossbred gilts (Southwood and Kennedy, 1990). The heritability estimate for number of stillborn (0.08) is lower than the 0.17 obtained from a population under long-term selection for litter size, while this study's heritability estimate for number of mummified fetuses (0.10) was similar to the 0.12 obtained in that population (Johnson et al., 1999)

In this study, estimates of variance components for individual birth weight are adjusted for total number born. The direct and maternal heritabilities (0.03 and 0.13, respectively) are lower than comparable estimates reported for German pigs (0.08 and

0.22, respectively); on the other hand, our estimate for litter effect (0.18) is higher than the reported 0.09 (Roehe, 1999). Our heritability estimate for litter birth weight (0.08), unadjusted for litter size, agrees with that reported by Roehe (1999), but is lower than the 0.32 from a selection experiment for litter size (Johnson et al., 1999). This study's heritability estimates for BW, PW and PE (0.03, 0.25, and 0.18, respectively) are similar in magnitude to the 0.05, 0.18, and 0.29, respectively, obtained from pigs selected for ovulation rate or uterine capacity (Vallet et al., 2001). Similarly, when birth weight heritability was estimated by using a direct-maternal animal model, this study's estimates (0.03 and 0.13 direct and maternal, respectively) are very close to those obtained with European pigs (Grandinson et al., 2002; Knol et al., 2002).

Heritability of preweaning survival, a trait of the dam, was low in our study (0.05), agreeing with results obtained in other populations (Lamberson and Johnson, 1984; Knol et al., 2002). This suggests that direct selection for preweaning survival is unlikely to be effective.

In this experiment, selection for a linear index of litter size, birth weight, and placental weight was effective in changing placental weight and efficiency in the desired direction. Despite the difference in PE being larger in the present study than in that of Wilson et al. (1999), we did not detect a significant phenotypic difference in litter size, and the genetic trend was in the wrong direction. The genetic divergence trend observed was 0.07 and 0.06 piglets per generation for total born and born alive, respectively, in favor of the line with lower placental efficiency, which agrees with the negative sign on the genetic correlation between litter size and placental efficiency. The observed genetic trend agrees with the lower placental efficiency observed in a line with higher litter size

relative to its control (Mesa et al., 2003). Interestingly, in an evaluation of a line selected for increased uterine capacity, placental efficiency was not different from the control line, but was lower than in a line selected for increased ovulation rate (Vallet et al., 2001). If placental efficiency is in fact a key component of the increased fetal survival and uterine capacity observed in the prolific Meishan pig, all these results suggest that the positive association between placental efficiency and litter size does not hold in western breeds.

The selection index was designed to allow more space in the uterus by decreasing placental size while not allowing the unfavorable changes in BW that have been reported to accompany effective selection for increased litter size. The goal of minimizing the reduction that naturally occurs when litter size increases is justified by the need to avoid the undesired effects that reduced birth weight would have on postnatal survival (Johnson et al., 1999; Quiniou et al., 2002).

The lack of an unselected control line in this experiment makes the evaluation of asymmetry of response difficult. Nevertheless, a between lines comparison of genetic trends can still have value. The genetic trend for placental weight was 2.6 times greater in the L than the H line. Similarly, the genetic trend for placental efficiency was 1.6 times greater in the L line. Considering that birth weight was not different between lines, the asymmetry of the response suggests a lower limit in placental weight after which fetal survival may be compromised, and in this way explains the unfavorable trend in litter size observed.

Even though litter size has the biggest impact on the economic efficiency of the swine industry, problems associated with other reproductive traits, such as weak estrus symptoms and high piglet mortality, should be kept in mind when setting goals for long-

term selection programs (Rydhmer, 2000). It should be remembered that after the number of piglets born alive, preweaning viability has the highest impact upon economic efficiency (Legault, 1983; Tess et al., 1983). The direct and maternal genetic variability observed for birth weight suggest that selection schemes for increased litter size can be designed to control reduction in birth weight and consequently improve piglet survival to weaning.

Selection for increased litter size has been effective, but the process requires complicated surgical procedures to measure components of litter size such as ovulation rate, embryo survival, and uterine capacity (Christenson et al., 1987; Johnson et al., 1999). These approaches are possible in the academic field, but in practice are not desirable or cost effective (Webb, 1998). Other successful selection systems, such as the hyperprolific scheme (Bidanel et al., 1994), require big centralized sets of performance records and are difficult to implement. In addition, the success of increasing litter size is associated with an increase in the number of stillborns to the point that only half of the response obtained in an experiment was represented by live pigs (Johnson et al., 1999). The increased time from beginning to end of parturition in large litters may be the cause of the increased number of stillborn piglets (Johnson et al., 1999). The selection procedure used in the present experiment could alleviate the negative environmental effect on piglet survival because it requires the constant presence of a technician during parturition. This person can supervise farrowing and increase the probability of survival of small and weak piglets. In this experiment, 3.5% of the pigs were stillborn. This proportion differs significantly from the 7% average observed in first parity gilts from the

Maternal Line National Genetic Evaluation Program (Moeller et al., 2004) and the 8.2% (mummies plus stillborn) of the NAHMS survey of commercial farms (USDA, 2002).

The complexity of the interactions among the component traits of litter size makes the manipulation of this trait difficult. According to the current understanding of the physiology of litter size, this trait will increase only when the most limiting of its components is enhanced (Bennett and Leymaster, 1989; 1990a; 1990b). Comparison of the results of the present experiment and the literature available on the Meishan breed and other selection experiments leads to the conclusion that in any specific population, prolificacy can be increased, but through different physiological mechanisms. Additional comparisons of litter size components (including ovulation rate, embryo survival, uterine capacity, and placental efficiency) in those populations would allow a better understanding of their relationships.

Fetal development and survival are ultimately dependent on the transfer of nutrients and removal of waste materials through the placenta. A possible explanation for the negative genetic correlation between placental efficiency and litter size found in this study is that, without compensatory increases in physiologically relevant traits for placental function, a reduction in placental weight compromises fetal survival. This type of compensatory increase has been shown in the Meishan breed, where placental vascularity increases in the last third of pregnancy to allow survival of the fetus (Biensen et al., 1999). If these compensatory mechanisms do not exist in western breeds, attempts to increase litter size must focus on traits relevant to uterine capacity. Relevant traits that merit attention include fetal erythropoiesis, endometrial gland function, placental

hormone secretion, and placental vascularity (Vallet and Christenson, 1993; Pearson et al., 1998; Vallet, 2000; Kim et al., 2001).

Based on the negative direct genetic correlation between litter size and placental efficiency found in this experiment, it seems unlikely that litter size can be increased as a correlated response to higher placental efficiency. However, it would be interesting to investigate if a population expressing high placental efficiency can be successfully utilized in crosses with lines in which uterine capacity is limiting. Alternatively, selection for an index of litter size, birth weight, and placental weight can be a valuable tool to use in populations where preweaning viability can be potentially increased by selecting for heavier piglets.

Implications

Previous experiments that have effectively increased litter size have not yielded maximum benefits because of low birth weight and increased perinatal and preweaning mortality. There is little evidence that selection for improved placental efficiency will increase litter size. Use of birth weight and placental weight in combination with increased litter size may a yield response in litter size with less compromise in birth weight and preweaning survival.

Table 1. Number of parents per line and generation

Generation	Line	Number of Females	Number of Males
0	Base Population	40	10
1	High line	24	7
	Low line	25	11
2	High line	24	10
	Low line	13	6
3	High line	22	7
	Low line	17	7
4	High line	13	5
	Low line	15	5

Table 2. Estimates of (co)variance components and genetic parameters with standard errors (se[#]) from single-trait models for individual birth weight, placental weight, placental efficiency, and selection index, and litter birth and placental weight produced by the dam

Parameter*	Birth weight, g	Placental weight, g	Placental efficiency, ratio	Selection Index	Litter birth weight, kg	Litter placental weight, kg
σ^2_a	2593.9	2336.2	0.28	0.10	1.06	0.06
σ^2_m	12931.9	799.0	0.05	0.00	1.97	0.19
σ_{am}	-1911.2	-700.5	-0.12	-0.02	-1.45	-0.06
σ^2_l	16890.8	1572.5	0.19	0.15	3.46	0.00
σ^2_e	65578.7	5329.0	1.17	0.71	9.51	0.79
σ^2_p	84446.1	9336.1	1.57	0.94	14.56	0.98
h^2_a	0.03 (0.09)	0.25 (0.12)	0.18 (0.08)	0.11 (0.07)	0.07 (0.37)	0.06 (0.27)
h^2_m	0.13 (0.10)	0.09 (0.08)	0.03 (0.05)	0.00 (0.05)	0.14 (0.32)	0.19 (0.29)
r_{am}	-0.33 (0.85)	-0.51 (0.34)	-1.00 (0.44)	-1.00 (#)	-1.00 (1.00)	-0.53 (0.92)
l^2	0.18 (0.06)	0.17 (0.05)	0.12 (0.03)	0.16 (0.04)	0.24 (0.22)	0.00 (0.20)
e^2	0.68 (0.06)	0.57 (0.08)	0.74 (0.06)	0.75 (0.05)	0.65 (0.23)	0.80 (0.18)
Mean	1389.5	304.8	4.90	1.83	14.80	2.62
SD	334.2	99.3	1.27	0.98	4.08	1.01

*$\boldsymbol{\sigma^2_a}$=additive variance, $\boldsymbol{\sigma^2_m}$=maternal variance, $\boldsymbol{\sigma_{am}}$=covariance between additive and maternal effects, $\boldsymbol{\sigma^2_l}$=variance of litter effect, $\boldsymbol{\sigma^2_e}$=environmental variance, $\boldsymbol{\sigma^2_p}$=phenotypic variance, $\boldsymbol{h^2_a}$=additive heritability (se), $\boldsymbol{h^2_m}$=maternal heritability (se), $\boldsymbol{r_{am}}$=correlation between additive and maternal genetic effects (se), $\boldsymbol{l^2}$=proportion of phenotypic variance due to litter effect (se), $\boldsymbol{e^2}$=proportion of phenotypic variance due to environmental effects (se), **SD**=standard deviation, [#]Standard error estimate > 1.0

Table 3. Estimates of (co)variance components and genetic parameters with standard errors (se[#]) from single-trait models for litter traits

Parameter*	Total number born	Number born alive	Number Stillborn	Number Mummies	Number Weaned	Preweaning survival, %
σ^2_a	0.93	1.07	0.11	0.16	0.29	8.85
σ^2_m	0.91	0.96	0.08	0.19	0.17	3.91
σ_{am}	0.92	1.01	-0.09	0.17	0.22	5.88
σ^2_l	1.25	1.52	0.00	0.00	0.80	0.00
σ^2_e	8.17	8.24	1.21	1.09	8.18	161.98
σ^2_p	12.17	12.80	1.31	1.63	9.66	180.63
h^2_a	0.08 (0.30)	0.08 (0.35)	0.08 (0.38)	0.10 (0.39)	0.03 (0.29)	0.05 (0.30)
h^2_m	0.07 (0.35)	0.08 (0.35)	0.06 (0.28)	0.12 (0.29)	0.02 (0.27)	0.02 (0.27)
r_{am}	1.00 (#)	1.00 (#)	-1.00 (#)	1.00 (#)	1.00 (#)	1.00 (#)
l^2	0.10 (0.22)	0.12 (0.21)	0.00 (0.21)	0.00 (0.19)	0.08 (0.18)	0.00 (0.20)
e^2	0.67 (0.20)	0.64 (0.23)	0.93 (0.24)	0.67 (0.26)	0.85 (0.19)	0.90 (0.20)
Mean	11.03	10.61	0.59	0.81	9.62	90.40
SD	3.27	3.34	1.12	1.19	3.25	14.15

* $\boldsymbol{\sigma^2_a}$=additive variance, $\boldsymbol{\sigma^2_m}$=maternal variance, $\boldsymbol{\sigma_{am}}$=covariance between additive and maternal effects, $\boldsymbol{\sigma^2_l}$=variance of litter effect, $\boldsymbol{\sigma^2_e}$=environmental variance, $\boldsymbol{\sigma^2_p}$=phenotypic variance, $\boldsymbol{h^2_a}$=additive heritability (se), $\boldsymbol{h^2_m}$=maternal heritability (se), $\boldsymbol{r_{am}}$=correlation between additive and maternal genetic effects (se), $\boldsymbol{l^2}$=proportion of phenotypic variance due to litter effect (se), $\boldsymbol{e^2}$=proportion of phenotypic variance due to environmental effects (se), **SD**=standard deviation.

Standard error estimate > 1.0

Table 4. Estimates of direct [a] and maternal [b] genetic correlations and standard errors (se[#]) from two-trait analyses

	Birth weight	Placental weight	Placental efficiency	Selection Index	Litter size
Birth weight		0.96 (0.69)	-0.66 (0.35)	-0.76 (#)	-0.28 (#)
Placental weight	0.60 (0.60)		-0.89 (0.15)	-0.55 (#)	-0.98 (#)
Placental efficiency	0.06 (0.57)	-0.95 (0.07)		0.91 (0.21)	-0.12 (#)
Selection Index	-0.71 (0.62)	-0.87 (0.24)	0.96 (0.08)		-0.56 (#)
Litter size	-0.33 (#)	-1.0 (#)	-0.63 (#)	-0.18 (#)	

[a] Below the diagonal. [b] Above the diagonal. [#] Standard error estimate > 1.0

Table 5. Coefficients (b) and standard errors (se) of regression of mean breeding value on generation for individual and litter traits

Trait	High line b (se)	Low line b (se)	P-value for divergence
Birth weight, g	2.4 (0.4)	2.3 (0.4)	0.91
Placental weight, g	-5.8 (0.8)	14.9 (2.5)	<0.001
Placental efficiency, ratio	0.14 (0.004)	-0.09 (0.03)	<0.001
Selection Index	0.08 (0.002)	-0.04 (0.02)	0.003
Total born, piglets	-0.02 (0.02)	0.05 (0.01)	<0.01
Born alive, piglets	-0.01 (0.02)	0.05 (0.01)	0.02
Litter birth weight, g	26.3 (3.8)	2.3 (4.3)	<0.01
Litter placental weight, g	-6.37 (2.0)	10.3 (0.7)	<0.001

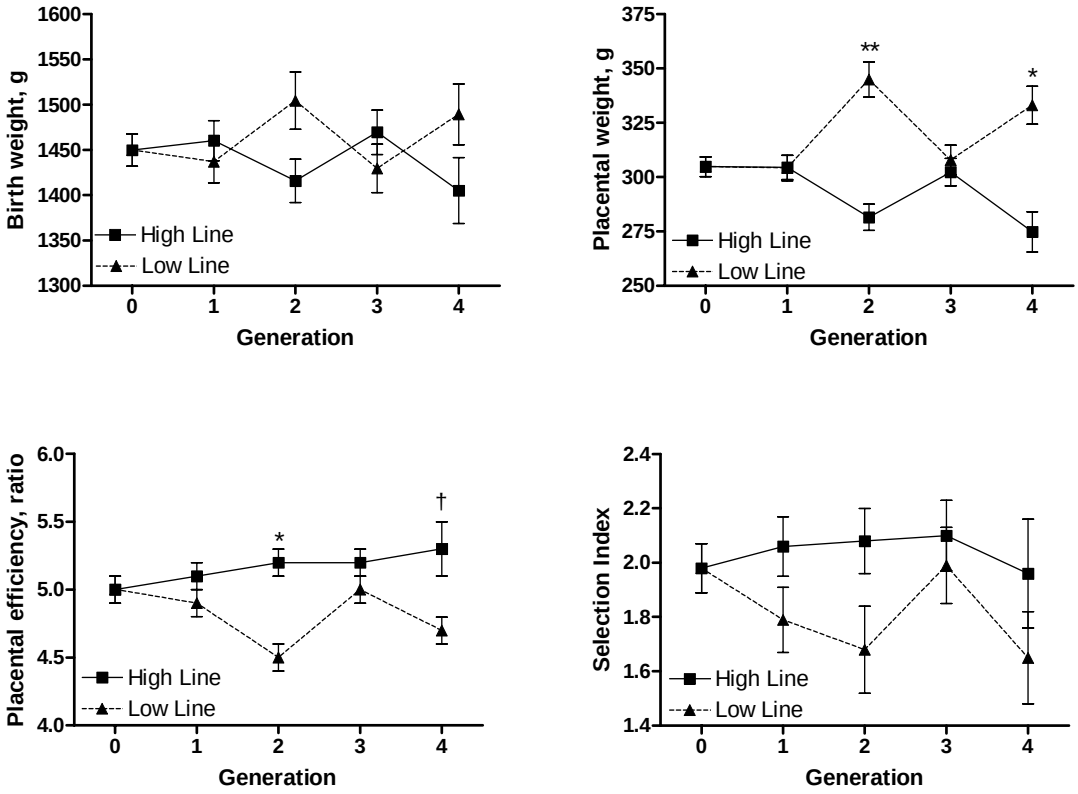

Figure 1. Line phenotypic least-squares means plotted by generation for birth weight, placental weight, placental efficiency, and the selection index.
** $P < 0.01$, * $P < 0.05$, † $P < 0.10$

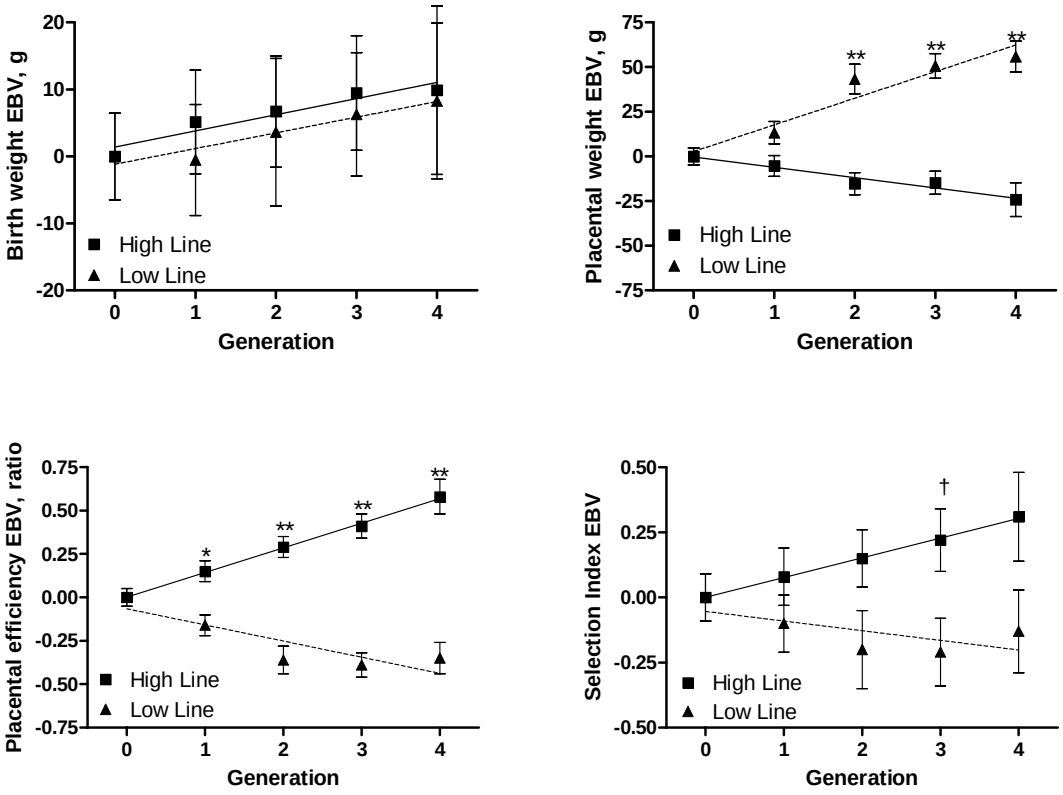

Figure 2. Estimated breeding value means and regression of means on generation for birth weight, placental weight, placental efficiency, and the selection index. Divergence trends were 20.7 ± 2.7 g, 0.24 ± 0.03, and 0.11 ± 0.02 per generation for placental weight, placental efficiency, and the selection index, respectively.
** $P < 0.01$, * $P < 0.05$, † $P < 0.10$

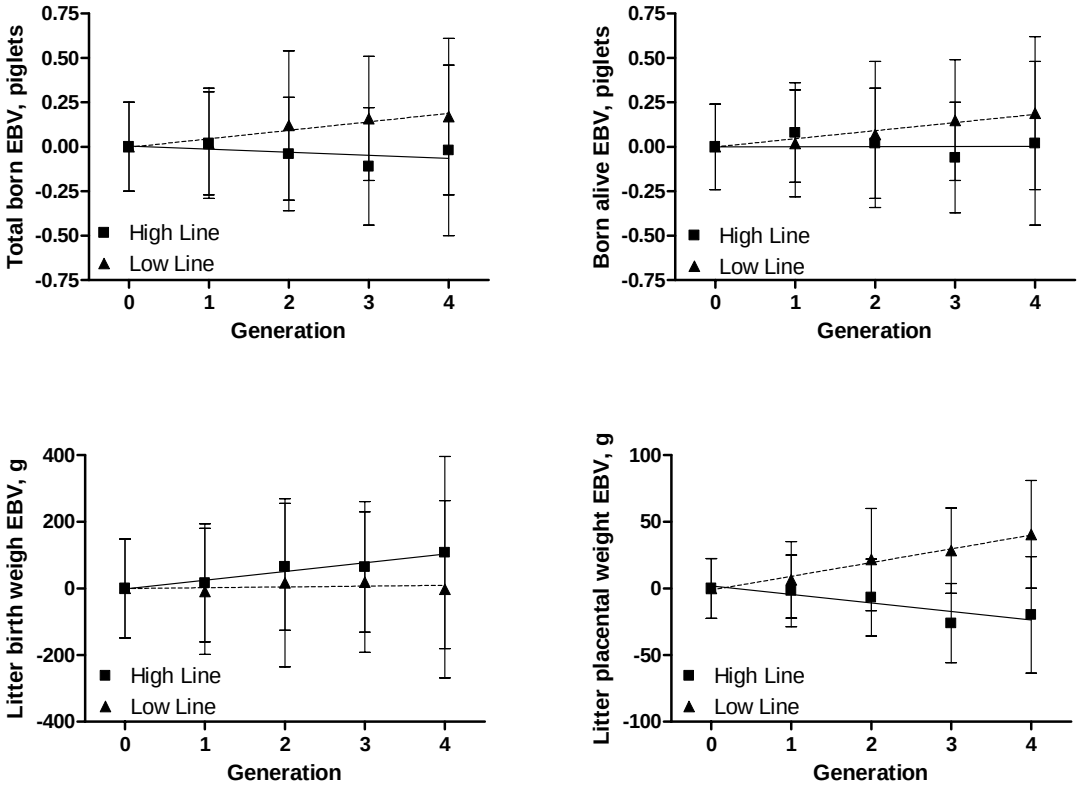

Figure 3. Estimated breeding value means and regression of means on generation for total born, born alive, litter birth weight, and litter placental weight. Divergence trends were 0.07 ± 0.02, 0.06 ± 0.02, 24.0 ± 5.8 g, and 16.7 ± 2.2 g per generation for total born, born alive, litter birth weight, and litter placental weight, respectively.

CHAPTER IV

CONCEPTUS DEVELOPMENT IN SWINE DIVERGENTLY SELECTED FOR PLACENTAL EFFICIENCY

ABSTRACT

The objective of this study was to evaluate correlated responses in conceptus development and traits physiologically relevant for placental function in animals from a selection experiment that resulted in differences in placental weight **(PW)** and efficiency **(PE)**. Fifty generation-3 second parity females from two lines with either high PE **(H)** or low PE **(L)** were mated within line to produce generation-four litters for evaluation at d 30, 50, 70, 90, and 110 of gestation. Uterine length was not different between lines at any gestational age, but increased from 275.0 ± 23.1 cm at d 30 to 338.3 ± 23.3 cm at d 50 (P = 0.06), and remained relatively unchanged to d 110. Fetal weight was not significantly different between lines from d 30 to d 90, but was lower in H than L at d 110 (1280.6 ± 77.0 vs. 1551.1 ± 75.3 g, respectively; P = 0.02). Crown-rump length was not significantly different between lines from d 30 to 70, but tended to be longer in H than L at d 90 (265.8 ± 8.8 vs. 241.2 ± 10.6 mm, respectively; P = 0.09) and was shorter in H than L at d 110 (290.6 ± 5.0 vs. 304.9 ± 4.5 mm, respectively; P = 0.04). Placental weight

increased in both lines from d 30 to 50, at which point it remained relatively unchanged through the rest of pregnancy, except in L that showed a second increase from d 90 to 110. As a result, placental weight was not significantly different between lines from d 30 to 90, but was lower in H than L at d 110 (244.6 ± 32.3 vs. 379.2 ± 24.5 g, respectively; $P < 0.01$). Line differences in placental efficiency were not significant at any gestational age. Implantation site length increased slowly for both lines from d 30 to 90, where it remained unchanged to d 110. Implantation site area was significantly higher in H than L at d 30 and 50, but was not different between lines for the remainder of pregnancy. These results suggest that in western breeds, a reduction in placental weight through selection is not accompanied by physiological compensation and may result in decreased prenatal survival.

Introduction

In swine, there are more viable embryos at 30 d of pregnancy than piglets born at term (Fenton et al., 1972; Knight et al., 1977; Pope, 1994). The maximum number of fetuses a female can support through pregnancy is termed uterine capacity and is considered the limiting factor to increasing litter size (Bennett and Leymaster, 1989). Placental function in nutrient supply is highly dependent on blood flow and area of placental exchange (Schneider, 1991), making endometrial surface area available for placentation a critical factor in prenatal survival and thus uterine capacity in swine (Wrathall, 1971). Placental surface area has a high, positive correlation with placental weight (Knight et al., 1977). For that reason the ratio of birth weight to placental weight has been used as an indicator of placental efficiency (Leiser and Kauffmann, 1994; Ford, 1997; Biensen et al., 1998; Wilson et al., 1999; Vallet et al., 2001).

In the prolific Meishan breed, there is a positive association between litter size and placental efficiency (Ashworth et al., 1990; Biensen et al., 1998; Wilson et al., 1998). Similar results were reported after one generation of selection for placental efficiency (Wilson et al., 1999), but results from other genetic selection experiments suggest that the same association is not present in western breeds (Vallet et al., 2001; Mesa et al., 2003; Mesa et al., 2005). The objective of this study was to evaluate correlated responses in conceptus development and traits physiologically relevant for placental function through gestation in animals from a four generation selection experiment for an index of reproductive components that resulted in differences in placental weight and efficiency.

Materials and Methods

Second parity females from generation 3 (n = 50) of a selection experiment for an index of reproductive components were mated within line to produce generation-four litters for evaluation. The selection procedures and results were described previously (Mesa et al., 2005). Briefly, divergent selection was performed on an index that included total number born, birth weight, and placental weight. Animals were ranked on this index and the highest and lowest ranking individuals within line were selected to produce divergent lines with either high **(H)** or low **(L)** placental efficiency, calculated as the ratio of birth weight to placental weight. Selection produced significant genetic and phenotypic differences between lines in placental weight and placental efficiency. The differences in placental efficiency resulted from piglets of similar weight associated with smaller placentas in the H line.

All females that produced generation four of the selection experiment (n = 28) and females that didn't farrow within the time period designated for data collection (n = 22),

were heat checked once daily with a mature, intact boar. Sows were hand-mated to boars of the same line at the onset of behavioral estrus and again 24 h later. Pregnant females remained in dirt lots until transported to the University of Missouri abattoir to be sacrificed at the scheduled time. Animals were fed a corn-soybean meal based diet formulated to meet or exceed nutritional requirements (N.R.C., 1998). Management of animals was done in accordance with approved procedures at the University of Missouri South Farm Swine Pasture Unit (MUIACUC protocol # 3198).

Five females per line were slaughtered at each d 30, 50, 70, 90, and 110 of gestation. These five gestational ages were chosen to represent the completion of the placentation process (d 30) (Marrable, 1971; Leiser and Dantzer, 1988), the beginning (d 50) and end (d 70) of a period with high incidence of fetal death due to competition for space among fetuses (Knight et al., 1977), a period of rapidly increasing fetal demands (d 90) (Ford, 1997; Wilson et al., 1998), and a point close to parturition (d 110). Females were, on average, sacrificed within one day of the target gestational age.

After slaughter, the reproductive tract was removed, placed on ice, and transported to the laboratory for processing. The broad ligament was removed and the uterine horns extended. Each ovary was dissected to count the number of corpora lutea to estimate ovulation rate (**OR**). Each uterine horn was then measured along the internal curvature from the junction with the cervix to the utero-tubal junction, and uterine length (**UL)** calculated as the sum of both values. The uterus was finally opened along the antimesometrial border to expose its contents and evaluate other maternal traits including total number of fetuses (**TF**), number of viable fetuses (**VF**), number of dead fetuses (**DF**) including mummies, and survival rate (**SR**) calculated as [VF/OR]*100. For each

female the total occupied (**TO**) and total unoccupied (**TU**) length of the uterus was measured, and the proportion of uterine length occupied by fetuses (**PO**) was calculated.

Fetuses were removed and sex, weight (**FW**), and crown-rump length (**CRL**) recorded. Three conceptuses per horn were randomly chosen for measurement of liver and stomach weight when possible. Placentas were stripped from the endometrium and weighed (**PW**). Placental efficiency (**PE**) was calculated as the ratio FW:PW. Implantation length (**IL**) was measured as the length of the vascular area of the uterus associated with each placenta. Implantation site area (**IA**) was measured by cutting the uterine wall around the vascular implantation site for each conceptus, spreading the tissue on heavy paper, and drawing its contour. All placental outlines were then scanned into an electronic format and sent to the Center for Environmental Technology at the University of Missouri were ER Mapper software v6.1 (Earth Resource Mapping Inc., San Diego, CA) was used to determine the area of the implantation site.

Statistical analyses were performed by using the MIXED procedure of SAS (SAS Inst. Inc., Cary, NC). Maternal and fetal traits were analyzed by using a model including the fixed effects of line and gestational age, and the random effect of sire within line. The GROUP option of the MIXED procedure was used to account for unequal variances across gestational age groups for all fetal traits.

Results

Uterine length was not different between lines at any gestational age in this study, but increased from 275.0 ± 23.1 cm at d 30 to 338.3 ± 23.3 cm at d50 ($P = 0.06$), and remained relatively unchanged to d 110. No line differences were detected for TO, TU or PO at any gestational age. Total uterine space occupied increased from 158.0 ± 20.3 cm

at d 30 to 241.9 ± 20.6 cm at d 50 (P = 0.04), and remained relatively constant to d 110. Conversely, total uterine space unoccupied decreased from 96.2 ± 14.0 cm at d 30 to 48.7 ± 14.2 cm at d 50 (P = 0.02), and remained relatively unchanged to d 110. As a result, the proportion of uterine length occupied increased from 62.0 ± 4.9% at d 30 to 83.0 ± 5.0% at d 50 (P = 0.03), and remained unchanged to d 110. No line or gestational age group effects were detected for the other maternal traits recorded; overall line means are presented in Table 6.

Least-squares means for fetal traits are presented in Figures 4 and 5 for all line x gestational age group combinations. Fetal weight was not significantly different between lines from d 30 to 90, but was lower in H than L at d 110 (1,280.6 ± 77.0 vs. 1,551.1 ± 75.3 g, respectively; P = 0.02). Crown-rump length was not significantly different between lines from d 30 to 70, but tended to be higher in H than L at d 90 (265.8 ± 8.8 vs. 241.2 ± 10.6 mm, respectively; P = 0.09) and was lower in H than L at d 110 (290.6 ±5.0 vs. 304.9 ± 4.5 mm, respectively; P = 0.04). Line differences were not significant at any gestational age for liver weight or stomach weight.

Placental weight increased in both lines from d 30 to 50, at which point it remained relatively unchanged through the rest of pregnancy, except in L that showed a second increase from d 90 to 110. As a result, placental weight was not significantly different between lines from d 30 to 90, but was lower in H than L at d 110 (244.6 ± 32.3 vs. 379.2 ± 24.5 g, respectively; P < 0.01). Line differences in placental efficiency were not significant at any gestational age. Implantation site length increased slowly for both lines from d 30 to 90, where it remained unchanged to d 110. Implantation site area was

higher in H than L at d 30 and 50, but was not different between lines for the remainder of pregnancy.

Discussion

In this experiment, fetal traits such as weight, crown-rump length, and liver and stomach weight showed a numerical tendency to be higher in H than L up to d 90 of pregnancy. This tendency fits the known history of four generations of selection for a higher weight at birth in H and for lower weight at birth in L. Between d 90 and 110 this tendency was reversed to the extent that fetal weight and crown-rump length are significantly higher in L than H. During the same period (d 90 to 110) placental weight remained relatively constant in H, but increased significantly in L fitting the expectation of a line selected for higher placental weight at birth. This last observation is similar to that observed in a comparison of Meishan and Yorkshire conceptuses, in which Yorkshire placentas increase in size between d 90 and 110, while Meishan placentas increase vascularity to maintain fetal growth (Wilson et al., 1998). Since fetal weight is highly dependent on placental weight (Knight et al., 1977), a heavier placenta in L may explain the presence of heavier fetuses at d 110 in this line. The increase in placental weight observed in this study between d 90 and 110 in line L agrees with that observed in a study of crossbred western breeds (Vonnahme et al., 2001), while the growth pattern in H resembles that of the Meishan pig (Biensen et al., 1998).

Increased placental weight in L is not associated to increased implantation length or implantation site area. These results indicate that reduction of placental weight in western breeds is not accompanied by the appropriate physiological response to ensure fetal survival trough pregnancy.

Data about birth weight, placental weight, and placental efficiency had been already collected during the selection phase of the experiment from 28 of the females that produced the litters in this study. In that analysis, no line differences were detected in birth weight, but placental weight was higher in L ($P < 0.05$) resulting in a higher placental efficiency in H ($P < 0.10$) (Mesa et al., 2005). Those results contrast with this study's results at d 110, which are a higher fetal weight at d 110 in L along with higher placental weight resulting in an absence of line differences in placental efficiency. These results may be explained in terms of parity number and age differences. On average, females produced their first litter at 1.5 years of age, and the second litter was produced between 6 and 12 mo later. It is conceivable that in gilts uterine space limited the growth of the placenta in L and thus limited the effect of a heavier placenta on birth weight. In contrast, longer uteri at parity two (P2) allowed the placenta in L to express more of its growth potential and resulted in an increased fetal weight. A second and complementary possibility is that uterine blood flow is higher in older females, therefore influencing the total mass of feto-placental units that can be supported (Père and Etienne, 2000).

In the selection phase of the experiment, a difference in favor of H of 0.6 ± 0.1 units of placental efficiency was detected at birth ($n = 186$; $P = 0.06$). It is likely that a smaller sample size at d 110 in this experiment ($n = 115$) is the cause of the failure to detect as significant a difference in favor of H of 1.4 ± 1.7 units in placental efficiency. Alternatively, greater variation in PE in this experiment, and not sample size, may be the cause of the reduced statistical power. An F-ratio test of variances between data from gilts and P2 females supports this conclusion. Both PW and PE are more variable in conceptuses produced by P2 females ($P < 0.0001$), while BW variance is not significantly

different. We hypothesize that this greater variation is of biological significance. If uterine space does not restrict placental growth in P2 females, individual conceptuses in both lines can express more of their intrinsic potential for placental growth.

In the Meishan conceptus vascular density of the placenta and the endometrium doubles between d 70 and 90 of gestation but placental surface area does not increase, while the Yorkshire conceptus doubles placental surface area between d 90 and 110 but maintains a constant placental and endometrial vascular density. In addition, Meishan and Yorkshire conceptuses gestated together in a Yorkshire uterus have similar birth weight but the placenta of Meishan conceptuses are lighter, which results in higher placental efficiency for Meishan conceptuses (Biensen et al., 1998). Changes in uterine gland and vascular density through pregnancy need to be evaluated in the population of the present experiment.

Conceptus development was studied in generation four of the divergently selected population initiated by Wilson et al. (1999). Placental weight was reported to be lower at d70 and d90 in the high line than the low and control lines, and although fetal weight was higher in the low line at d110, placental efficiency was always higher in the high line (Vonnahme and Ford, 2003). Although statistically significant, a PE difference of only 0.3 units between the high and the low lines at d 90 does not seem to be of biological importance. However, this difference was reported to be positively associated with differences in the expression pattern of the VEGF system and a difference in litter size of five piglets (statistical significance not reported) (Vonnahme and Ford, 2003). To the best of our knowledge, the population size and selection procedures followed during the three intervening generations of selection have not been reported in the literature. Considering

the small size of the population from which those lines originated, it is possible that the physiological differences observed between lines in that population are the result of genetic drift and do not represent a cause-effect relationship between selection for placental efficiency and prolificacy.

Implications

The high prolificacy of the Meishan pig has been linked in part to the high placental efficiency displayed by its conceptuses. However, it is possible that in western breeds of pigs, the absence of physiological compensatory mechanisms will reduce the probability of prenatal survival as a result of selection for a reduced placental weight. Selection for increased placental efficiency is thus unlikely to result in a correlated increase in litter size.

Table 6. Line least-squares means ± standard errors for maternal traits

Maternal Trait	High Line	Low Line
Ovulation rate, CL	20.1 ± 1.0	22.1 ± 1.2
Total number fetuses	12.9 ± 0.9	12.7 ± 1.0
Number viable fetuses	11.3 ± 1.0	11.9 ± 1.1
Number dead fetuses	1.3 ± 0.3	0.9 ± 0.3
Survival rate, %	57.7 ± 6.1	56.2 ± 6.5

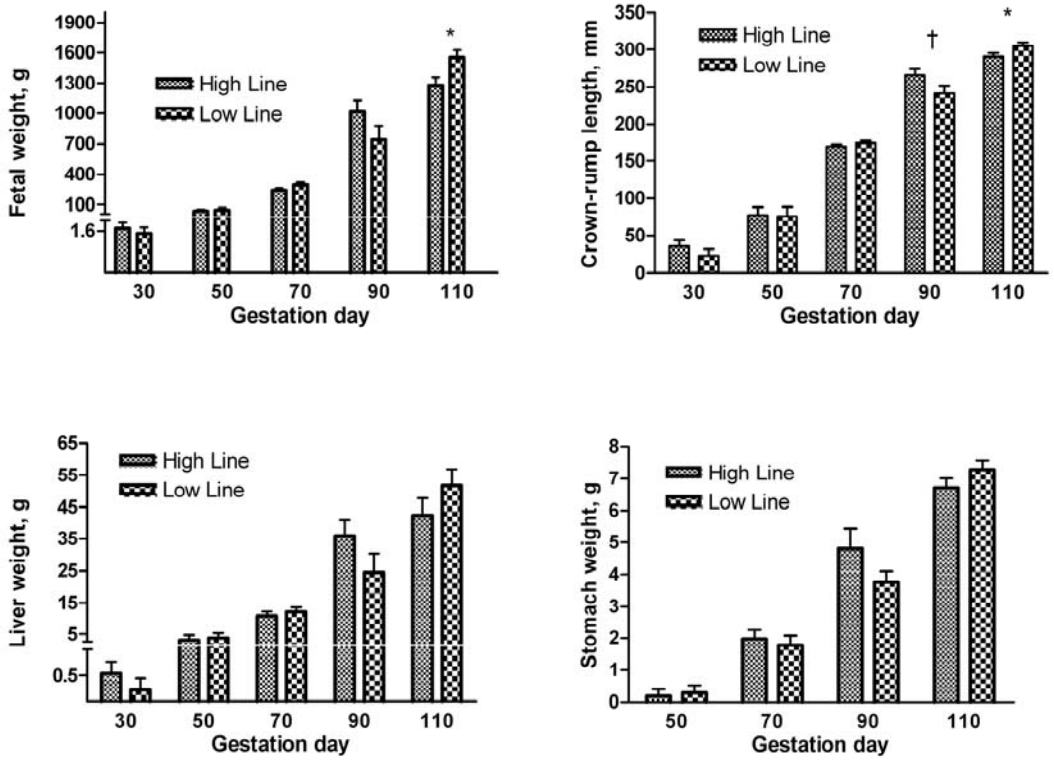

Figure 4. Least-squares means by line and gestational age for fetal weight, crown-rump length, liver weight and stomach weight
* $P < 0.05$, † $P < 0.10$ within gestation day

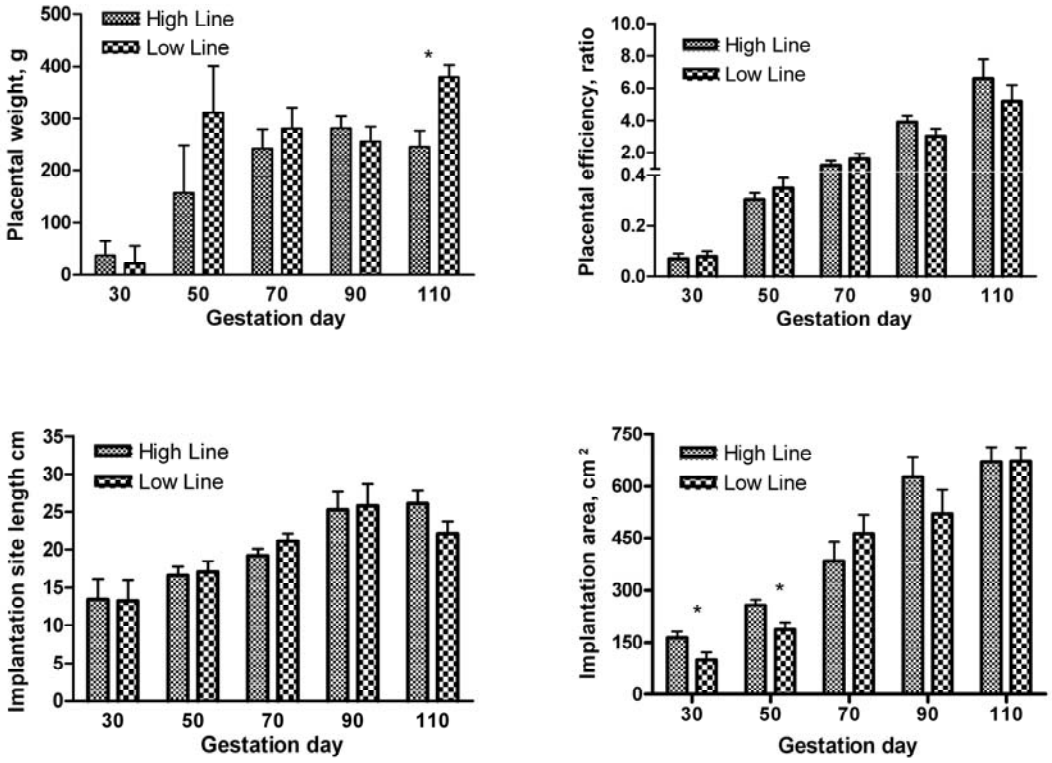

Figure 5. Least-squares means by line and gestational age for placental weight, placental efficiency, implantation site length, and implantation site area
* $P < 0.05$, † $P < 0.10$ within gestation day

CHAPTER V

SURVIVAL AT FARROWING AND AT WEANING IN SWINE AND THEIR RELATION TO BIRTH AND PLACENTAL WEIGHT

ABSTRACT

Data obtained during four generations of divergent selection for placental efficiency were used to determine factors influencing survival at farrowing and at weaning in litters produced by first parity females. Data were collected from 193 litters and included records on 2,053 individuals. Farrowing survival (**FS)** and weaning survival (**WS**) were considered traits of the piglet and were scored as 1 if the individual was alive at those time points or as 0 if dead. (Co)variance components and breeding values (**EBV**) for FS and WS were estimated for direct and maternal additive effects by using an animal model with MTDFREML procedures. Estimates of direct heritability were 0.16 and 0.18 for FS and WS, respectively. Estimates of maternal heritability were 0.14 and 0.10 for FS and WS, respectively. Genetic correlation estimates between direct and maternal effects were high and negative for both traits. The direct genetic correlation between FS and WS was 0.92. Variables associated with FS and WS were determined using logistic regression procedures. Farrowing survival EBV and the total number of piglets born in that litter

were the best predictors of FS. Weaning survival EBV and FS EBV best predicted WS, indicating that genetic effects that favor survival at farrowing also affect survival at weaning. In the absence of estimates of genetic merit for survival, birth weight, placental weight, their interaction, and total born can be used as predictors of survival at farrowing. The same model, excluding TB, is the best predictor for WS. In the presence of birth weight information, placental efficiency does not improve the prediction of survival probability. Results from this experiment suggest that it is possible to select for increased survival at farrowing and at weaning, provided that the negative correlations between direct and maternal effects are accounted. Information on a piglet's birth weight, placental weight, litter average birth weight, and the individual's deviation from litter average birth weight can be used to optimize those values at levels resulting in high survival probability without unnecessarily exceeding them.

Introduction

Litter size at weaning is a trait of major economic importance to swine producers (Tess et al., 1983). It has been demonstrated that it is possible to effectively increase litter size by selection (Lamberson et al., 1991; Bidanel et al., 1994; Johnson et al., 1999), although its heritability is low. A correlated response to selection for increased litter size has been decreased birth weight (Johnson et al., 1999; Mesa et al., 2003). Low birth weight, and particularly low birth weight within a litter, has been linked to high piglet mortality (Damgaard et al., 2003). A survey of U.S. swine producers in 2000 revealed that average litter size was 10.9 pigs, of which 10.0 were born alive, and 8.9 survived to weaning. Thus, of those pigs born alive, average preweaning mortality rate was 11.0 percent, with more than 50% of preweaning deaths due to being crushed by the sow

(USDA, 2002). Direct selection for increased preweaning survival is unlikely to be effective, as the heritability has been reported to be very low (Lamberson and Johnson, 1984; Grandinson et al., 2002), although the heritability of stillbirths was reported to be somewhat higher (Grandinson et al., 2002).

These traits are, in part, connected by prenatal growth of the piglet, which is in turn influenced by the placenta. Emphasis on placental efficiency, defined as the ratio of birth weight to placental weight at birth, may be a mechanism through which litter size can be increased while maintaining adequate birth weight (Wilson et al., 1999). Data for the current study were collected during four generations of divergent selection for placental efficiency. The objective of this study was to determine factors influencing survival at farrowing and at weaning in swine.

Materials and Methods

Selection procedures and results of the selection experiment that provided the data for this study have been reported previously (Mesa et al., 2005). Briefly, divergent selection was performed on an index that included total number born **(TB)**, birth weight (**BW**), and placental weight (**PW**). Animals were ranked on this index, and the highest and lowest ranking individuals were selected to produce divergent lines with either high **(H)** or low **(L)** placental efficiency (**PE**), calculated as the ratio of birth weight to placental weight. Selection produced significant genetic and phenotypic differences between lines in placental weight and placental efficiency. The differences in placental efficiency resulted from piglets of similar weight associated with smaller placentas in the H line.

Data were collected from 193 litters produced over five generations. To facilitate data collection each farrowing group was limited to a seven-day period. Generation interval was one year, and females produced only one litter. At 107 d of pregnancy, females were transferred to the Animal Sciences Research Center farrowing facility where parturition was supervised 24 h per day. In the morning of the fifth day of the seven-day farrowing period, parturition was induced in the remaining females with two i.m. injections of 10 mg of dinoprost (Lutalyse, Pharmacia and Upjohn Co., Kalamazoo, MI; 5 mg/mL), given 12 h apart.

At birth, to match each piglet to its placenta, the umbilical cord of each fully formed piglet was double tagged with identically numbered mouse ear tags (Gey Band & Tag Co., Norristown, PA). One tag was placed approximately 10 cm from the piglet and the umbilical cord severed so the first tag retracted into the birth canal with the cord stump. The second tag was placed on the piglet's umbilical cord stump approximately 5 cm from the abdomen. Piglets were weighed immediately after birth, before suckling began, and all placentas were collected and individually weighed at delivery. Approximately 21% of the placentas were not tagged because the umbilical cord broke during the tagging process or the piglet was already detached from it at birth.

Piglets were processed and ear notched within 24 h of farrowing. Fostering was minimal; therefore, the natural mother and the nurse effect were confounded in all analyses. Piglets were weaned when the oldest litter was 21 d old (average 18 d) and subsequently maintained in environmentally controlled nursery facilities. Survival at farrowing (**FS)** and at weaning (**WS**) were each considered a binary trait of the piglet and

scored as 1 if the individual was alive at those time points or as 0 if it was dead. Stillborn piglets were accurately differentiated from early postnatal deaths as a result of the constant farrowing supervision. Piglets were considered born alive even if they died within minutes after being born. Unthrifty piglets sacrificed before weaning were classified as dead even if they may have survived to weaning.

Analyses of survival traits in this study are retrospective; in consequence, management practices were not designed to facilitate the interpretation of such analyses. For example, obstetric assistance was provided to those females having difficulty at farrowing and this obviously increases an individual's ability to survive at farrowing. However, the results from this study can be extrapolated to swine herds in which obstetric assistance is routine. Similarly, the cause and time of death of piglets dead at weaning was not recorded.

The relationship between birth weight and placental weight was explored by fitting segmented and nonlinear regression curves to the data. A quadratic regression with plateau and a nonlinear model (Brody curve) describing changes in BW dependent on PW were fitted by using PROC NLIN (SAS Inst. Inc., Cary, NC).

(Co)variance components and breeding values (**EBV**) for survival at farrowing and weaning were estimated for direct and maternal additive effects using an animal model with MTDFREML procedures (Boldman et al., 1993). Threshold models fit binary data better than linear mixed models; however, both approximations perform equally well in estimation of variance components over a range of different incidence levels (Mäntysaari et al., 1991). The pedigree file represented seven generations and included

2,236 individuals. Farrowing survival and weaning survival were analyzed by using a model including contemporary group and sex as fixed effects, birth weight and total born as linear covariates, and litter as an uncorrelated random effect. Two-trait analyses of FS and WS with BW, PW, or PE excluded the linear adjustment for BW.

Variables associated with farrowing and weaning survival were determined by using logistic regression procedures (PROC LOGISTIC, SAS Inst. Inc., Cary, NC). Each trait was fitted to three sets of models exploring different combinations of explanatory variables. Set I (models 1 to 3) tested the effects of birth weight, placental weight, and placental efficiency. Set II (models 4 to 6) tested the effects of litter average for BW, PW, and PE and the individual's deviation from its litter mean for each trait. Set III (model 7) tested the effect of the individuals' EBV for farrowing survival and weaning survival. All models also included the effect of total number born. A detailed description of the models evaluated is presented in Table 7. Main effects or their interactions were entered into a model one at a time using the FORWARD model selection option. After all variables with significant effects in each model had been entered, the best model from each set was selected for goodness of fit. Model selection was based on log likelihood ratio tests after the data was trimmed to ensure that models were compared while using the same number of observations.

Probabilities of survival at farrowing and at weaning were simulated by using logistic regression estimates obtained from models 1 and 4. The predicted change of probability of survival at birth and at weaning was calculated for deviations from the mean for significant effects in a model using the inverse link function

$p_i = \frac{e^{(X\beta)}}{[1+e^{(X\beta)}]}$ where p_i is the probability estimate, X is the coefficient matrix and β is the solution vector (Kaps and Lamberson, 2004).

Results

Descriptive statistics for litter traits and traits tested for association with farrowing survival and weaning survival are presented in Tables 8 and 9, respectively.

A Brody curve and a segmented regression curve describing the relationship between birth weight and placental weight are plotted in Figure 6.

The Brody curve was of the form:

$$BW_i = A - (A - BW_{100})e^{-k(PW_i - PW_{100})}$$

where:

A = 1,893 g	the asymptotic birth weight
BW_{100} = 661.3 g	estimated birth weight at PW_{100}
PW_{100} = 100 g	lower placental weight associated to a viable piglet
k = 0.00515	the growth rate index

The segmented regression curve was of the form:

$$BW_i = a + (b \times PW_i) + (c \times PW_i^2) \qquad \text{for } PW_i \leq X_0$$

$$BW_i = a + (b \times X_0) + (c \times X_0^2) \qquad \text{for } PW_i > X_0$$

where:

a = 213.4 g	intercept
b = 5.76	linear regression coefficient
c = -0.005	quadratic regression coefficient

X_0 = 529.2 g inflexion point on the X axis

and,

Birth weight plateau = 1,738 g for all PW ≥ X_0

The segmented regression analysis of birth weight on placental weight shows that birth weight increases to a plateau of 1,738 g with increasing placental weight up to 529 g. This indicates that within the range of placental weights observed in most populations, a heavier placenta will always allow the expression of growth potential to produce a heavier piglet.

Estimates of variance components and genetic parameters from single-trait models are presented in Table 10. The direct and maternal heritability for FS and WS show that there is significant additive genetic variation for these two traits. The correlations between direct and maternal effects for both traits were high and negative. There was a significant common environmental litter effect for FS, but the estimate for WS was not significantly different from zero.

Estimates of direct and maternal genetic correlations between FS and WS and BW, PW, and PE are presented in Table 11. Both direct and maternal correlations between FS and WS were close to one, indicating that essentially the same genetic effects influence both traits. Direct genetic correlations were positive and high between birth weight and both FS and WS. Placental weight had the lowest direct and maternal correlations with FS and WS. The direct and maternal correlations between PW and FS were positive, but the direct correlation between PE and WS was negative.

Of the models describing FS in terms of BW, PW, PE, and TB (Set I), the best fit was obtained when BW, PW, BWxPW, and TB were included (model 1, Table 7). When

FS was modeled in terms of litter mean birth weight (**mBW**), litter mean placental weight (**mPW**), litter mean placental efficiency (**mPE**) and the individual's deviation from each mean (**dBW**, **dPW**, and **dPE**, respectively; Set II), it was found that mPW, mPE, dPW, and dPE have no predictive value. Therefore, model 4 (mBW, dBW, and their interaction) was selected for further analyses. Predictably, EBV for farrowing survival and total number of piglets born significantly affected FS (model 7).

Of the models describing WS in terms of BW, PW, PE, and TB (Set I) the best fit was obtained when BW, PW, and BWxPW were included (model 1). When WS was modeled in terms of mBW, mPW, mPE and the individual's deviation from the mean (Set II), model 4 (mBW, dBW and their interaction) had the best fit. Probability of survival to weaning was significantly influenced by the individuals' EBV for farrowing and weaning survival (model 7).

Logistic regression coefficients and their significance for effects included in models 1, 4, and 7 are presented for both survival traits in Table 12. A response surface describing the probability of survival at farrowing simulated using model 1 is presented in Figure 7. Farrowing survival probability is dramatically reduced when birth weight drops below the population average (1,390 g), but is not substantially increased for piglets weighing more than average. For piglets with BW in the range from 800 to 1,000 g, increasing PW has a slight positive effect on FS. Conversely, if an individual's BW is above 1,500 g, the highest FS results from having a placenta weighing under 350 g.

A response surface describing the probability of survival at farrowing simulated by using model 4 is presented in Figure 8. Individuals from litters with an average BW at and above the population mean (1,421 g) and that do not deviate negatively from their

litter's mean have the highest FS probability. If both litter and individual weight increase above the average, FS is not substantively increased, but reduction of both values drastically reduces the probability of survival at farrowing.

Probability of survival at weaning simulated by using model 1 is presented in Figure 9. An increase in both BW and PW positively affects WS. The effect of increasing PW is detectable up the higher end of the range but is maximized around 80%. Increasing BW above the population mean does not produce a substantial increment in WS. Interestingly, when both BW and PW are in the higher end of the spectrum WS falls below 80%.

Weaning survival simulated by using model 4 is presented in Figure 10. Similar to the trend already described, WS was maximized when litter mean birth weight is at the population average and individuals within that litter are at or above the average. Reduction of any of those values below their average rapidly reduces the probability of survival to weaning.

Discussion

The proportion of stillborn piglets in this study (3.5%) is significantly lower than the average 8.3% reported for the U.S swine industry (USDA, 2002) and is likely the result of constant supervision at farrowing and obstetric assistance. This indicates that benefits to the swine industry could be achieved initially by changes in management practices that provide an environment conducive to survival. Management practices can then be supplemented with selection strategies that produce piglets with a high potential for survival.

Previous estimates of the direct and maternal heritability of weaning survival were low and suggested that selection for increased survival was not likely to be effective (Lamberson and Johnson, 1984). Similarly, estimates of direct and maternal heritability for survival at farrowing and at weaning obtained in a within-line analysis were consistently low (Knol et al., 2002). On the other hand, estimates of direct and maternal heritability and their correlation for weaning survival were 0.11, 0.09, and -0.56, respectively, in a study involving more than 50,000 piglets (van Arendonk et al., 1996). The results presented here agree well with those of van Arendonk et al. (1996).

Survival traits are often categorized as survival at farrowing and total survival, the latter encompassing survival from the onset of parturition to weaning. In this type of analysis, the heritability of farrowing survival and total survival were estimated at 0.15 and 0.05, respectively, with no discrimination between direct and maternal effects (Grandinson et al., 2002).

In agreement with the results of this study, a higher EBV for FS was found to increase the probability of survival at farrowing (Leenhouwers et al., 2003). Based on the log likelihood results presented in Table 7, it is obvious that by far the best predictors of probability of survival at farrowing are the individual genetic merit for survival and the total number of piglets born in that litter. Weaning survival is best described by a model including the individual genetic merit for farrowing survival and weaning survival, indicating that genetic effects that favor survival at farrowing also affect survival at weaning. The effect of total born on both survival traits in all models in which this effect was included was always positive, which contradicts the notion that the environmental effect of increasing litter size will decrease survival directly. The results of this study

indicate that selection for increased survival is likely to be effective. As the maternal heritability for both survival traits are of similar magnitude to the direct heritabilities, and are negatively correlated to the direct effects, a genetic evaluation and selection program will need to include both types of effects to be successful. The high direct genetic correlation between farrowing survival and weaning survival ($r_G = 0.92$), and the significant effect of farrowing survival EBV on weaning survival, would indicate that selection for increased FS can result in positive correlated responses in WS. Birth weight, placental weight, and their interaction provide a model that could be used to help in the prediction of probability of survival traits. In the presence of birth weight information, placental efficiency does not improve the prediction of survival probability.

Piglets in litters with high variation in birth weight, especially if the litter's mean was low, have lower weaning survival probability (Milligan et al., 2002). Similarly, the average birth weight of the litter and the variation in BW within the litter decreased when the maternal EBV for FS increased (Leenhouwers et al., 2003). The results presented here indicate that the same two traits negatively affect probability of survival when they decrease below the population average. Selection for a sow's ability to produce uniform litters is possible based on the heritability estimate of 0.08 for within-litter variation found in a study including more than 2,000 litters (Damgaard et al., 2003). In the present study, the heritability estimate for the standard deviation of piglet weights produced by a sow was 0.03 ± 0.34 (data not shown).

In a study focused on the physiological components of increased piglet ability for total survival (from the onset of parturition to weaning), it was found that pigs with higher genetic merit for total survival have lower birth weights, and their high genetic

merit was not related to differences in progress of farrowing, early postnatal behavior or rectal temperature 24 h after birth (Leenhouwers et al., 2001). Their results contradict those reported here; increasing birth weight always increased survival probability as long as both birth and placental weight were not in the high end of the spectrum (Figure 7). The difference could reflect the fact that Leenhouwers et al. (2001) did not provide obstetrical assistance in their experiment, while heavy pigs experiencing difficulty passing through the birth canal were always assisted in this study.

In late gestation, litters with high genetic merit for total survival had lower average placental weight and lower variation in this trait, while placental efficiency tended to be higher. On the other hand, average fetal weight and variation in this trait were not correlated to genetic merit for survival (Leenhouwers et al., 2002a). Fetal cortisol levels were higher in fetuses with high genetic merit for survival, and most likely accounted for the maturity differences observed (Leenhouwers et al., 2002a). Those results mark a sharp contrast between pre- and post-natal life. Placental weight and efficiency account for differences in survival potential before birth, but after birth, BW becomes the major factor in the piglets' ability to survive.

Based on the results of this experiment, piglet survival at farrowing and weaning is satisfactory at birth weights around 1,400 g, and increased birth weight beyond this level does not result in substantial benefits in piglet survival. In our view, this means that allocation of extra fetal mass to piglets of high birth weight is inefficient.

Our results suggest that is possible to select for increased genetic merit for piglet survival. Additionally, information on a piglet's birth and its placental weight can be used to assist in this effort. Conceivably, litters with more homogeneous birth weight would

have acceptable individual piglet survival at even lower weights. We suggest that at current uterine capacity levels, it is possible to produce 13 to 14 viable piglets at birth that survive to weaning by selecting for uniformity and minimum birth weight. This alone would result in big benefits to the swine without the need to get involved in measuring and selecting for increased uterine capacity.

In conclusion, the results from this experiment suggest that it is possible to select for increased survival at farrowing and at weaning, provided that both the direct and maternal effects are taken into account in the estimation of breeding values. Information on a piglet's birth weight, placental weight, litter average birth weight, and the individual's deviation from that mean can be used to optimize those values at levels resulting in high survival probability without unnecessarily exceeding them.

Implications

The probability of piglet survival from birth to weaning has a large environmental component. Most rapid progress in number of piglets weaned can be achieved through application of improved management practices. Then long term improvements can be achieved by genetically enhancing a piglet's ability to survive, and that effort can be facilitated by the use of information on the piglet's birth and placental weight.

Table 7. Models used to test the association of trait combinations with farrowing and weaning survival

Set	Model Number[a]	Farrowing Survival		Weaning Survival	
		Effects Tested[b]	Log Likelihood[e]	Effects Tested[b]	Log Likelihood[e]
I	1	BW[c], PW[c], BWxPW[c], TB[c]	-206.65	BW[d], PW[d], BWxPW[d], TB	-486.11
	2	PW, PE, TB[c]	-221.57	PW, PE, TB[d]	-489.34
	3	BW[c], PE, TB[c]	-211.75	BW[d], PE[d], TB	-488.89
II	4	mBW[c], dBW[c], TB[c]	-216.51	mBW[d], dBW[d], mBWxdBW[d], TB	-492.26
	5	mPW, dPW, TB[c]	-221.57	mPW, dPW[d], TB[d]	-514.59
	6	mPE, dPE, TB[c]	-221.57	mPE[d], dPE[d], TB	-511.49
III	7	FSebv[c], WSebv, TB[c]	-81.67	FSebv[d], WSebv[d], TB	-231.93

[a] Each model tested included all possible linear interactions of its components.
[b] BW= birth weight, PW= placental weight, PE= placental efficiency, mBW= litter mean birth weight, mPW= litter mean placental weight, mPE= litter mean placental efficiency, dBW= deviation from litter mean birth weight, dPW= deviation from litter mean placental weight, dPE= deviation from litter mean placental efficiency, FSebv= farrowing survival estimated breeding value, WSebv= weaning survival estimated breeding value, TB= total born.
[c] Denotes effects selected for inclusion in a model of farrowing survival.
[d] Denotes effects selected for inclusion in a model of weaning survival.
[e] Log likelihood values refer to the model with all significant effects entered.

Table 8. Numbers of litters and descriptive statistics for litter traits

Variable	n	Mean	Std. Dev.	Minimum	Maximum
Total born	193	11.0	3.3	2.0	18.0
Born alive	193	10.4	3.3	2.0	17.0
Stillborn	193	0.6	1.2	0.0	9.0
Mummies	193	0.8	1.2	0.0	8.0
Number weaned	193	9.5	3.3	0.0	17.0

Table 9. Numbers of observations and descriptive statistics for farrowing and weaning survival and associated traits

Variable	n	Mean	Std. Dev.	Minimum	Maximum
Farrowing survival	2,053	0.96	0.18	0	1.0
Weaning survival	1,981	0.89	0.31	0	1.0
Farrowing survival EBV*, %	2,053	-0.30	2.47	-15.8	11.4
Weaning survival EBV*, %	2,053	2.11	4.69	-20.2	18.0
Birth weight (BW), g	2,050	1,390	334	75	2,530
Litter mean BW (mBW), g	193	1,421	236	808	2,173
Deviation from mBW, g	2,050	0.0	248	-1,000	988
Placental weight (PW), g	1,630	305	99.3	54	714
Litter mean PW (mPW), g	189	311	67.9	135	569
Deviation from mPW, g	1,630	0.0	76.1	-241	315
Placental efficiency (PE), g	1,630	4.9	1.27	1.7	15.9
Litter mean PE (mPE), g	189	4.9	0.74	3.37	7.84
Deviation from mPE, g	1,630	0.0	1.07	-3.6	8.9

*Estimated breeding value

Table 10. Estimates of (co)variance components and genetic parameters with standard errors (se) from single-trait models for farrowing survival and weaning survival

Parameter*	σ^2_p	h^2_a	h^2_m	r_{am}	l^2	e^2
Farrowing Survival	0.03075	0.16 (0.12)	0.14 (0.08)	-1.0 (0.16)	0.15 (0.05)	0.70 (0.08)
Weaning Survival	0.08763	0.18 (0.10)	0.10 (0.06)	-0.77 (0.19)	0.00 (0.02)	0.83 (0.07)

*$\boldsymbol{\sigma^2_p}$=phenotypic variance, $\boldsymbol{h^2_a}$=additive heritability (se), $\boldsymbol{h^2_m}$=maternal heritability (se), $\boldsymbol{r_{am}}$=correlation between additive and maternal genetic effects (se), $\boldsymbol{l^2}$=proportion of phenotypic variance due to litter effect (se), $\boldsymbol{e^2}$=proportion of phenotypic variance due to environmental effects (se).

Table 11. Estimates of direct and maternal genetic correlations from two-trait analyses involving farrowing survival and weaning survival

		Farrowing survival	Weaning survival	Birth weight	Placental weight	Placental efficiency
Farrowing survival	Direct	-	0.92	0.83	0.09	0.26
	Maternal	-	0.99	0.01	0.00	0.69
Weaning survival	Direct	0.92	-	0.82	0.16	-0.41
	Maternal	0.99	-	0.01	0.00	0.23

Table 12. Logistic regression coefficients and their significance for effects included in models used for predicting survival traits

Independent variable	Model Number	Effects[a]	Logistic Regression Coefficient	P value
Farrowing Survival	1	Intercept	-2.7678	0.019
		BW	0.00443	<0.0001
		PW	0.00469	0.221
		BWxPW	-6.28 E-6	0.0104
		TB	0.1393	0.0047
	4	Intercept	-1.3138	0.2820
		mBW	0.00219	0.0013
		dBW	0.00181	0.0013
		TB	0.1605	0.0012
	7	Intercept	4.3696	<0.001
		FSebv	91.528	<0.001
		TB	0.1921	0.0288
Weaning Survival	1	Intercept	-2.6267	0.0016
		BW	0.00422	<0.001
		PW	0.00602	0.0444
		BWxPW	-6.3 E-6	0.0015
	4	Intercept	0.5887	0.3047
		mBW	0.00121	0.0034
		dBW	0.00715	0.002
		mBWxdBW	-3.5 E-6	0.0319
	7	Intercept	2.9177	<0.001
		FSebv	11.8067	0.0501
		WSebv	52.9984	<0.001

[a] See Table 1 for trait acronym descriptions.

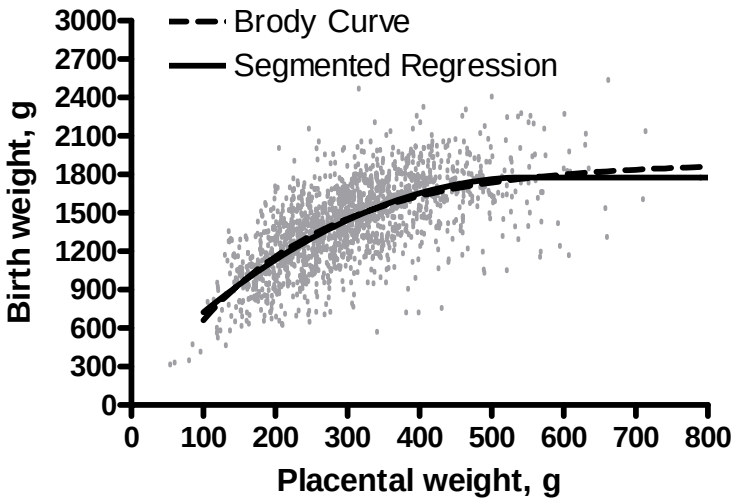

Figure 6. Scatter plot of the relationship between birth weight and placental weight and fitted Brody curve and segmented regression curve with plateau.

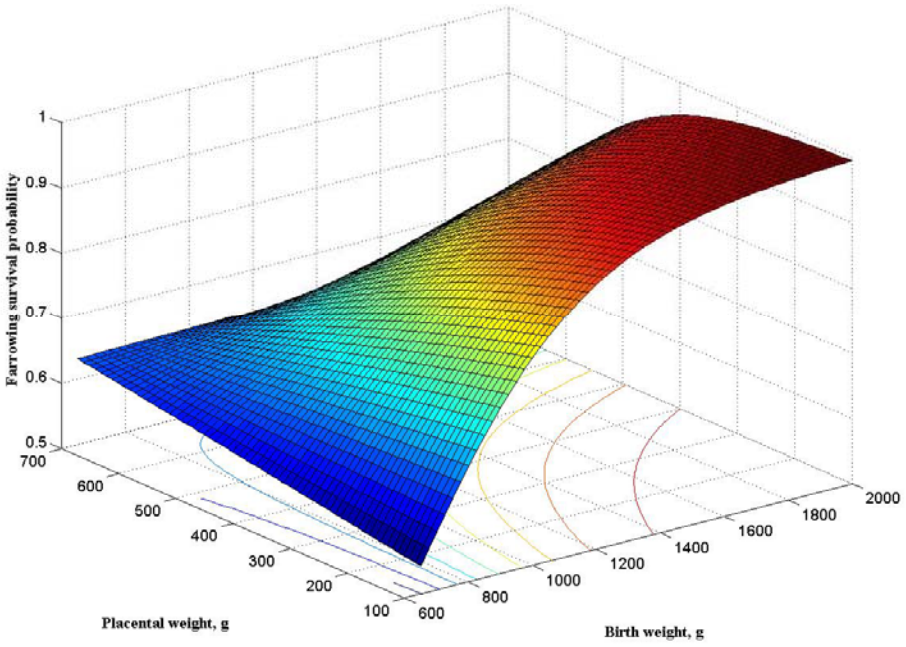

Figure 7. Response surface of probability of survival at farrowing as affected by birth weight and placental weight.

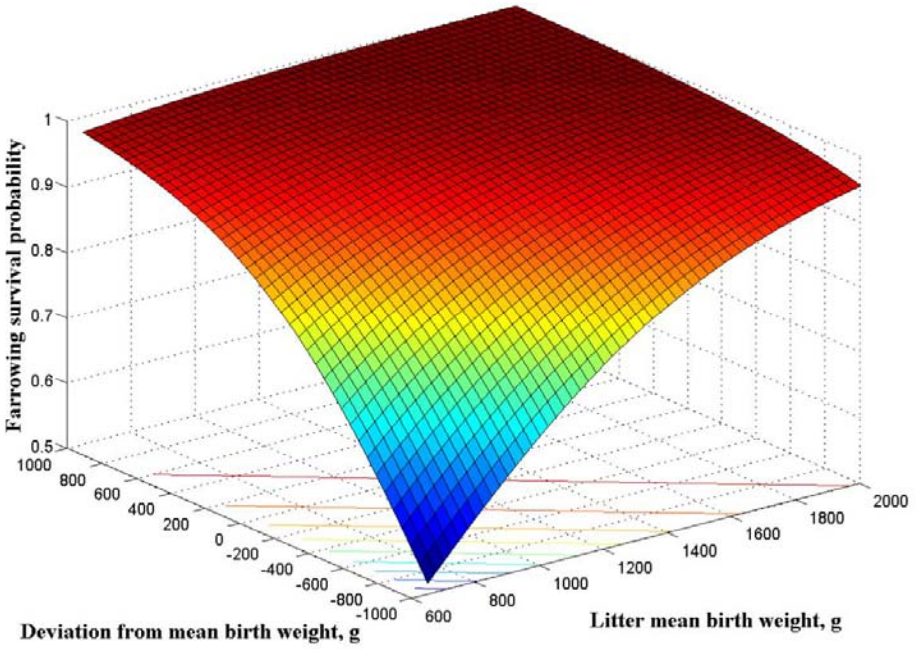

Figure 8**.** Response surface of probability of survival at farrowing as affected by litter mean birth weight and individual deviation from the mean.

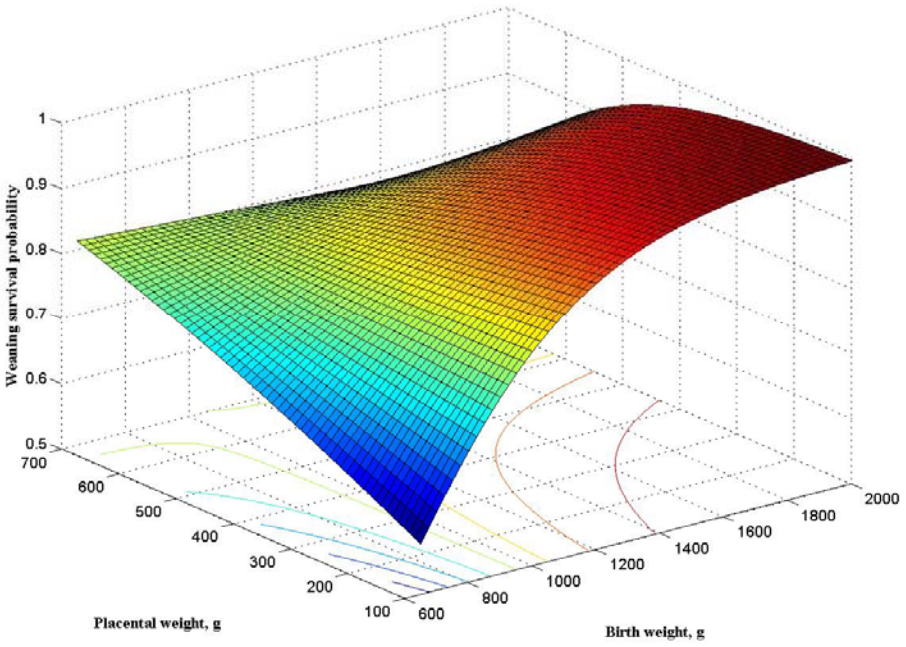

Figure 9. Response surface of probability of survival at weaning as affected by birth weight and placental weight.

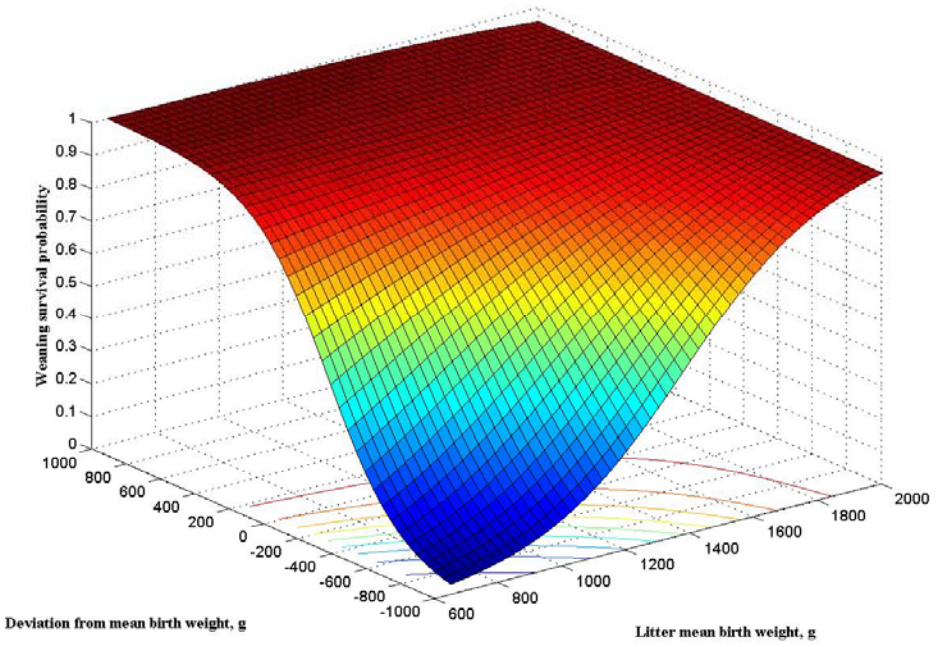

Figure 10. Response surface of probability of survival at weaning as affected by litter mean birth weight and individual deviation from the mean.

CHAPTER VI

GENERAL DISCUSSION

Placental weight and efficiency have important additive genetic components that allow selection to be carried out to modify both traits in the desired direction. In this context, placental efficiency is defined as the ratio between a piglet's birth weigh and its placental weight, a convenient measurement that may not reflect the functional efficiency of the placenta. The reduced weight ratio has been in fact linked to the outstanding prolificacy of the Meishan pig and is complemented by an increased vascular density that allows for adequate supply of nutrients to the growing fetus (Ford, 1997; Biensen et al., 1998; 1999). The same association between the weight ratio and prolificacy has not been observed in western lines of pigs showing increased prolificacy due to selection (Vallet et al., 2001; Mesa et al., 2003). In this experiment we found that successful selection for increased placental efficiency, defined as the weight ratio, is correlated with a negative genetic trend in litter size. From a physiological perspective, this result can be explained if the smaller placenta resulting in a high ratio lacks the compensatory mechanisms for nutrient supply observed in Meishan conceptuses. Since ultimately the transfer efficiency of the placenta is dependent on exchange surface area, a relatively smaller placenta is more likely to result in prenatal death due to placental insufficiency (Knight et al., 1977).

Uterine capacity is frequently defined as the number of piglets that a female can carry to term when ovulation rate is not limiting (Bennett and Leymaster, 1989). Alternatively, uterine capacity can be defined as the maximum fetal weight that can be carried by a female, and is dependent on female weight at breeding (van Oijen et al., 1993). Since uterine capacity is in part limited by uterine volume and blood supply, the latter definition is physiologically more appropriate. Uterine blood flow is more closely related to litter weight than litter size. Uterine blood flow at 111 d of gestation in swine is 2.84 $L \cdot min^{-1} \cdot horn^{-1}$, resulting in a blood flow of 0.42 $L \cdot min^{-1} \cdot kg\ fetus^{-1}$(Père and Etienne, 2000). This would mean that approximately 13.5 kg of piglet could be produced. In this experiment the average total piglet mass carried by a female was 15.3 kg. Simulation studies suggest that the maximum fetal mass the uterus can carry in the average female bred at 119 kg of live weight is 20.3 kg (van Oijen et al., 1993). This could be interpreted as meaning that there is much room for increasing uterine capacity. However, selection strategies to increase uterine capacity would require technical procedures such as unilateral hysterectomy and measurement of blood flow, techniques that are very difficult to implement at an industry level.

The presence of embryos at d 30 of pregnancy not represented by live fetuses at term has been extensively discussed in the literature. In the same light, variation in piglet weight at birth results in suboptimal litter size and weight at weaning. Within a litter, piglet survival is highly dependent on birth weight because light piglets have to compete with heavier littermates for colostrum (English and Wilkinson, 1982; Fraser, 1990). However, across lines or breeds, higher preweaning survival is associated with litter uniformity and a higher physiological maturity at birth (Leenhouwers et al., 2002a).

Below 1 kg birth weight, >11% of piglets are stillbirths and subsequently >17% die within the first 24 h; while above 1 kg birth weight, 4% are stillbirths and 3% die within 24 h (Quiniou et al., 2002). The proportion of piglets below 1 kg birth weight increases form 14% to 23% if litter size increases from 15 to ≥16 (Quiniou et al., 2002).

Based on the results of this experiment, piglet survival at farrowing and weaning is satisfactory at birth weights around 1,400 g, and increased birth weight beyond this level does not result in substantial benefits in piglet survival. In our view, this means that allocation of extra fetal mass to piglets of high birth weight is inefficient.

Our results suggest that it is possible to select for increased genetic merit for piglet survival. Additionally, information on a piglet's birth and its placental weight can be used to assist in this effort. Conceivably, litters with more homogeneous birth weight would have acceptable individual piglet survival at even lower weights. In conclusion, we suggest that at current uterine capacity levels, it is possible to produce 13 to 14 viable piglets at birth that survive to weaning by selecting for uniformity and minimum birth weight. This alone would result in big benefits to the swine industry without the need to get involved in measuring and selecting for increased uterine capacity.

LITERATURE CITED

Allan, G. J., D. J. Flint, and K. Patel. 2001. Insulin-like growth factor axis during embryonic development. Reproduction 122: 31-39.

Amoroso, E. C. 1952. Placentation. In: A. S. Parkes (ed.) Marshall's Physiology of Reproduction. p 127-294. Longmans, Cambridge.

Anderson, L. L. 1978. Growth, protein content and distribution of early pig embryos. Anat. Rec. 190: 143-153.

Anderson, L. L. 1993. Pigs. In: E. S. E. Hafez (ed.) Reproduction in Farm Animals. p 343-360. Lea and Febiger, Philadelphia.

Anthony, R. V., S. L. Pratt, R. Liang, and M. D. Holland. 1995. Placental-fetal hormonal interactions: Impact on fetal growth. J. Anim. Sci. 73: 1861-1871.

Ashworth, C. J., A. M. Finch, K. R. Page, M. O. Nwagwu, and H. J. McArdle. 2001. Causes and consequences of fetal growth retardation in pigs. Reproduction Suppl. 58: 233-246.

Ashworth, C. J., C. S. Haley, R. P. Aitken, and I. Wilmut. 1990. Embryo survival and conceptus growth after reciprocal embryo transfer between Chinese Meishan and Landrace x Large White gilts. J. Reprod. Fert. 90: 595-603.

Bazer, F. W., A. J. Clawson, O. W. Robinson, and L. C. Ulberg. 1969. Uterine capacity in gilts. J. Reprod. Fertil. 18: 121-124.

Bennett, G. L., and K. A. Leymaster. 1989. Integration of ovulation rate, potential embryonic viability and uterine capacity into a model of litter size in swine. J. Anim. Sci. 67: 1230-1241.

Bennett, G. L., and K. A. Leymaster. 1990a. Genetic implications of a simulation model of litter size in swine based on ovulation rate, potential embryonic viability and uterine capacity: I. Genetic theory. J. Anim. Sci. 68: 969-979.

Bennett, G. L., and K. A. Leymaster. 1990b. Genetic implications of a simulation model of litter size in swine based on ovulation rate, potential embryonic viability and uterine capacity: II. Simulated selection. J. Anim. Sci. 68: 980-986.

Bidanel, J. P., J. Gruand, and C. Legault. 1994. An overview of twenty years of selection for litter size in pigs using "hyperprolific" schemes. In: Proc. 5th World Congr. Genet. Appl. Livestock Prod., Armidale, Australia. p 512-515.

Biensen, N. J., M. E. Wilson, and S. P. Ford. 1998. The impact of either a Meishan or Yorkshire uterus on Meishan or Yorkshire fetal and placental development to days 70, 90, and 110 of gestation. J. Anim. Sci. 76: 2169-2176.

Biensen, N. J., M. E. Wilson, and S. P. Ford. 1999. The impacts of uterine environment and fetal genotype on conceptus size and placental vascularity during late gestation in pigs. J. Anim. Sci. 77: 954-959.

Boldman, K. G., L. A. Kriese, L. D. Van Vleck, and S. D. Kachman. 1993. A manual for use of MTDFREML. A set of programs to obtain estimates of variances and covariances. ARS-USDA, Clay Center, NE.

Bolet, G., J. P. Bidanel, and L. Ollivier. 2001. Selection for litter size in pigs. II. Efficiency of closed and open selection lines. Genet. Sel. Evol. 33: 515-528.

Bolet, G., L. Ollivier, and P. Dando. 1989. [Selection for prolificacy in the pig. I. Results of an eleven-generation selection experiment] [in French]. Genet. Sel. Evol. 21: 93-106.

Boylan, W. J., W. E. Rempel, and R. E. Comstock. 1961. Heritability of litter size in swine. J. Anim. Sci. 20: 566-568.

Breier, G. 2000. Angiogenesis in embryonic development- a review. Placenta 21 (Suppl. A): S11-S15.

Chen, P., T. J. Baas, J. W. Mabry, K. J. Koehler, and J. C. M. Dekkers. 2003. Genetic parameters and trends for litter traits in U.S. Yorkshire, Duroc, Hampshire, and Landrace pigs. J. Anim. Sci. 81: 46-53.

Chen, Z. Y., and P. J. Dziuk. 1993. Influence of initial length of uterus per embryo and gestation stage on prenatal survival, development, and sex ratio in the pig. J. Anim. Sci. 71: 1895-1901.

Christenson, R. K. 1993. Ovulation rate and embryonic survival in Chinese Meishan and White crossbred pigs. J. Anim. Sci. 71: 3060-3066.

Christenson, R. K., and K. A. Leymaster. 2000. Effects of selection for ovulation rate or uterine capacity on gravid uterine, farrowing, and weaning traits in swine. J. Anim. Sci. 78 (Suppl.1): 202.

Christenson, R. K., K. A. Leymaster, and L. D. Young. 1987. Justification of unilateral hysterectomy-ovariectomy as a model to evaluate uterine capacity in swine. J. Anim. Sci. 65: 738-744.

Constancia, M., M. Hemberger, J. Hughes, W. Dean, A. Fergusson-Smith, R. Fundele, F. Stewart, G. Kelsey, A. Fowden, C. Sibley, and W. Reik. 2002. Placental-specific IGF-II is a major modulator of placental and fetal growth. Nature 417: 945-948.

Cunningham, P. J., M. E. England, L. D. Young, and D. R. Zimmerman. 1979. Selection for ovulation rate in swine: Correlated response in litter size and weight. J. Anim. Sci. 48: 509-516.

Damgaard, L. H., L. Rydhmer, P. Lovendahl, and K. Grandinson. 2003. Genetic parameters for within-litter variation in piglet birth weight and change in within-litter variation during suckling. J Anim. Sci. 81: 604-610.

Dantzer, V. 1984. Scanning electron microscopy of exposed surfaces of the porcine placenta. Acta Anat. 118: 96-106.

Dantzer, V., and H. Winther. 2001. Histological and immunohistochemical events during placentation in pigs. Reproduction: 209-222.

Dziuk, P. J. 1985. Effect of migration, distribution and spacing of pig embryos on pregnancy and fetal development. J. Reprod. Fertil. Suppl. 33: 57-63.

Engelhardt, H., B. A. Croy, and G. J. King. 2002. Conceptus influences the distribution of uterine leukocytes during early porcine pregnancy. Biol. Reprod. 66: 1875-1880.

Engelhardt, H., and G. J. King. 1996. Uterine natural killer cells in species with epitheliochorial placentation. Nat. Immun. 15: 53-69.

English, P. R., and V. Wilkinson. 1982. Management of the sow and litter in late pregnancy and lactation in relation to piglet survival and growth. In: D. J. A. Cole and G. R. Foxcroft (eds.) Control of Pig Reproduction. p 479-506. Butterworths, London.

Fenton, F. R., F. L. Schwartz, F. W. Bazer, O. W. Robison, and L. C. Ulberg. 1972. Stage of gestation when uterine capacity limits embryo survival in gilts. J. Anim. Sci. 35: 383-388.

Ferrara, N. 2000. Vascular endothelial growth factor and the regulation of angiogenesis. Recent Progress in Hormone Research 55: 15-36.

Ferrara, N., and T. Davis-Smyth. 1997. The biology of vascular endothelial growth factor. Endocrine Reviews 18: 4-25.

Ford, S. P. 1997. Embryonic and fetal development in different genotypes of pigs. J. Reprod. Fertil. Suppl. 52: 164-176.

Ford, S. P., and R. K. Christenson. 1979. Blood flow to uteri of sows during the estrous cycle and early pregnancy: Local effects of the conceptus on the uterine blood supply. Biol. Reprod. 21: 617-624.

Fowden, A. L. 2003. The insulin-like growth factors and feto-placental growth. Placenta 24: 803-812.

Fraser, D. 1990. Behavioral perspectives on piglet survival. J. Reprod. Fert. Suppl. 40: 355-370.

Friess, A. E., F. Sinowatz, R. Skolek-Winnish, and W. Träutner. 1980. The placenta of the pig. I. Finestructural changes of the placental barrier during pregnancy. Anat. Embryol. 158: 179-191.

Friess, A. E., F. Sinowatz, R. Skolek-Winnish, and W. Träutner. 1982. Structure of the epitheliochorial porcine placenta. Biblthca Anat. 22: 140-143.

Geisert, R. D., J. W. Brookbank, R. M. Roberts, and F. W. Bazer. 1982a. Establishment of pregnancy in the pig. II. Cellular remodeling of the porcine blastocyst during elongation on day 12 of pregnancy. Biol. Reprod. 27: 941-955.

Geisert, R. D., R. H. Renegar, W. W. Thatcher, R. M. Roberts, and F. W. Bazer. 1982b. Establishment of pregnancy in the pig. I. Interrelationships between preimplantation development of the pig blastocyst and uterine endometrial secretions. Biol. Reprod. 27: 925-939.

Geisert, R. D., and R. A. M. Schmitt. 2002. Early embryonic survival in the pig: Can it be improved? J. Anim. Sci. 80: E54-E65.

Gille, H., J. Kowalski, B. Li, J. LeCourter, B. Moffat, T. F. Zioncheck, N. Pelletier, and N. Ferrara. 2001. Analysis of biological effects and signalling properties of Flt-1 (VEGFR-1) and KDR (VEGFR-2). J. Biol. Chem. 276: 3222-3230.

Grandinson, K., M. S. Lund, L. Rydhmer, and E. Strandberg. 2002. Genetic parameters for the piglet mortality traits crushing, stillbirth and total mortality, and their relation to birth weight. Acta Agric. Scand., Sect. A, Animal Sci. 52: 167-173.

Gray, C. A., F. F. Bartol, B. J. Tarleton, A. A. Wiley, G. A. Johnson, F. W. Bazer, and T. E. Spencer. 2001. Developmental biology of uterine glands. Biol. Reprod. 65: 1311-1323.

Gunsett, F. C. 1984. Linear index selection to improve traits defined as ratios. J. Anim. Sci. 59: 1185-1193.

Irgang, R., J. A. Favero, and B. W. Kennedy. 1994. Genetic parameters for litter size of different parities in Duroc, Landrace, and Large White sows. J. Anim. Sci. 72: 2237-2246.

Johnson, R. K., M. K. Nielsen, and D. S. Casey. 1999. Responses in ovulation rate, embryonal survival, and litter traits in swine to 14 generations of selection to increase litter size. J. Anim. Sci. 77: 541-557.

Johnson, R. K., D. R. Zimmerman, and R. J. Kittok. 1984. Selection for components of reproduction in swine. Livest. Prod. Sci. 11: 541-558.

Kaps, M., and W. R. Lamberson. 2004. Biostatistics for Animal Science. CABI Publishing, Cambridge.

Kim, J. G., J. L. Vallet, and R. K. Christenson. 2001. Characterization of uterine epidermal growth factor during early pregnancy in pigs. Domest. Anim. Endocrinol. 20: 253-265.

King, G. J. 1993. Comparative placentation in ungulates. J. Exp. Zool. 256: 588-602.

Knight, J. W., F. W. Bazer, W. W. Thatcher, D. E. Franke, and H. D. Wallace. 1977. Conceptus development in intact and unilaterally hysterectomized-ovariectomized gilts: Interrelations among hormonal status, placental development, fetal fluids and fetal growth. J. Anim. Sci. 44: 620-637.

Knol, E. F., B. J. Ducro, J. A. M. Arendonk, and T. van der Lende. 2002. Direct, maternal and nurse sow genetic effects on farrowing-, pre-weaning- and total piglet survival. Livest. Prod. Sci. 73: 153-164.

Korpelainen, E. I., and K. Alitalo. 1998. Signaling angiogenesis and lymphangiogenesis. Curr. Opin. Cell Biol. 10: 159-164.

Lamberson, W. R. 1990. Genetic parameters for reproductive traits. In: L. D. Young (ed.) Genetics of Swine. p 70-76. Publication NC-103. University of Nebraska, Lincoln, NE.

Lamberson, W. R., and G. R. Eckardt. 1996. Local changes in uterine dimensions in the pregnant pig. Anim. Reprod. Sci. 43: 35-41.

Lamberson, W. R., and R. K. Johnson. 1984. Preweaning survival in swine: Heritability of direct and maternal effects. J. Anim. Sci. 59: 346-349.

Lamberson, W. R., R. K. Johnson, D. R. Zimmerman, and T. E. Long. 1991. Direct responses to selection for increased litter size, decreased age at puberty, or random selection following selection for ovulation rate in swine. J. Anim. Sci. 69: 3129-3143.

Leenhouwers, J. I., C. A. de Almeida Júnior, E. F. Knol, and T. van der Lende. 2001. Progress of farrowing and early postnatal pig behavior in relation to genetic merit for pig survival. J Anim. Sci. 79: 1416-1422.

Leenhouwers, J. I., E. F. Knol, P. N. de Groot, H. Vos, and T. van der Lende. 2002a. Fetal development in the pig in relation to genetic merit for piglet survival. J Anim. Sci. 80: 1759-1770.

Leenhouwers, J. I., E. F. Knol, and T. van der Lende. 2002b. Differences in late prenatal development as an explanation for genetic differences in piglet survival. Livest. Prod. Sci. 78: 57-62.

Leenhouwers, J. I., P. Wissink, T. van der Lende, H. Paridaans, and E. F. Knol. 2003. Stillbirth in the pig in relation to genetic merit for farrowing survival. J Anim. Sci. 81: 2419-2424.

Legault, C. 1983. Breeding for larger litters in swine. In: Pork Industry Conference, Urbana, IL. p 1-26.

Leiser, R., and V. Dantzer. 1988. Structural and functional aspects of porcine placental microvasculature. Anat. Embryol. 117: 409-419.

Leiser, R., and P. Kauffmann. 1994. Placental structure: in a comparative aspect. Exp. Clin. Endocrinol. 102: 122-134.

Leymaster, K. A., and R. K. Christenson. 2000. Direct and correlated responses to selection for ovulation rate or uterine capacity in swine. J. Anim. Sci. 78 (Suppl. 1): 68.

Mäntysaari, E. A., R. L. Quaas, and Y. T. Gröhn. 1991. Simulation study on covariance component estimation for two binary traits in an underlying continuous scale. J. Dairy Sci. 74: 580-591.

Marrable, A. W. 1971. The embryonic pig. A chronological account. Pitman Medical, Great Britain.

Mesa, H., T. J. Safranski, K. A. Fischer, K. M. Cammack, and W. R. Lamberson. 2005. Selection for placental efficiency in swine: Genetic parameters and trends. J Anim. Sci. Submitted.

Mesa, H., T. J. Safranski, R. K. Johnson, and W. R. Lamberson. 2003. Correlated response in placental efficiency in swine selected for an index of components of litter size. J. Anim. Sci. 81: 74-79.

Milligan, B. N., D. Fraser, and D. L. Kramer. 2002. Within-litter birth weight variation in the domestic pig and its relation to pre-weaning survival, weight gain, and variation in weaning weights. Livest. Prod. Sci. 76: 181-191.

Moeller, S. J., R. N. Goodwin, R. K. Johnson, J. W. Mabry, T. J. Baas, and O. W. Robison. 2004. The National Pork Producers Council Maternal Line National Genetic Evaluation Program: A comparison of six maternal genetic lines for female productivity measures over four parities. J. Anim. Sci. 82: 41-53.

N.R.C. 1998. Nutrient Requirements of Swine (9th Ed.). National Academy Press, Washington, DC.

Neal, S. M., R. K. Johnson, and R. J. Kittok. 1989. Index selection for components of litter size in swine: response to five generations of selection. J. Anim. Sci. 67: 1933-1945.

NSIF. 1996. Guidelines for uniform swine improvement programs. National Swine Improvement Federation, Ames, Iowa.

Ollivier, L. 1973. Five generations of selection for increasing litter size in swine. Genetics 74 (Suppl. 2): 202-203.

Ollivier, L., and G. Bolet. 1981. [Selection for prolificacy in the pig: Results of a 10 generation selection experiment] [in French]. Journees Rech. Porcine en France 13: 261-267.

Owens, J. L. 1991. Endocrine and substrate control of fetal growth: Placental and maternal influences and insulin-like growth factors. Reprod. Fert. Dev. 3: 501-517.

Pearson, P. L., H. G. Klemcke, R. K. Christenson, and J. L. Vallet. 1998. Uterine environment and breed effects on erythropoiesis and liver protein secretion in late embryonic and early fetal swine. Biol. Reprod. 58: 911-918.

Père, M. C., and M. Etienne. 2000. Uterine blood flow in sows: Effects of pregnancy stage and litter size. Reprod. Nutr. Dev. 40: 369-382.

Pérez-Enciso, M., and J. P. Bidanel. 1997. Selection for litter size components: a critical review. Genet. Sel. Evol. 29: 483-496.

Perry, J. S. 1981. The mammalian fetal membranes. J. Reprod. Fert. 62: 321-335.

Perry, J. S., and J. G. Rowell. 1969. Variations in foetal weight and vascular supply along the uterine horn of the oig. J. Reprod. Fert. 19: 527-534.

Perry, J. S., and I. W. Rowlands. 1962. Early pregnancy in the pig. J. Reprod. Fertil. 4: 175-188.

Petry, D. B., and R. K. Johnson. 2004. Responses to 19 generations of litter size selection in the Nebraska Index line. I. Reproductive responses estimated in pure line and crossbred litters. J. Anim. Sci. 82: 1000-1006.

Pope, C. E., R. K. Christenson, V. A. Zimmerman-Pope, and B. N. Day. 1972. Effect of number of embryos on embryonic survival in recipient gilts. J. Anim. Sci. 35: 805-808.

Pope, W. F. 1994. Embryonic mortality in swine. In: M. T. Zavy and R. D. Geisert (eds.) Embryonic Mortality in Domestic Species. p 53-77. CRC Press, Boca Raton, FL.

Quiniou, N., J. Dagorn, and D. Gaudré. 2002. Variation of piglets' birth weight and consequences on subsequent performance. Livest. Prod. Sci. 78: 63-70.

Reynolds, L. P., S. P. Ford, and C. L. Ferrel. 1985. Blood flow and steroid and nutrient uptake of the gravid uterus and fetus of sows. J. Anim. Sci. 61: 968-974.

Reynolds, L. P., and D. A. Redmer. 1995. Utero-placental vascular development and placental function. J. Anim. Sci. 73: 1839-1851.

Reynolds, L. P., and D. A. Redmer. 2001. Angiogenesis in the placenta. Biol. Reprod. 64: 1033-1040.

Roehe, R. 1999. Genetic determination of individual birth weight and its association with sow productivity traits using Bayesian analyses. J. Anim. Sci. 77: 330-343.

Ruíz-Flores, A., and R. K. Johnson. 2001. Direct and correlated responses to two-stage selection for ovulation rate and number of fully formed pigs at birth in swine. J. Anim. Sci. 79: 2286-2297.

Rydhmer, L. 2000. Genetics of sow reproduction, including puberty, oestrus, pregnancy, farrowing and lactation. Livest. Prod. Sci. 66: 1-12.

Schneider, H. 1991. Placental transport function. Reprod. Fertil. Dev. 3: 345-353.

See, M. T., J. W. Mabry, and J. K. Bertrand. 1993. Restricted maximum likelihood estimation of variance components from field data for number of pigs born alive. J. Anim. Sci. 71: 2905-2909.

Sherer, D. M., and O. Abulafia. 2001. Angiogenesis during implantation, and placental and early embryonic development. Placenta 22: 1-13.

Smith, G. C. S., E. J. Stenhouse, J. A. Crossley, D. A. Aitken, A. D. Cameron, and J. M. Connor. 2002. Early-pregnancy origins of low birth weight. Nature 417: 916.

Southwood, O. I., and B. W. Kennedy. 1990. Estimation of direct and maternal genetic variance for litter size in Canadian Yorkshire and Landrace swine using an animal model. J. Anim. Sci. 68: 1841-1847.

Southwood, O. I., and B. W. Kennedy. 1991. Genetic and environmental trends for litter size in swine. J. Anim. Sci. 69: 3177-3182.

Spencer, T. E., and F. W. Bazer. 2004. Uterine and placental factors regulating conceptus growth in domestic animals. J. Anim. Sci. 82 (E. Suppl.): E4-E13.

Sterle, J. A., T. C. Cantley, W. R. Lamberson, M. C. Lucy, D. E. Gerrard, R. L. Matteri, and B. N. Day. 1995. Effects of recombinant porcine somatotropin on placental size, fetal growth, and IGF-I and IGF-II concentrations in pigs. J. Anim. Sci. 73: 2980-2985.

Stroband, H. J. W., and T. Van der Lende. 1990. Embryonic and uterine development during early pregnancy. J. Reprod. Fert.: 261-277.

Tess, M. W., G. L. Bennett, and G. E. Dickerson. 1983. Simulation of genetic changes in life cycle efficiency of pork production. II. Effects of components on efficiency. J. Anim. Sci. 56: 354-368.

USDA. 2002. Part III: Reference of swine health and environmental management in the United States, 2000. USDA:APHIS:VS, CEAH, National Animal Health Monitoring System. #N361.0902, Fort Collins, CO.

Vallet, J. L. 2000. Fetal erythropoiesis and other factors which influence uterine capacity in swine. J. Appl. Anim. Res. 17: 1-26.

Vallet, J. L., and R. K. Christenson. 1993. Uterine space affects placental protein secretion in swine. Biol. Reprod. 48: 575-584.

Vallet, J. L., K. A. Leymaster, J. P. Cassady, and R. K. Christenson. 2001. Are the hematocrit and placental efficiency selection tools for uterine capacity in swine? J. Anim. Sci. 79 Suppl. 2: 89.

van Arendonk, J. A. M., C. van Rosmeulen, L. L. G. Janss, and E. F. Knol. 1996. Estimation of direct and maternal genetic (co)variances for survival within litters of piglets. Livest. Prod. Sci. 46: 163-171.

van Oijen, M. A. A. J., W. J. Koops, T. Zandstra, and B. Kemps. 1993. Modelling fetal growth in pigs. Anim. Prod. 57: 447-453.

Vonnahme, K. A., and S. P. Ford. 2003. Placental vascular endothelial growth factor receptor system mRNA expression in pigs selected for placental efficiency. J Physiol 554.1: 194-201.

Vonnahme, K. A., and S. P. Ford. 2004. Differential expression of the vascular endothelial growth factor-receptor system in the gravid uterus of Yorkshire and Meishan pigs. Biol. Reprod. 71: 163-169.

Vonnahme, K. A., M. E. Wilson, and S. P. Ford. 2001. Relationship between placental vascular endothelial growth factor expression and placental/endometrial vascularity in the pig. Biol. Reprod. 64: 1821-1825.

Wang, T., G. L. Chou, C. Y. Chen, and R. J. Xu. 2003. The piglet as a model for studying intrauterine growth retardation. In: R.-J. Xu and P. Cranwell (eds.) The Neonatal Pig. Nottingham University Press, Nottingham.

Webb, A. J. 1998. Objectives and strategies in pig improvement: An applied perspective. J. Dairy Sci. 81: 36-46.

Whitelaw, P. F., and B. A. Croy. 1996. Granulated lymphocytes of pregnancy. Placenta 17: 533-543.

Wilson, M. E., N. J. Biensen, and S. P. Ford. 1999. Novel insight into control of litter size in pigs, using placental efficiency as a selection tool. J. Anim. Sci. 77: 1654-1658.

Wilson, M. E., N. J. Biensen, C. R. Youngs, and S. P. Ford. 1998. Development of Meishan and Yorkshire littermate conceptuses in either a Meishan or Yorkshire uterine environment to day 90 of gestation and to term. Biol. Reprod. 58: 905-910.

Winther, H., A. Ahmed, and V. Dantzer. 1999. Immunohistochemical localization of vascular endothelial growth factor (VEGF) and its two specific receptors, Flt-1 and KDR, in the porcine placental and non-pregnant uterus. Placenta 20: 35-43.

Wise, T. H., and R. K. Christenson. 1992. Relationship of fetal position within the uterus to fetal weight, placental weight, testosterone, estrogens, and Thymosin β4 concentrations at 70 and 104 days of gestation in swine. J. Anim. Sci. 70: 2787-2793.

Wise, T. H., A. J. Roberts, and R. K. Christenson. 1997. Relationships of light and heavy fetuses to uterine position, placental weight, gestational age, and fetal cholesterol concentrations. J. Anim. Sci. 75: 2197-2207.

Wootton, R., I. R. McFadyen, and J. E. Cooper. 1977. Measurement of placental blood flow in the pig and its relation to placental and fetal weight. Biol. Neonate 31: 333-339.

Wrathall, A. E. 1971. Prenatal survival in pigs. Part 1. Ovulation rate and its influence on prenatal survival and litter size in pigs. In: Review Series No 9, Farnham Royal, England

Wu, M. C., M. D. Hentzel, and P. Dziuk. 1987. Relationship between uterine length and number of fetuses and prenatal mortality in pigs. J. Anim. Sci. 65: 762-770.

Wu, M. C., M. D. Hentzel, and P. J. Dziuk. 1988. Effect of stage of gestation, litter size and uterine space on the incidence of mummified fetuses in pigs. J. Anim. Sci. 66: 3202-3207.

Zumkeller, W. 2000. The role of growth hormone and insulin-like growth factors for placental growth and development. Placenta 21: 451-467.

VITA

Henry Mesa Echeverri was born in Bogotá, Colombia on March 24 of 1972. When he was 2 years old, his parents moved to the city of Manizales where he was raised. He received a degree in Veterinary Medicine and Animal Science from the Universidad de Caldas in 1995. He then received a scholarship from the COLCIENCIAS-FULBRIGHT-LASPAU program to pursue his graduate studies. He received a Master of Science degree in Animal Science in 2002 and a Doctor of Philosophy degree in Animal Science in 2004 from the University of Missouri-Columbia. He married Catalina Valencia in 1998.