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The endocrine cycle and the role of nutrition

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A major challenge for the pig industry is to achieve acceptable levels of sow fertility in management situations that are nor primarily designed to optimize sow reproductive performance. For example, the move to SEW systems to maintain improved health status of the weaned pig presents a series of challenges to the breeding herd manager. Faced with the challenge of adapting breeding herd management to meet other production objectives, an understanding of the key biological mechanisms that regulate the fertility of the lactating and weaned sow can be a great asset. On the basis of this understanding, management strategies can be developed that will minimize the detrimental effect of lactation on breeding herd performance. Analysis of most breeding herd records will show that the reproductive performance of the first parity sow after weaning is a major limitation to herd productivity. This may be seen as increased weaning to estrus intervals, decreased conception rates, increased culling rates, and a reduction or only a marginal increase in the size of the second litter. Therefore, this paper will review current knowledge on the endocrine status of the lactating and weaned sow, with particular focus on nutritional effects that may reduce fertility in the first parity female.

The physiology of the lactating and weaned sow

The physiological mechanisms that are the major regulators of reproductive function in the sow during lactation and after weaning can be considered in three categories:

- mechanisms that mediate effects of time after farrowing on the function of the reproductive system;
- mechanisms that mediate effects of suckling as the primary block to reproduction during lactation; and,
- mechanisms that mediate effects of nutrition and metabolic state during lactation and after weaning on sow fertility.

The relative importance of these factors will change, depending on the sexual and physical maturity of the sow and the length of lactation. Therefore, the management of the sow must allow for the dynamic changes over successive lactations. However, in practice, improved management of the first parity sow must be given a high priority.

Effects of time after farrowing on the reproductive system

We must accept that there is an unavoidable period of infertility in the early postpartum period. Pregnancy in large mammals requires massive adaptation on the part of the mother to provide for the needs of the fetus. This long-term commitment terminates in the dramatic changes associated with parturition, not the least of which are the hormonal changes that control the delivery of the young, and the onset of milk production and nursing behavior. Generally, these changes are not conducive to good fertility immediately after birth, and the metabolic demands of lactation—on top of the earlier metabolic demands of gestation—result in a period of lactational anoestrus. During this period the reproductive tract undergoes a period of recovery at all levels and key aspects of this recovery include uterine involution and recovery of the brain and pituitary.

Uterine involution

This term describes the gradual return of the uterus to its non-pregnant state, having increased in all proportions during pregnancy. Although information on uterine involution in the sow is not extensive, the data available suggest that involution is not finally complete until around 21 days postpartum. As suckling is the critical stimulus for rapid uterine involution, early weaning will delay the involution process. Although early weaning studies clearly indicate that complete uterine involution is not essential for the next pregnancy to be established, it is generally accepted that incomplete uterine involution is probably one factor that contributes to poor embryonic survival, and reduced litter size, in early weaned sows.

Recovery of the brain and pituitary

As the sow comes into estrus, the secretion of the pituitary gonadotropic hormones, Luteinizing Hormone (LH), and Follicle Stimulating Hormone (FSH) promotes the growth of pre-ovulatory follicles and may, in part, regulate the number of ovulations that occur (ovulation rate). A major "surge" in LH is also needed to actually cause ovulation. Thus if LH and FSH secretion is limited because the sow is weaned early, there may be consequences for sow fertility. In earlier studies such effects were clearly evident in sows weaned after either 3- or 5-week lactations (Edwards and Foxcroft, 1983a,b). Even more relevant to the early weaned sow situation are the data of Kirkwood et al. (1984), which showed that LH concentrations at estrus were lower in sows weaned at 10 compared to 35 days of lactation. These data indicate that not only the uterus, but also the central components of the reproductive system (the brain and pituitary), need some time to recover after farrowing.

Even this brief review of the biology of the postpartum sow indicates why fertility may be reduced if the sow is weaned very early and bred at the first observed estrus.

Suckling as the primary block to reproductive activity in lactation

The mechanisms mediating the effects of suckling on lactational anestrus were extensively reviewed by Varley and Foxcroft (1990) and Foxcroft et al. (1995). Active LH and FSH secretion can be observed in sows immediately after farrowing and this period has therefore been described as the "hypergonadotrophic" phase of lactation (Britt, 1996). If the litter remains with the sow, this uninhibited period of LH secretion is eventually suppressed around day 3 of lactation, as the inhibitory effects of suckling become established at the level of the brain and pituitary. This would then represent the "hypogonadotrophic" phase. An extension of the "hypergonadotropic" pattern of LH secretion and associated ovarian follicular development, as a result of removing the litter from the sow at farrowing (zero weaning), demonstrates the importance of suckling as the primary inhibitor of LH secretion. Although zero weaning can be associated with observed estrus, in many cases the pattern of follicular development is abnormal and ovulation does not occur. As lactation progresses, there appears to be a gradual increase in LH secretion (a "recovery" phase), as long as the sow does not become seriously catabolic. A number of experiments have suggested that factors that increase LH secretory activity in lactation will also produce increased fertility after weaning, indicating that the priming of the ovary by LH in lactation may be important.

Partial removal of the inhibitory effects of suckling—by reducing the size of the litter suckling (split or partial weaning)—produces a transient increase in LH secretion, but longer lasting effects on ovarian development (Grant, 1989). This suggests that manipulation of litter size before weaning (split weaning) can be an effective management tool for increasing ovarian development and sow fertility. Because the gonadotropin response to split weaning is so transient, Britt (1996) suggested that split weaning should only occur 2 to 3 days before final weaning. Another interpretation of existing data is that any period of reduced suckling will give beneficial results. Clearly, further information is needed to allow the optimal use of split weaning protocols to improve fertility after weaning.

The pattern of follicular development observed during lactation reflects the pattern of gonadotropin secretion. A number of large ovarian follicles may be present immediately after farrowing, but a week later follicular development is minimal. Then, as lactation progresses there is a gradual increase in the number of medium to large sized follicles. The lack of ovarian activity in early lactation appears to be primarily suckling dependent and the suckling-induced inhibition of LH secretion is the primary cause of lactational anestrus. Unfortunately, although we understand something of the mechanisms by which suckling acts on the brain to inhibit LH secretion (Foxcroft,1992), it has not been possible to develop a practical treatment to reliably induce a fertile estrus during lactation. The follicles are responsive to gonadotropins because treatment of sows with eCG (PMSG), or with repeated pulses of Gonadotropin Releasing Hormone (GnRH) to increase LH secretion, results in the growth of ovulatory follicles. However, even if such techniques are used to drive follicular development, the detrimental effects of poor metabolic state in the lactating, primiparous sow discussed later, would probably still result in reduced ovarian responses to such treatments and reduced fertility.

An immediate increase in LH secretion is invariably observed in response to weaning and is the primary stimulus for ovarian follicular development. The magnitude of the increase in LH secretion after weaning has not been consistently related to the weaning-to-estrous interval, or to ovulation rate at first post-weaning estrus. However, as discussed earlier, a number of studies have reported a relationship between the pattern of LH secretion during lactation and fertility after weaning, and there has been one report of a relationship between FSH concentrations after weaning and ovulation rate. Evidence that changes in LH and FSH secretion in late lactation and immediately after weaning affect sow fertility, may explain the efficacy of treating sows with low doses of exogenous gonadotropins (products like PG600) at weaning.

Overall, these data indicate that suckling is the primary inhibitor of the reproductive system during lactation. Therefore, one effective way to improve fertility in the lactating and weaned sow is to further refine techniques such as split weaning, that reduce the inhibitory effects of suckling. Because the phase of lactation induced by the inhibitory effects of suckling coincides with the period when uterine involution may still be incomplete, this is a period in lactation when the reproductive system is particularly inactive. Weaning during this period will predictably result in low fertility and yet, unfortunately, weaning may be preferred in this period in SEW systems.

Effects of metabolic state during lactation and after weaning on sow fertility

Inadequate voluntary feed intake during lactation in first parity sows is often a problem and there is extensive data to show that loss of body condition in lactation can have very negative effects on sow fertility after weaning.

Centrally mediated effects of nutrition

As the pattern of LH secretion is a key regulator of ovarian function, it is not surprising that nutritionally mediated differences in sow fertility after weaning are associated with differences in LH secretion. This point is well illustrated in the results of Zak et al. (1997a), an experiment that involved three patterns of feeding during lactation in primiparous sows. Sows were either fed ad libitum (100%) throughout a 28-day lactation, fed ad libitum from days 1–21 and then restrict fed to 50% of ad libitum feed intake from days 22–28, or restrict fed from days 1–21 and then ad libitum from days 22–28. In this way it was possible to determine whether the pattern of change in the body condition and metabolic state of the sows, as well as the absolute amount of body tissue loss, was affecting subsequent fertility. Notwithstanding the dominant inhibitory effect of suckling, differences in the pattern of feed intake during lactation produced significant effects on episodic LH secretion during lactation and on post-weaning fertility (see **Table 1**). These results clearly indicate that the pattern of metabolic change during lactation can affect different components of sow productivity, such as ovulation rate and embryonic survival (and thus potential litter size), and weaning to service interval (and thus non-productive days).

Work from the University of Minnesota also led to the hypothesis that restricted feed intake and catabolism in early lactation, and the associated reduction in LH secretion, had lasting consequences for the fertility of the sow after weaning (Tokach et al. 1992; Koketsu 1994; Yang, 1998). These data also suggested that reductions in feed intake in the first or second week of lactation has a more profound effect on sow fertility than reductions in feed intake in later lactation. However, our extensive studies on the endocrine mechanisms mediating effects of nutrition on ovarian function in the primiparous sow, led us to conclude that the pattern of LH secretion immediately before weaning is a more critical determinant of subsequent fertility. Also, we know that effects of metabolic state on subsequent fertility involve both central (gonadotropin-mediated), as well as local ovarian, effects (Cosgrove and Foxcroft, 1996; Cosgrove et al., 1997; Foxcroft et al, 1995, 1996).

Locally mediated effects of nutrition

Relatively short-term effects of nutritional state on ovarian function can be found in the work on nutritional flushing in the gilt (Beltranena et al., 1991) and in the studies of Cox and her colleagues on the influence of energy and insulin treatment on the final stages of ovarian follicular development before ovulation (Cox et al., 1987; Matamoros et al., 1990, 1991). Relating these results to the sow, we suggest that periods of catabolism in late lactation, which carry over into the period after weaning when ovarian development occurs, will be most detrimental to fertility. The hormonal status of sows that are catabolic in late lactation supports this idea. Hormones such as insulin and insulin-like growth factor-1 (IGF-1), that are known to act locally to promote ovarian function, are increasingly depressed as sows become more catabolic. If

Table 1. Effects of pattern of feed intake over a 28-day lactation on postweaning fertility in primiparous sows bred at first postweaning estrus.

	Group AA	Group AR	Group RA
Weight loss in lactation (kg)	11.00[a]	21.12[b]	24.75[b]
Backfat loss in lactation (mm)	2.19[c]	4.61[b]	5.38[b]
Ovulation rate	19.86[c]	15.44[b]	15.43[b]
Embryo survival (%) to day 28	87.53[a]	64.43[b]	86.50[a]
Weaning- to- estrous interval (days)	3.7[a]	5.1[b]	5.6[b]

Superscripts [b] and [a] denote treatment differences at P<.002, and [c] denotes differences at P<.05. (from Zak et al., 1997a) this situation applies in late lactation, then the follicles that are "recruited" to ovulate immediately after weaning will have been inadequately primed by these key metabolic hormones. One mechanism by which nutrition affects ovulation rate is by changing the number of maturing follicles available for recruitment into the ovulatory population. Thus, in the sow, the sensitivity of the ovary to gonadotropin stimulation immediately after weaning, and hence the number of follicles that are finally ovulated, will be affected by both the previous and current metabolic status of the sow. For example, reported associations between nutritionally mediated differences in insulin status during lactation and subsequent fertility likely involve direct ovarian effects (see Cox, 1997).

The "imprinting" of follicles in early lactation may have other, lasting, consequences for follicle development at weaning, as the quality of follicles that grow and ovulate is important for normal oocyte maturation and early embryonic development after fertilization (Ding and Foxcroft, 1994). Differences in follicle quality at weaning due to different metabolic states during lactation, and related differences in the quality of oocytes destined to be fertilized, may therefore be another important factor determining subsequent embryonic survival. Data supporting this hypothesis have been reported by both Zak et al. (1997b) and Yang (1998).

Importance of the pattern and duration of nutritionally induced effects

The discussion above highlights the different mechanisms by which changes in metabolic state at all stages of lactation affect the fertility of the sow after weaning. Although the negative effects of marked catabolism in early lactation on embryonic survival can apparently be reversed by feeding to appetite immediately before weaning, effects on ovulation rate apparently cannot. Longer-term strategies may therefore be needed to ensure optimal ovulation rates after weaning. As it has been proposed that the final growth of follicles in the pig to ovulatory size covers a period of about 19 days, in very early weaned sows the follicles that ovulate after weaning may be affected by the metabolic state of the sow during late gestation (see Cosgrove and Foxcroft, 1996; Foxcroft et al, 1995). As many conventionally managed sows become catabolic in late gestation, negative effects on fertility of early weaned sows may already occur before farrowing!

Because the pattern of weight loss, and resulting dynamic changes in metabolic state, are likely the key regulators of the reproductive status of lactating and weaned sows, feeding programs that control the relative metabolic state of the sow during lactation may produce improvements in breeding performance after weaning. If sows are simply fed to appetite throughout lactation, unexpected periods of reduced appetite in late lactation may result in very negative effects on fertility after weaning, even if overall weight loss in lactation may be within acceptable limits. In contrast, by implementing a more controlled pattern of lactation feed intake, it may be possible to ensure that sows are always increasingly less catabolic as weaning approaches, even if overall weight loss in lactation is greater. Recent data from a study with primiparous sows weaned after a 21-day lactation support this concept (Foxcroft, unpublished data).

Breeding herd managers should therefore be encouraged to consider more innovative patterns of feeding as a means of improving the consistency of production from first parity sows.

The paramount importance of parity

The data in Table 1 illustrate an essential feature of recent studies of primiparous lactating sows that cannot be over-emphasized. Even when sows are fed to appetite throughout lactation, many primiparous sows still lose considerable bodyweight and backfat during lactation. In comparison, higher parity sows are able to satisfy the demands of lactation through adequate feed intake, and may even be anabolic during lactation. The resulting differences in metabolic state of sows of different parities underlies the need to consider different management strategies for primiparous, as compared to multiparous, sows.

References

Beltranena, E., G.R. Foxcroft, F.X. Aherne and R.N. Kirkwood (1991) Endocrinology of nutritional flushing in gilts. Canadian Journal of Animal Science 71, 1063–1071.

Britt, J.H. (1996) Biology and management of the early weaned sow. In: Proceedings of the Leman Conference Workshop on "Biology and Management of the Breeding Herd", Part 1, pp46–59.

Clowes, E.J., F.X. Aherne, and G.R. Foxcroft (1994) Effect of delayed breeding on the endocrinology and fecundity of sows. J. Anim. Sci. 72:283–29

Cosgrove, J.R. and Foxcroft, G.R. (1996) Nutrition and Reproduction in the Pig: Ovarian Aetiology. Proceedings of 13th International Conference on Animal Reproduction, Sydney, Australia. Animal Reproduction Science, 42, 131–141.

Cosgrove, J.R., Kirkwood, R.N., Aherne, F.X., Clowes, E. J., Foxcroft, G.R. (1997) A Review - Management and nutrition of the early weaned sow. In: Manipulating Pig Production VI, Ed. P.D. Cranwell, APSA, Werribee, Australia; pp 33–56.

Cox, N.M. (1997) Control of follicular development and ovulation rate in pigs. J.Reprod. Fert., Suppl. 52, 31–46.

Cox, N.M., M.J. Stuart, T.G. Althen, W.A. Bennett, and H.W. Miller (1987) Enhancement of ovulation rate in gilts by increasing dietary energy and administering insulin during follicular growth. Journal of Animal Science 64, 507–516. 1987. Enhancement of ovulation rate in gilts by increasing dietary energy and administering insulin during follicular growth. J. Anim. Sci. 64: 507–516.

Ding, J. and Foxcroft, G.R. (1994) Conditioned media produced by follicle shells of different maturity affect maturation of pig oocytes. Biol. Reprod., 50, 1377–1384.

Edwards, S. and G.R. Foxcroft (1983a) Endocrine changes in sows weaned at two stages of lactation. Journal of Reproduction and Fertility 67, 161–172.

Edwards, S. and G.R. Foxcroft (1983b) The response of sows to oestradiol benzoate treatment after weaning at two stages of lactation. Journal of Reproduction and Fertility 67, 173–180.

Foxcroft, G.R. (1992) Nutritional and lactational regulation of fertility in sows. J. Reprod. Fert. Suppl. 45: 113–125.

Foxcroft, G.R., F.X. Aherne, E.C. Clowes, H. Miller and L.J. Zak. (1995) Sow fertility: The role of suckling inhibition and metabolic status. In: Animal Science Research and Development; Moving Toward a New Century. Ed. M. Ivan, Centre for Food and Animal Research, Ottawa, Canada. pp 377–393.

Foxcroft, G.R., Cosgrove, J.R. and Aherne, F.X. (1996) Relationship Between Metabolism and Reproduction. In: Proceedings of the 14th International Pig Veterinary Society Congress, Bolgna, Italy, pp 6–9.

Grant, S.A. (1989) Control of follicular development in the cyclic gilt and weaned sow. PhD Thesis, University of Nottingham, Nottingham, UK.

Kirkwood, R.N., K.R. Lapwood, W.C. Smith and I.L. Anderson. (1984) Plasma concentrations of LH, prolactin, oestradiol-17 and progesterone in sows weaned after lactation for 10 or 35 days. Journal of Reproduction and Fertility 70, 95–102.

Koketsu, Y. (1994) Influence of feed intake and other factors on the lactational and postweaning reproductive performance of sows. PhD thesis, University of Minnesota.

Matamoros, I.A., N.M. Cox, and A.B. Moore (1990) Exogenous insulin and additional energy affect follicular distribution, follicular steroid concentration, and granulosa cell human chorionic gonadotropin binding in swine. Biol. Reprod. 43: 1–7.

Matamoros, I.A., N.M. Cox, and A.B. Moore (1991) Effects of exogenous insulin and body condition on metabolic hormones and gonadotropin-induced follicular development in prepuberal gilts. J. Anim. Sci. 69: 2081–2091.

Tokach, M.D., J.E. Pettigrew, G.D. Dial, J.E. Wheaton, B.A. Crooker, and L.J. Johnston (1992). Characterization of luteinizing hormone secretion in primiparous, lactating sow: relationship to blood metabolites and return-to-estrus interval. Journal of Animal Science 70, 2195–2201.

Varley, M.A. and G.R. Foxcroft (1990) Endocrinology of lactation. J. Reprod. Fert. 40:47–61.

Yang, H. (1998) PhD thesis, University of Minnesota.

Zak, L.J., J.R. Cosgrove, F.X. Aherne, and G.R. Foxcroft (1997a) Pattern of feed intake, and associated metabolic and endocrine changes, differentially affect post-weaning fertility in the primiparous lactating sow. Journal of Animal Science 75 :208–216.

Zak, L.J., Xu, X., Hardin, R.T. and Foxcroft, G.R. (1997) Impact of different patterns of feed intake during lactation in the primiparous sow on follicular development, oocyte maturation and embryo survival. J. Reprod. Fertil., 110, 99–106.