Pre-natal Programming of Variation in Post-Natal Performance – How and When?

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Introduction

As intensive pork production systems continue to evolve, increasing attention is being paid to the concept of segregated management systems. The reasons for adopting segregated production flows vary, but the underlying principle remains the same – the net advantages that come from managing particular subpopulations of the pork production chain. Segregation may be a spatial concept, in a geographic sense, to improve the control of disease transmission at different levels of the production pyramid. Increasingly, segregation involves separation of sub-populations on the basis of their susceptibility to disease challenges compared to say more mature animals, or because this segregation allows specialized management to be applied in a cost-effective way to these segregated populations. Segregation in this instance can be on-site within a farm, or even within-barn, depending on the goals and situation.

To begin this review, the overall production advantages that might result from segregated production management will be briefly considered, and from a number of perspectives may have little to do with any inherent differences in the growth potential in individual pigs, or sub-populations of pigs. However, there appears to be a substantial area of conceptual overlap, in which the advantages of adopting segregated management of sows and their off-spring may be intimately linked to growing evidence for pre-natal programming of post-natal development. The origins of these programming effects may be very different and in the second part of this review we will address this topic from a biological perspective. Finally, we will return to a consideration of segregated management systems that takes full account of recent information on the biology of pre-natal programming effects. We hope this discussion will open the minds of those involved in integrated systems of pork production and processing to an intriguing number of possibilities that exist to improve the consistency and quality of pork as a competitive product in the world food market place.

Approaching the Question from the Perspective of Production Management

As reviewed by Moore (2005), the origins of segregated parity management systems vary, and have initially been directed to improving the management of the gilt and first litter sow. However, this trend has also simultaneously recognized the problems of co-mingling the progeny of different parity sows, and the advantages to be gained from adopting segregated nursery systems for at least the progeny of parity 1 sows, compared to the progeny of higher parity females. The latter strategy was largely driven by the observation of higher mortalities encountered when parity 1 and higher offspring were co-mingled in the same nurseries. This appeared to be mainly due to the detrimental influence that the higher risk parity 1 offspring brought to the offspring from more mature sows, rather than even worse performance by the parity 1 offspring per se. These concepts were expanded in the discussion of Deen (2005), who discussed the risk factors associated with offspring born in the lower percentile of birth weights per se. By definition, the proportion of offspring from gilts litters falling into these lower weight percentiles is higher (**Figure 5**). Therefore, there is good reason to think that segregated management of these offspring at the nursery level will bring overall improvements to a production system.

Many of the production advantages of segregated parity management of litters born have initially been thought to reflect better management of immune status and pre-weaning survival. However, consistent with the concept of pre-natal programming effects discussed later in this review, parity 1 segregation may also address less obvious differences in post-natal growth potential. These differences may be open to cost effective manipulations much later in the grow-finish stage. For example the opportunity to take advantage of responses to specialized diets and use of growth partitioning agents, that are particularly cost-effective in slower growing, less well-muscled, individuals. At the other end of the breeding herd distribution, Boyd et al. (2006) discussed strategies for improving the provision of micro-nutrients to older “geriatric” sows to maintain their productivity. This additional level of parity segregation seeks to address overall under-formulation of diets for mature sows relative to their metabolic requirements. However, given the changing dynamics of pre-natal loss discussed later, it is relevant to recognize Boyd’s suggestion that the inflammatory response occurring in older females may be open to therapeutic treatments. Collectively, these aspects of segregated parity management may open a Pandora’s box of functional nutrients that will be cost-effective when applied to sows at specific stages in their reproductive life cycle. In all these discussions, there should be as much focus on the quality, as on the quantity, of pigs produced per sow lifetime.

▪ Approaching the Problem from a Biological Perspective

In domestic species like the pig, the number of offspring born is an important economic trait, and the components of litter size (ovulation rate, embryonic survival and uterine capacity) responsive to genetic selection are well established (Johnson et al., 1985, 1999). However, as selection for ovulation rate has been associated with selection against early embryonic survival, and because birth weight decreased as litter size increased, Johnson et al. (1999) concluded that selection for uterine capacity might be the most productive approach in genetic selection programs. A recent study of associations among within-litter variation in birth weight and pre-weaning survival and weight gain, also led to the conclusion that selection for increased litter size that results in more low-birth-weight piglets may not be beneficial, unless measures are taken to improve the survival of the low-birth-weight offspring (Milligan et al., 2002). Thus, both the developmental competence of the pigs born, as well as the size of the litter, needs critical consideration.

Existing literature indicates that a considerable amount of the variation in growth performance after birth may be largely determined, and essentially pre-programmed, during fetal development in the uterus (Foxcroft and Town, 2004). Furthermore, it is likely that these pre-programmed limitations in growth performance will only finally express themselves in the late grower and early finisher stage of production. There is also preliminary evidence that differences in fetal development can affect postnatal growth performance in the absence of any associated effects on birth weight (Town, 2004). Therefore, from a practical perspective, sorting pigs by weight at the nursery and grower stages will not resolve the variation in growth performance that is still an inherent characteristic of particular pigs or litters. In this review, of the biological basis for pre-natal programming, which expands on the review of Foxcroft et al. (2006), we will discuss the concept that ***"an inability to compensate for either, 1) direct epigenetic effects on embryonic development related to previous catabolism in the sow before breeding or 2), indirect negative effect of intra-uterine crowding on placental development in early pregnancy, leads to reprogramming of fetal development and poorer post-natal growth performance and meat quality at slaughter"***.

The effects of prenatal programming on postnatal performance are not limited to effects on muscle development and growth. As reviewed by Harding et al.

(2006a,b), the earlier epidemiological studies in human infants born with phenotypic characteristics indicating intra-uterine growth retardation (IUGR) had an increased risk of developing cardiovascular disease as adults (Barker et al., 1989, 1990). This and other epidemiological studies led to the “Barker hypothesis” (Barker, 1994) linking pre-natal programming of the fetus to lifetime health outcomes. The implications of prenatal programming for postnatal health outcomes are just as real. Harding et al. (2006a,b) discussed this in the context of development of the immune system and early postnatal survival. Furthermore, analysis of brain sparing effects that are indicative of IUGR showed that the organs most notably affected in stillborn pigs with low birth weight were the heart, liver and spleen. These complications undoubtedly underlie the problems of managing low birth weight pigs through the lactation and nursery stages of production, and provides the rationale for adopting segregated parity management of nursery flows as discussed by Moore (2005).

▪ Uterine Capacity as the Ultimate Limitation on Litter Size

The concept of uterine capacity was established using different experimental approaches to study effects of uterine crowding in the pig. These included uterine ligation, oviduct resection, unilateral hysterectomy and ovariectomy (UHO), super-ovulation and embryo transfer, and led to the conclusion that when the number of embryos exceeded 14, intrauterine crowding was a limiting factor for litter size born (Dziuk, 1968). Bazer et al. (1969 a, b) also concluded that increased embryonic loss, associated with a greater number of embryos in the uterus, was due to maternal limitations and not to inherent limitations of the embryo. They suggested that two physiological mechanisms might be involved. Initially, embryo selection might be the result of competition among embryos for some biochemical factor in the uterus necessary for their continued development. However, in later gestation, intrauterine competition for the establishment of adequate surface area for nutrient exchange between fetal and maternal circulations may act to limit litter size.

In the context of variation in development in the uterus, the concept has been advanced that mechanisms promoting competition among embryos in the pre-implantation period will act to reduce within-litter variation in development by selectively removing the least developed embryos (van der Lende et al., 1990). Nevertheless, the more recent results of Père et al. (1997) confirm that, even in sows with "normal" ovulation rates, uterine capacity can affect both litter size and the average birth weight of the litter. Furthermore, information from large populations of higher parity commercial sows, supports our central hypothesis that the dynamics of in-utero development tends to become more variable as sows advance to higher parities. In turn, we believe this creates greater variation in the birth weight characteristics of the litters born and unresolved problems for the appropriate post-weaning management of these litters.

When does uterine capacity impact fetal survival and development?

Fenton et al. (1970) determined that uterine capacity only becomes a limiting factor for fetal survival after d 25 of gestation. Knight et al. (1977) further defined d 30 to 40 of gestation as the critical period when uterine capacity exerts its effects. Subsequent studies in both intact and UHO females support this conclusion (Vallet, 2000). Vallet et al. (2003) suggested that fetal growth rate is less sensitive to intrauterine crowding than placental growth rate and, as in the prolific Meishan female (Ford and Youngs, 1993), within certain limits of uterine capacity an increase in placental efficiency may initially protect the developing fetus from a limitation in placental size. However, in some populations of commercial sows identified in recent studies (Town, 2004), increased placental efficiency did not compensate poor placental development in sows with even relatively modest intra-uterine crowding (15 vs. 9 embryos surviving to d 30) and classic effects of intrauterine growth retardation (IUGR) were present at d 90 of gestation.

In the context of results from earlier studies of within-litter variation in prenatal development (Adams, 1971; Widdowson, 1971; Hegarty and Allen, 1978; Flecknell et al., 1981), Wooton et al. (1983) suggested that the extremes of IUGR or "runting" were identified within a discrete sub-set of fetuses. Furthermore, based on data from subsequent studies of the association between within-litter differences in prenatal development and postnatal survival and growth, van der Lende and de Jager (1991) concluded that the lower pre-weaning growth of the runt pigs born could not be entirely explained on the basis of their lower birth weight and suggested that IUGR or runting had a more complex effect on the developmental potential. Interestingly, data from the same laboratory led to the suggestion that the extent of IUGR within a litter was associated with specific patterns of embryonic survival (van der Lende et al., 1990) and the larger the litters were in the uterus, the greater the chance that runt fetuses would be present. Furthermore, these data were consistent with the conclusion that within-litter variation in development was already established at the early fetal stage (d27 to 35) of gestation.

Changing Patterns of Pre-natal Loss and Developmental Potential

Pre-implantation embryonic losses are still considered to be the largest proportion of prenatal loss in the pig, with some lesser loss in the post-implantation period that will ultimately reflect uterine capacity (as reviewed by

Ashworth and Pickard, 1998). In commercial practice, this generalization likely reflects the situation in gilts in which ovulation rates of 10 to 15, associated with some degree of embryonic loss, are the primary factors limiting litter size. Weaned, first parity sows also tend to fall into this category. Although ovulation rate may be higher (15 to 20 ovulations), many sows tend to be in a catabolic state, and this generally decreases embryonic survival to 60 to 65% (Foxcroft, 1997). However, the dynamics of prenatal loss in existing commercial dam-lines may be changing (Foxcroft, 1997; **Figure 1**). In these populations, it appears that several generations of direct selection for litter size have indirectly resulted in a discrepancy between the number of conceptuses surviving to the post-implantation period and uterine capacity. As a consequence of markedly increased ovulation rates, associated with good or even modest embryonic survival in the pre-implantation period, the number of embryos surviving to the immediate post-implantation period (d25 to 30) initially greatly exceeds uterine capacity. As a result, a substantial proportion of prenatal loss is now occurring in the post-implantation period in these animals.

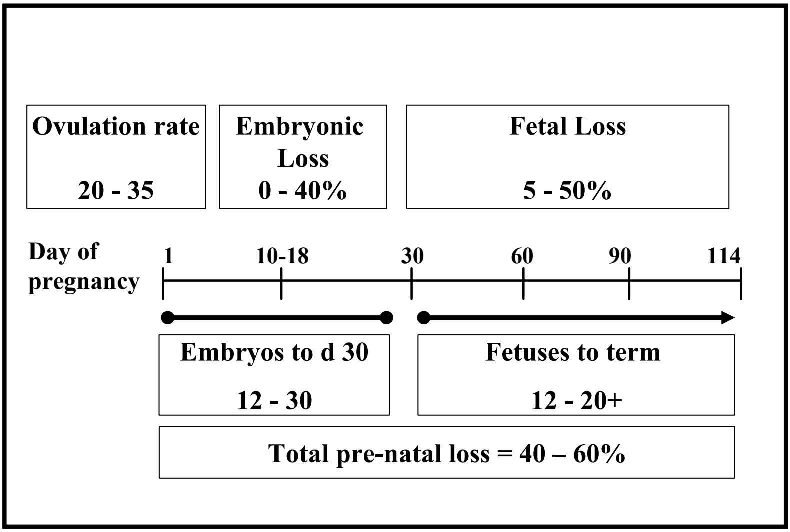

Figure 1. Schematic representation of the changing pattern of prenatal loss observed in multiparous sows in recent studies. Ovulation rate from total number of corpora lutea present at time of embryonic or fetal dissection.

Even in individual gilts with 20 or more ovulations, embryonic survival rate can be 100% at d28 of gestation (Almeida et al., 2000), whereas average first litter size is still only 10 to 12 piglets. In higher parity females, the situation may be even more extreme, with an increasing proportion of higher parity sows having more than 25 ovulations (**Figure 2**). Despite relatively poor embryonic survival to d30, numbers of conceptuses in the uterus at d30 (15 or more) still exceeded uterine capacity for normal development. Consistent with the literature reviewed earlier, uterine capacity then exerted its effects and a significant reduction in the number of conceptuses occurs by d45 to 50 of gestation. An example of these changing trends can be seen in the data in **Table 1**, which represent the same sub-populations of sows in different parity groupings shown in Figure 2, but only includes data from sows having ovulation rates greater than 25. As we have shown in earlier studies, even modest increases in uterine crowding around d30 of gestation decreased placental volume (Almeida et al., 2000) and placental weight (Vonnahme et al., 2002) and this restriction in placental weight at d30 persisted to d90 (Town et al, 2004; **Figure 3**).

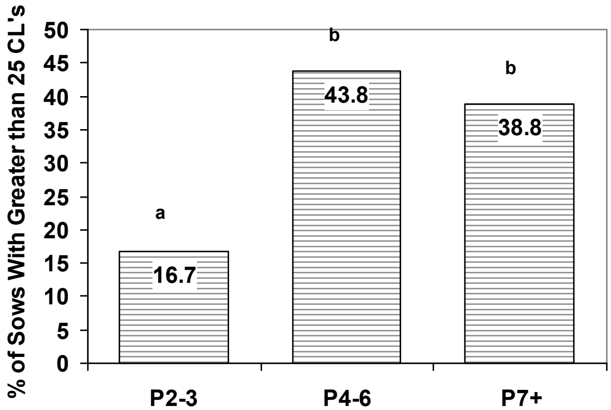

Figure 2. Percent of sows with ovulation rates 25 or higher within parity (P) grouping. (SRTC, unpublished , 2006) (N = 504)

Table 1. Ovulation rate and numbers of viable embryos at day 30 and fetuses at d50 for sows with ovulation rates 25 or higher in parities 2-3, 4-6 and 7+. (SRTC, unpublished, 2006)

Variable	P2-3	P4-6	P7+
Ovulation Rate	27.0	28.3	27.4
Viable Embryos - d30	16.8	16.8	13.3
Viable Fetuses - d50	15.3	11.9	10.5

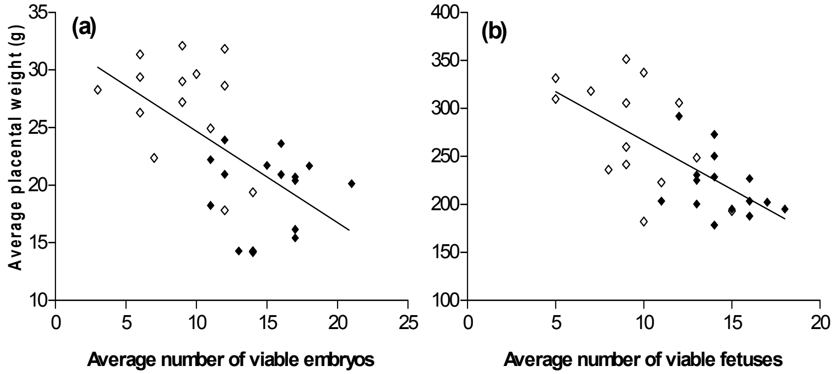

Figure 3. Correlation between average placental weight and (a) number of viable embryos at d 30 of gestation (r = -0.61; P = 0.0003) and (b) number of viable fetuses at day 90 of gestation (r = -0.67; P < 0.0001) (Control, CTR ◆; Unilateral oviduct ligated, LIG sows ◇) (Town et al., 2004).

Although the size and weight of the embryo was not seen to be affected by crowding up to d44 of gestation, potential impacts on fetal development need careful study. If placental compensatory mechanisms are not adequate, crowding of the uterus in the early post-implantation period of gestation may affect fetal development of surviving conceptuses in a manner analogous to IUGR. This raises important questions for both fetal and postnatal development. In the context of commercial grow-finish performance, a specific interest in effects on the development of fetal muscle fibers, which start to differentiate around d35 of gestation in the pig, is particularly important. In contrast to situations in which the occurrence of IUGR is limited to a discrete subpopulation of runt fetuses (Royston et al., 1982; Wooton et al., 1983), we hypothesized that ***"a changing pattern of embryonic loss that results in uterine crowding in early gestation would produce a more uniform effect on placental development that would affect the development of all surviving fetuses"*** (Foxcroft, 1997; Foxcroft and Town, 2004).

Implications of Crowding for Muscle Development in the Pig

A series of studies in the pig have demonstrated that maternal nutrition during gestation has an effect on piglet birth weight, and that low birth weight is primarily associated with a reduced number of secondary muscle fibers

(Handel & Stickland, 1987; Dwyer et al., 1994). Consistent with earlier data of Hegarty and Allen (1978) indicating that runts in the litter have reduced muscle growth potential, Dwyer et al. (1993) also established a positive correlation between the total number of muscle fibers and postnatal growth potential, and littermates with a high numbers of fibers grew faster and more efficiently than littermates with a lower number of fibers. Dwyer et al. (1994) further demonstrated that the effect of maternal nutrition occurred between d 25 and 50 of gestation, the period immediately preceding secondary muscle fiber hyperplasia.

Effects of maternal nutrition during gestation on fetal development are widely reported, and this area of literature was the subject of an excellent review by Robinson et al. (1999). Furthermore, Maltin et al. (2001) extensively discussed the impact of manipulating myogenesis by various intra-uterine manipulations on subsequent muscle development. The early period of myogenesis, involving the differentiation of primary muscle fibers, is generally considered to be resistant to nutritional manipulation, whereas nutritional effects on differentiation and hyperplasia of secondary fibers have been demonstrated between d25 and 90 of gestation. However, Rehfeldt and Khun (2006) suggest that nutrition may also affect the number of primary fibers differentiating.

From the perspective of using nutritional intervention and other treatments to reduce the variation in birth weight and postnatal growth within litters, it is interesting to note that the greatest reported impact of increased maternal nutrition (Dwyer et al., 1994), treatment with exogenous somatotropin during early gestation (Rehfeldt et al., 2001), and breed of sow (Ashworth et al., 1998), was on the smallest pigs within the litter. These results suggest that relative under-nutrition of the smallest fetuses in the uterus is the driver of low birth weight and poor postnatal growth performance. Furthermore, the early data of Widdowson (1976) showed that if limited nutrition initially results in the runting of pigs before and after birth, high subsequent feed intakes do not result in a normal development during compensatory growth, again implying that some form of intra-uterine fetal re-programming had occurred. Based on the schematic representation of muscle fiber development shown in **Figure 4**, this led to the central hypothesis tested in a number of our recent studies, that ***"by detrimentally affecting placental size in early gestation, uterine crowding will also affect fetal organ development and the number and type of muscle fibers, analogous to the situation of IUGR in nutritionally challenged sows".***

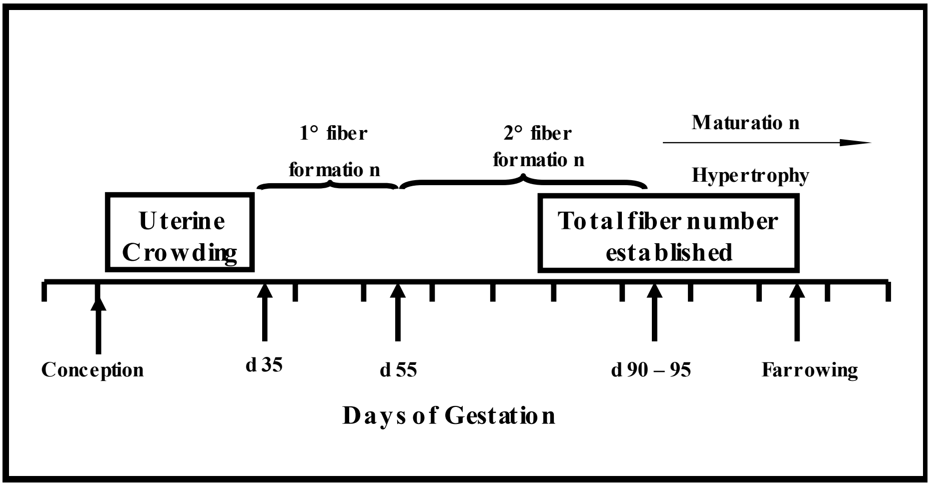

Figure 4. Schematic representation of the time-course of muscle fiber development in the pig, indicating a critical window in early pregnancy when crowding effects limit placental development and set in place detrimental effects on fetal development and lifetime growth performance.

Preliminary data from an initial experiment involving analysis of fetal and placental weights at term, and associations with IUGR effects measured in the neonate, indicated that even when the number of conceptuses in the uterus does not significantly affect birth weight, crowding nevertheless results in measurable IUGR in the fetus (Town, 2004). In another study, unilateral oviduct ligation was used as a surgical approach to vary the number of fetuses developing in the uterus. Even though the uterine crowding observed was not at the level that probably occurs in existing commercial dam-line sows, a higher number of fetuses in the uterus resulted in measurable developmental changes. As shown in Figure 3, there were again effects of increasing numbers of conceptuses and fetuses in the uterus on placental development (Town et al., 2004). Furthermore, in the same study, among the various measures of IUGR, there were specific effects on the brain:muscle weight ration, brain to muscle fiber number ration, estimated total number of secondary muscle fibers, and associated differences in the wet weight and cross sectional area of the semitendinosus muscle (**Table 2**). ***This provides some of the first evidence that the variation in the number of conceptuses surviving to the post-implantation period will affect not only placental, but also fetal, development.*** In the literature cited earlier, comparable effects on muscle fiber development, created by maternal under-nutrition during gestation, resulted in lifetime limitations in growth performance and muscle mass. It is thus reasonable to assume that the observed effects of embryo crowding in the uterus on the number of secondary muscle fibers will be associated with similar limitations in post-natal growth performance.

Table 2. Muscle fiber development data (means ± SEM) for day 90 fetuses from control (CTR) and unilaterally oviduct ligated (LIG) sows (N=28). Muscle data were derived from analysis of the semitendinosus (ST) muscle. (after Town et al., 2004)

Parameter	**Treatment group** **CTR (n=14)** **"*Crowded*"**	 **LIG (n=14)** **"*Non Crowded*"**
Muscle weight (g)	1.25 ± 0.06a	1.47 ± 0.09b
Muscle CSA (mm2)	47.71 ± 2.85a	58.78 ± 2.65b
Brain: liver weight ratio	1.17 ± 0.04a	0.97 ± 0.04b
Brain: ST muscle weight ratio	10.49 ± 0.43a	9.25 ± 0.33b

Means in rows with different post-scripts a, b were significantly different ($P < 0.05$)

The extent of uterine crowding that we have managed to create in the above study, and a number of comparable studies in both gilts and higher parity sows, has been less than the crowding we predict in at least a sub-population of higher parity sows in existing commercial dam-lines (Vonnahme et al, 2002; Foxcroft and Town, 2004). Nevertheless, we appear to be able to demonstrate that differences in intra-uterine crowding in the pre-natal period in individual females have consequences for the pattern of fetal muscle fiber development. Furthermore, in embryonic tissues harvested from the sows reported in the study of Town et al. (2004), we have since been able to study the effect of moderate crowding on the expression of the myogenic regulatory factors *myogenin* and *myoD*. This study provided direct evidence that crowding at d30 of gestation can impact the differentiation of muscle fibers through reductions in *myogenin* expression in this experimental paradigm, and, interestingly, most of the overall litter effect was found to originate from selective effects on *myogenin* expression in the male embryos in the litter (Tse, 2005).

Together with the earlier literature reviewed above, these results support our earlier suggestion that environmental influences on embryonic and fetal development are likely an important component of the biological origins of the variability in post-natal growth performance encountered in the pork production industry (Foxcroft and Town, 2004).

▪ Catabolic (Epigenetic) Effects on Subsequent Embryonic Survival and Development.

Increased catabolism during the last week of lactation in primiparous sows is known to reduce embryonic survival and development to d30 of gestation in the subsequent litter (Foxcroft, 1997). Using a refinement of the experimental paradigm reported by Zak et al. (1997), Vinsky et al. (2006a) confirmed a detrimental effect of catabolism in late lactation on embryonic survival. The greater deficit in overall net energy balance in feed restricted sows led to increased loss of both protein and fat mass during lactation. The thresholds of maternal tissue loss, above which there was an increased likelihood of embryonic loss and developmental delays, were consistent with thresholds reported by Clowes et al. (2003a,b). Furthermore, Vinsky et al. (2006a) used sex-typing to demonstrate that the increased loss of embryos before d 30 of gestation was female biased (**Table 3a**).

The etiology of this selective loss of female embryos before d 30 of gestation is unknown. Vinsky et al. (2006a) suggested that female embryo loss could be due to epigenetic defects originating from the oocyte, as the timing of feed restriction coincides with the final stages of oocyte maturation (Foxcroft 1997) and with epigenetic establishment seen in other species (Lucifero et al. 2002). Based on the data of Vinsky et al. (2006b), we suggested that a sub-population of embryos within a proportion of litters from nutritionally restricted sows were epigenetically defective and lost before d 30 of gestation and surviving embryos in these sows were also developmentally retarded. Heterogeneity and competition within litters is believed to be a primary cause of decreased litter survival before d 30 of gestation, and has been suggested to have an epigenetic component (Geisert and Schmitt 2002). By studying epigenetic traits of early stage embryos further, it should be possible to determine the ontogeny of epigenetic defects leading to changes in embryonic survival and development. Such epigenetic effects of sow catabolism on embryonic development and survival clearly represent a very different set of dynamics that will affect the characteristics of the litters born. In contrast to the effects of intra-uterine crowding discussed above, these effects of previous catabolism during the period of follicular development are seen as direct effects on embryonic development, with little evidence of effects on placental development (**Table 3b**). The term “phenotypic plasticity” has been used recently to capture the concept that environmental effects can result in different phenotypic outcomes in individuals that have identical genotypes.

Table 3. Gender-specific loss of embryos in sows made increasingly catabolic in the last week of a three-week lactation (Vinsky et al., 2006).

a) Least square means (± s.e.m.) for sow reproductive performance and embryonic survival data.

Item	Control (*n* = 16)	Restrict (*n* = 17)
Wean-to-oestrous interval (days)	5.3 ± 0.3	5.4 ± 0.3
Ovulation rate	18.3 ± 0.7	18.2 ± 0.6
Pregnancy rate (% of sows bred)	100	100
Day of gestation at slaughter	30.3 ± 0.2	30.1 ± 0.2
Number of live embryos*	14.4 ± 0.8	12.3 ± 0.8
Embryonic survival rate (%)*	79.2 ± 4.0	67.9 ± 3.9
Number of males	7.7 ± 0.6	7.5 ± 0.6
Number of females*	6.5 ± 0.6	4.7 ± 0.6

*$P < 0.05$ compared with Control sows.
Analysis of embryonic survival rate performed on arcsin transformed data

b) Least-square means (± s.e.m.) for sex-specific embryo characteristics collected at day 30 of gestation

Characteristic	Control males (*n* = 124)	Restrict males (*n* = 128)	Control females (*n* = 104)	Restrict females (*n* = 80)
Embryo weight (g)**	1.55 ± 0.07	1.39 ± 0.07	1.51 ± 0.07	1.37 ± 0.07
Crown–rump length (mm)*	23.87 ± 0.44	23.21 ± 0.43	23.75 ± 0.44	23.13 ± 0.43
Allantochorion volume (mL)	251.31 ± 17.86 (*n* = 59)	225.96 ± 17.29 (*n* = 58)	235.88 ± 17.86 (*n* = 46)	233.11 ± 17.29 (*n* = 39)
Placental weight (g)	22.87 ± 1.89 (*n* = 75)	23.38 ± 1.89 (*n* = 44)	22.31 ± 1.89 (*n* = 49)	22.13 ± 1.89 (*n* = 36)

*$P < 0.05$, **$P < 0.005$ difference only between treatments.

Implications for Developing Better Production Systems

If pre-natal development can have measurable effects on post-natal variation in growth performance, what are the possible practical resolutions to this problem? Firstly, it is likely that certain categories of sows, like high parity sows with increased ovulation rates and few problems with lactational catabolism, will produce the greatest incidence of altered developmental potential due to overcrowding in the uterus. In the extreme situations, developmental limitations will also be associated with low birth weights, and at least this population of pigs could be designated to segregated production flows at the nursery and grow-finish stages.

The Fate of the Runt Pig

The information reviewed above also indicates that the growth potential of runt pigs within a litter will forever be compromised. Therefore, simply mixing these pigs with smaller weight pigs that were not the runts within their respective litters, does not recognize that the developmental potential of these two sets of pigs will be very different. If we accept that runting and other forms of IUGR actually limits the number of muscle fibers, then it is probably unrealistic to consider that nutritional intervention can do much to alleviate this problem. Both muscle mass and meat quality at slaughter will be negatively impacted in runt pigs (see review of Rehfeldt and Ender, 2005; Bee, 2007 in these proceedings). Use of expensive nutritional programs to try and correct this problem may not, therefore, be money well spent. Because other data indicate that the survivability of runt pigs may also be seriously compromised, special attention may also be needed to keep them alive through the weaning and nursery stages of production.

Implications for Selection of Replacement Gilts as Terminal-line Production Females

Paradoxically, in selecting gilts for terminal line production when internal multiplication of replacement gilts occurs, managers must also be alert that low birth and weaning weights will tend to be inversely related to litter size born (**Figure 5**). There is longstanding evidence that the rate of sexual maturity and lifetime productivity of gilts raised in different sized litters is adversely affected by post-natal growth performance (Nelson and Robison, 1976; Van der Steen, 1985; Jorgenson, 1989). This impact of low birth weight from gilts born in large litters can be a major component of the effect of litter of origin in experiments where littermates are allocated to different treatments and litter is included in the statistical analysis. It is not surprising, therefore, that several publications report effects of litter of origin on a whole range of biological and production characteristics when included in the analytical model (Deligeorgis et al., 1984, 1985; Almeida et al., 2001). Furthermore, as discussed above, more recent research suggests that the lower initial growth performance is very likely also an imprinted effect due to competition in the uterus. In the most controlled selection systems, developed in collaboration with commercial producers, gilts born in gilt litters invariably weigh less than 1.5 kg at birth and are not selected as breeding herd replacements, because of the anticipated effects of low birth weight on subsequent growth performance (Moore, C; Robitaille Farms, Quebec; personal communication).

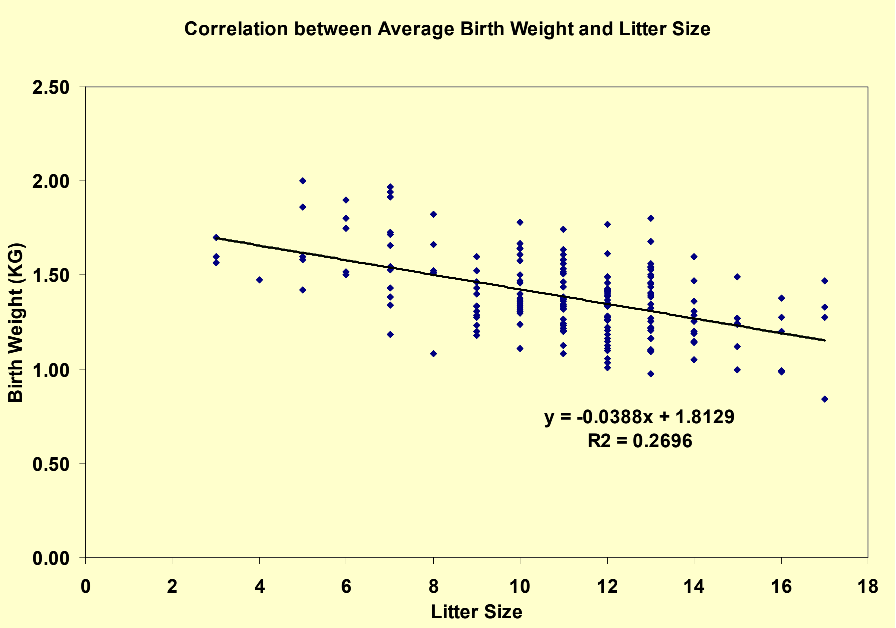

Figure 5. Data from commercial terminal-line gilts showing the distribution of birth weights for their progeny. (SRTC, unpublished production data, 2005-2006)

Implications for the Use of Hyper-prolific Sows for Increasing Litter Size Born

Given the impact of an imbalance between ovulation rate, embryonic survival, and uterine capacity on fetal and post-natal development, the reproductive characteristics of prolific dam-lines need careful consideration. Although the primary goal of increasing the number of pigs born per litter may be achieved, data from some of these prolific dam-lines leads us to suggest that many of the adverse pre-natal programming effects associated with inadvertent crowding of fetuses in the uterus may be prevalent in the mature sows in these populations. A consideration of the proportion of live-born vs. dead-born pigs within the litters of one population of hyper-prolific French sows (**Table 4**) suggests that the growth potential of the live-born pigs that survive to weaning will have been seriously compromised by intra-uterine competition with an increasing number of fetuses born dead. This conclusion is supported by data shown in **Table 5**, from this same population of sows, showing the relative birth weight of pigs born in different sized litters. We are presently investigating the reproductive characteristics of a similar line of French hyper-prolific sows being imported into Canada. Preliminary data (Harding, J.R., personal communication) confirm that in the higher parity sows in this population, high ovulation rates can be associated with substantial crowding of viable conceptuses at d30 of gestation, with obvious implications for deleterious effects of pre-natal programming on post-natal performance. Furthermore, the overall distribution of birth weights in these prolific sows shows a shift to a lower median weight and an increase in variance (Duggan, M., personal communication).

A better understanding of the characteristics of specific hyper-prolific dam-lines is needed. This information, and an increasing focus on the need to maximize total net revenues per sow in terms of the value of saleable pork products, relative to the input costs involved per kg of pork sold, should allow the most commercially acceptable terminal-line dams to be developed in the future. Ultimately, as in the case with the UHO experimental paradigm, selection of sows with increased uterine capacity offers the best opportunity for increasing the number of pigs born per litter without compromising the post-natal growth performance of these pigs. Perhaps at a population level, selection for litter size needs to include data from multiparous sows, with birth weight being used, in additional to litter size born live, as a means of identifying sows in which the dynamics of pre-natal loss does not result in detrimental pre-natal programming effects on post-natal growth potential.

Table 4. Production data recorded for individual hyperprolific white-type sows from commercial units in Brittany, France.[a]

Sow parity	Total pigs born	Pigs born dead	Pigs born live	Adjusted litter size 48 h after farrowing
7	***20***	***6***	***14***	***12***
2	15	2	13	13
5	***19***	***5***	***14***	***11***
2	15	1	14	11
9	***14***	***1***	***13***	***12***
5	***13***	***0***	***13***	***12***
4	19	1	18	13
2	12	0	12	12
5	***13***	***1***	***12***	***10***
5	***18***	***0***	***18***	***11***
4	16	1	15	12
1	10	2	8	12
4	16	0	16	12
5	***18***	***3***	***15***	***11***
8	***22***	***5***	***17***	***11***
5	***13***	***7***	***6***	***12***

[a] Individual higher parity sows (***data shown in bolded italics***) tend to show both an increase in total and dead born pigs per litter. Data are from personal communication (Leveneau, P.).

Table 5. Effect of litter size at birth on the average birth weight of pigs born to the hyper-prolific white-type sows in commercial production in France, for which data are shown in Table 2

Number of pigs in the data set	Average total pigs born	Average birth wt, kg	Percentage of pigs within specific weight ranges			
			< 1.0 kg	1.0 to 1.5 kg	1.5 to 2.0 kg	> 2.0 kg
2,637	12.6	1.49	7	37	43	13
432	17.4	1.27	15	57	26	2

Personal communication, Leveneau, P., France

Implications for the Use of Functional Nutrients to Improve Litter Size Born and Pre-natal Development.

As the different mechanisms mediating 1) effects of inadvertent uterine crowding on IUGR, and 2) epigenetic effects of sow catabolism on re-programmed embryonic development become better understood, the opportunities to ameliorate such effects with specific functional nutrients will also become clearer. The basis for developing functional nutrients as a means of correcting in utero programming of fetal development has become an area of intense interest. The background literature supporting this approach has recently been reviewed by Wu et al. (2006), with a specific focus on applying this information to the use of arginine as a functional nutrient in lactating sows. Further discussion of preliminary results from the use of L-Arginine and the potential application of other functional nutrients were also presented by Smits et al. (2006). These and other nutrient approaches to improving the fertility of the breeding sow offer further opportunities for refining breeding herd management in the future.

▪ Conclusions

The above review hopefully provides the reader with an understanding of the very complex interactions that determine the development of a market pig from conception to consumption. In the new era of epigenetic regulation of pre-natal development, and expanding information on the mechanisms controlling various levels of IUGR, the profound influence that the environment of the sow can have on the phenotypic characteristics of her off-spring are becoming evident. Clearly, simple selection of genetically superior sows and terminal line boars will determine the potential to produce a desired genotype in their terminal line off-spring. However, inappropriate management may interact with this genetic potential to produce a very different outcome. In this review, the profound effects of sow maturity, nutritional management, and their interaction have been considered. Observations from controlled experiments and from the analysis of the reproductive and developmental characteristics of existing commercial dam-line sows indicate the diversity of possible interactions. However, these studies start to provide a better understanding of the reported benefits of segregated parity management. Innovative approaches to addressing the problems, as well as the opportunities, presented by pre-natal fetal programming of post-natal performance will likely be the benchmark of the most profitable pork production systems in the next decade.

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