RESEARCH REPORT
ANIMAL SCIENCE

Title: Effect of glucosamine supplementation on litter size in a commercial setting - **NPB #14-238**

Investigator: Jeffrey L. Vallet

Coinvestigator: Shane Meyer

Institution: USMARC

Date Submitted: October 15, 2015

Industry Summary:

Litter size is a key determinant of the efficiency of pork production. In turn, placental function is a key determinant of whether an individual pig fetus survives during gestation and also influences piglet birth weights. Our previous results suggested that glucosamine supplementation during late gestation improved aspects of the structure of the placenta that likely affect placental efficiency, and also improved the number of live fetuses at 105 days of gestation, suggesting that it might be useful in improving litter size at farrowing. The objectives of this experiment were to further test the effect of glucosamine supplementation during late gestation on litter size and piglet birth weights. Sows (parity 2-8) were mated according to standard procedures and were treated with either 10 grams per day of glucosamine (128 sows) or glucose (127 sows) as a top dress on their feed from day 85 of gestation until farrowing. Total born, born alive, stillborn and mummies in the litter were recorded, and each piglet was weighed at birth and at weaning. Glucosamine supplementation increased total born by .4 piglets, born alive by .16 piglets, and increased stillborn piglets by .24 piglets. However, none of these overall differences were statistically significant. Birth weights were slightly greater in glucosamine (1.37 kg) compared to glucose (1.35 kg) supplemented sows and weaning weights were also slightly greater in glucosamine (5.48 kg) compared to glucose treated sows (5.43 kg). However, as with litter size results, these differences were not statistically significant. The incidence of stillbirth and preweaning mortality was numerically greater in glucosamine treated sows (9.9 and 16.7%, respectively) compared to glucose treated sows (8.4 and 16.0%, respectively), but once again these differences were not statistically different. However, the incidence of stillborn piglets was significantly greater in seventh and eight parity sows. We conclude that despite our previous results in gilts, glucosamine supplementation of sows from day 85 to farrowing did not improve litter size, birth weights or weaning weights, and increased stillbirth rate in late (7 and 8) parity sows.

Keywords:

Glucosamine, placenta, litter size, stillbirth, birth weight, weaning weight.

Scientific Abstract:

Litter size is influenced by ovulation rate, fertilization rate, embryo mortality and uterine capacity. Of these, the most limiting factor is uterine capacity, because increased ovulation rate results in increased number of embryos on day 30 of gestation, but this advantage is lost during later gestation. Uterine capacity is heavily influenced by placental function, making factors that influence placental development of interest in improving uterine capacity and litter size. Previous results indicated that glucosamine supplementation increased litter size in unilaterally hysterectomized-ovariectomized (UHO) gilts and increased the depths of the folds of the placental trophoblast-endometrial epithelial cell bilayer that represents the interface between the gilt and fetus. The objective of the current study was to determine whether glucosamine supplementation would increase litter size in intact sows under commercial conditions. Sows (parity 2-8) at a commercial farm in Diller NE were mated according to standard procedures and were then treated with either 10 grams per day of glucosamine (128 sows) or glucose (127 sows) as a top dress on their feed. Treatments began on day 85 of gestation and continued until farrowing. Total born, born alive, stillborn and mummies in the litter were recorded, and each piglet was weighed at birth and at weaning. Total born and born alive piglets after glucosamine supplementation were 15.6 ± 0.4 and 14.0 ± 0.3, respectively, compared to 15.2 ± 0.4 and 13.8 ± 0.3, respectively, for glucose supplementation, and did not differ between treatments. Piglet birth and weaning weights were 1.37 ± 0.02 and 5.48 ± 0.06 kg, respectively, for glucosamine supplemented sows compared to 1.35 ± 0.02 and 5.43 ± 0.06 kg, respectively, for glucose supplemented sows. As with litter size results, these means did not differ between treatments. In a separate analysis, the overall incidence of stillbirth and preweaning mortality did not differ between glucosamine treated sows (9.9 ± 0.9 and 16.7 ± 1.1%, respectively) compared to glucose treated sows (8.4 ± 0.8 and 16.0 ± 1.1%, respectively). However, there was a significant interaction between treatment and parity with regard to both the number of stillborn piglets and stillbirth rate. This interaction was due to increased stillbirth in glucosamine treated seventh and eighth parity sows compared to glucose treated seventh and eighth parity sows. Thus, results indicate that despite our previous results in UHO gilts, glucosamine treatment of sows during late gestation did not affect litter size, birth weights, or preweaning survival, but did increase stillbirth rate in late (7 and 8) parity sows.

Introduction:

Sow lifetime productivity is a major factor influencing the efficiency of swine production. One component of lifetime productivity is the number of piglets born alive for each parity. The number born alive is influenced by ovulation rate, fertilization rate, embryonic mortality, uterine capacity (Bennett and Leymaster, 1989) and the stillbirth rate (Vallet et al., 2010a). Ovulation rate is the ultimate limit on litter size, because in the absence of identical twinning, it controls the number of potential embryos available. From there the number of embryos is reduced due to fertilization rate, but this is typically (Polge, 1978) but not always (Flowers, 2013) relatively high. After fertilization, the number of embryos is reduced further during early pregnancy due to embryonic loss due to a variety of possible issues including embryo uterine environment asynchrony (Pope et al., 1990), possible chromosomal abnormalities (Zijlstra et al., 2008), or other failures associated with either maternal recognition of pregnancy or early implantation in swine (Geisert et al., 2006). Measured rates of loss during the embryonic period vary widely in previous reports, but have been summarized to be around 25% (Bennett and Leymaster, 1989). Notably, fertilization rate and embryonic loss are independent of the number of ova or embryos present, so increased ovulation rate results in increased number of embryos that survive to day 30 of gestation within the range of normal ovulation rates (Freking et al., 2007). By contrast, uterine capacity appears to be a true limit on litter size within a specific gestating sow, since it is known to be independent of ovulation rate

(Christenson et al., 1987). If the number of embryos exceeds uterine capacity, the extra embryos are lost during later gestation, typically between day 30 and 40 of gestation (Vallet et al., 2013; Freking et al., 2007; Town et al., 2005), but losses continue throughout gestation (Freking et al., 2007). Thus, factors influencing uterine capacity are a true limit on litter size in swine.

Uterine capacity is more than just uterine function. It is the combined effects of the ability of the uterus to accommodate multiple fetuses, plus the ability of each individual conceptus to survive the intrauterine environment. It has been shown that the uterus is capable of adjusting blood flow to accommodate more embryos, but this ability is limited (Père and Estienne, 2000). Within a given intrauterine environment, conceptuses are thought to vary in survival according to the size of each individual placenta, the efficiency of each placenta beyond its overall size, and the ability of each fetus to adjust its growth and metabolism in response to a limited intrauterine environment. The size of each placenta is likely to be fixed before day 30 of pregnancy, and size adjustments that result in functional improvements after that are limited (Vallet et al., 2011). Fetal adjustments to intrauterine crowding include birth weight reduction and reduction in the growth of individual organs (e.g., muscle development) while other organs (e.g. brain) are spared (Vallet and Freking, 2006). While this improves survival during gestation, it results in piglets at birth whose subsequent growth and survival are impaired (Spicer et al., 1986; Alvarenga et al., 2013). Placental factors that influence efficiency of nutrient transport beyond simple size are only beginning to be explored.

Placental factors that influence nutrient transport (excluding size) can be divided into structural aspects of the placenta that determine nutrient transport efficiency generally (i.e., affecting all nutrients), and those that are specific to individual nutrients (e.g., specific transporter proteins). The former includes aspects of the microscopic architecture of the interface between the sow and fetus. Leiser and Dantzer (1988) have described the architecture of the maternal and fetal capillary beds within the pig placenta. Their work indicated that capillaries are arranged on either side of the epithelial bilayer made up of fetal trophoblast epithelium and endometrial epithelium in a cross-countercurrent fashion. Arranged in this way, efficiency of nutrient transport will be affected by distance where the two capillary beds are in close proximity, which is within the folds of the epithelial bilayer (Vallet and Freking, 2007). Interestingly, the depth of these folds is not static. The folds deepen as gestation advances and are deeper in placenta of small fetuses compared to large fetuses (Vallet and Freking, 2007). This suggests that deepening of the folds may be an adaptive mechanism to reduced intrauterine space, and increase the importance of mechanisms governing the development of the folded bilayer.

The epithelial bilayer of the pig placenta develops within the confines of the placental stroma, which is made of a variety of extracellular matrix components. Previous results suggest that one limitation to the further development of the folded bilayer may be limited stromal development within the placenta of small fetuses. One major component of placental stroma is hyaluronan (Steele and Froseth, 1980; Vallet et al., 2010b), and differences in placental hyaluronidases are consistent with differences in epithelial fold bilayer development between placenta of small and large fetuses (Vallet et al., 2010b). Hyaluronan has a simple structure made up of repeating units of glucuronic acid and N-acetyl-glucosamine, which are both derivatives of glucose (Toole, 2000). Thus, one might conclude that the development of the folded bilayer, through its dependence on the extent of stromal development which is dependent on glucose, competes with the fetus for glucose. It is possible that in some placenta of small fetuses, this competition results in poor placental development, further reducing glucose transport, leading to fetal loss.

Glucose is transported across the placenta by one or more glucose transporters (Wood and Traylern, 2003). Interestingly, many glucose transporters can also transport glucosamine, in some cases preferentially to glucose (Uldry et al., 2002). Because glucosamine is a component of hyaluronan, which is a component of stroma, this led us to hypothesize that supplementation of glucosamine during gestation might preferentially support the placental stroma and promote placental folded bilayer development. In a recent experiment using unilaterally hysterectomized gilts to increase intrauterine crowding and provide a measure of uterine capacity, supplementation with

glucosamine was found to increase the width of the folded bilayer ($P < 0.05$) and uterine capacity ($P=0.09$). The effect of glucosamine supplementation on uterine capacity was 1.4 extra fetuses per uterine horn.

The UHO treatment was designed to measure uterine capacity directly without the influence of ovulation rate. Uterine capacity has some influence on litter size in intact female pigs, especially in modern sows where ovulation rates have been increased due to selection for litter size (Town et al., 2005). Thus, we further hypothesized that glucosamine supplementation may be useful in increasing litter size in intact sows if ovulation rate is sufficiently great. We tested this hypothesis by supplementing commercial sows during late gestation with glucosamine (compared to glucose supplementation as a control).

Objectives:

The objective will be to test the effect of glucosamine supplementation of sow diets from day 85 of gestation until farrowing on the number of piglets born alive and weaned per litter.

Materials & Methods:

This experiment was approved by the USMARC Animal Care and Use committee. The trial took place at a sow farm in Diller NE (Plymouth Ag Group, Diller NE). The farm farrowed approximately 255 sows over a two week period in two weekly batches. Sow parity in both weeks ranged from 2-8. Sows were managed and bred according to the normal protocols existing at the farm, and were then supplemented with either glucosamine (10 grams per day) or glucose (control, 10 g per day) as a top dress on their daily feed beginning on day 85 of gestation. Care was taken to evenly distribute glucosamine or glucose treatment among parities. Top dress was delivered using plastic scoops previously calibrated to deliver the appropriate amounts of glucosamine or glucose. During gestation, sows were housed in individual gestation stalls according to the standard procedure for the farm, allowing for them to be dosed independently on a daily basis. At day 115 of gestation, sows received an injection of estrumate (cloprostenol; Merck Animal Health, Madison NJ) to induce farrowing, which is also standard procedure for the management of farrowing on the farm. Number born, number born alive, number stillborn, number of mummies, and the number of piglets weaned were recorded for each litter. Birth and weaning weights for each piglet were also recorded for each litter. Pigs were weaned at an average age of 19.6 days (range 11 to 28 days)

Statistical Analysis

Litter size data were analyzed with a model that included the effects of farrowing week, treatment, parity and the treatment by parity interaction. Orthogonal contrasts were used when necessary to further evaluate differences amon treatment means. Birth and weaning weights were considered repeated measures of the sow and were therefore analyzed with a similar model to litter size data, including effects of farrowing week, treatment, parity and the treatment by parity interaction. Sow within week by treatment by parity interaction was included as a random effect. In addition, total born was included as a covariate in analysis of birth weights, and birth weights, age at weaning and the number weaned for each sow were included as covariates in the analysis of weaning weights. Finally, stillbirth rate and preweaning mortality were analyzed using PROC GLIMMIX, treating alive or dead at birth and weaning as binary variables. The model included effects of farrowing week, treatment, parity and treatment by parity, and the effect of sow within week by treatment by parity was included as a random effect. Total piglets born and weaned were included as covariates in the analysis of stillbirth rate and preweaning mortality, respectively.

Results:

There was a treatment by parity interaction for number of stillborn piglets and stillbirth rate. No treatment by parity interaction was observed for any of the other traits measured in this experiment. The treatment by parity least squares means for number of stillborn piglets and stillbirth rate are presented in Tables 1 and 2. For both number of stillborns and stillbirth rate, the interaction appeared to be due to greater stillbirth in glucosamine supplemented sows in later parities (parities 7 and 8).

Treatment least squares means for the other litter size and weight traits are presented in Table 3. There were no statistically significant effects of treatment on the number of total born, born alive, or mummies, or on birth weights, weaning weights, or preweaning survival.

Significant parity effects (Table 4) were observed for the number of total born ($P < 0.05$) and live born piglets ($P < 0.05$), and for birth ($P < 0.01$) and weaning weights ($P < 0.05$). Number of mummies and preweaning survival were not affected by parity. Total born and born alive increased gradually with increasing parity until parity 6, after which both litter size measures decreased. Birth weights were similar among parities until parity 6, after which they also decreased ($P < 0.05$). In contrast, average weaning weights increased progressively with increasing parity.

Table 1. Least squares means for the treatment by parity interaction for number of stillborn piglets is presented. The interaction contrast comparing the interaction between treatments and parities 2 through 6 combined versus parities 7 and 8 combined was statistically significant ($P < 0.05$), indicating that more stillborn piglets occurred in the glucosamine treated parity 7 and 8 sows compared to earlier parity sows.

	Treatment	
Parity	Glucosamine	Glucose
2	1.0 ± 0.3 (20)	0.8 ± 0.3 (20)
3	1.4 ± 0.3 (30)	1.0 ± 0.3 (30)
4	0.9 ± 0.4 (15)	1.3 ± 0.4 (16)
5	1.8 ± 0.4 (14)	1.8 ± 0.5 (11)
6	1.8 ± 0.4 (14)	2.2 ± 0.4 (15)
7	2.1 ± 0.3 (23)	1.5 ± 0.3 (23)
8	2.6 ± 0.4 (12)	1.2 ± 0.4 (12)

Table 2. Least squares means for the treatment by parity interaction for stillbirth rate is presented. The treatment by parity interaction ($P < 0.05$) was identical to that for number of stillborn piglets, glucosamine treatment increased the stillbirth rate in late parity sows (parity 7 and 8).

	Treatment	
Parity	Glucosamine	Glucose
2	0.06 ± 0.02	0.06 ± 0.02
3	0.08 ± 0.02	0.07 ± 0.01
4	0.06 ± 0.02	0.07 ± 0.02
5	0.09 ± 0.02	0.11 ± 0.03
6	0.10 ± 0.03	0.11 ± 0.03
7	0.14 ± 0.03	0.10 ± 0.02
8	0.22 ± 0.04	0.09 ± 0.03

Table 3. Litter size trait, birth and weaning weight least squares means for glucosamine and glucose supplemented sows are presented. Differences between glucosamine and glucose supplementation were not statistically significant.

	Treatment	
Variable	Glucosamine	Glucose
Total born	15.6 ± 0.4 (128)	15.2 ± 0.4 (127)
Born Alive	14.0 ± 0.3	13.8 ± 0.3
Mummies	0.56 ± 0.08	0.57 ± 0.08
Birth weights	1.37 ± 0.02 (1970)	1.35 ± 0.02 (1915)
Weaning weights	5.48 ± 0.06	5.43 ± 0.06
Preweaning mortality	0.17 ± 0.01	0.16 ± 0.01

Table 4. Litter size trait, birth and weaning weight least squares means for second through eighth parity sows are presented. Parity effects were statistically significant as indicated.

	Parity						
Variable	2	3	4	5	6	7	8
Total born[a]	14.7 ± 0.6 (40)	15.3 ± 0.5 (60)	15.5 ± 0.7 (31)	16.4 ± 0.8 (25)	17.3 ± 0.7 (29)	14.4 ± 0.6 (46)	14.5 ± 0.8 (24)
Born alive[a]	13.8 ± 0.6	14.1 ± 0.5	14.4 ± 0.6	14.6 ± 0.7	15.3 ± 0.7	12.6 ± 0.5	12.6 ± 0.7
Mummies	0.29 ± 0.14	0.59 ± 0.12	0.64 ± 0.16	0.53 ± 0.18	0.72 ± 0.17	0.69 ± 0.13	0.48 ± 0.18
Birth weights[b]	1.40 ± 0.03	1.42 ± 0.02	1.37 ± 0.03	1.40 ± 0.04	1.37 ± 0.03	1.28 ± 0.03	1.28 ± 0.04
Weaning weights[c]	5.27 ± 0.09	5.30 ± 0.08	5.35 ± 0.11	5.41 ± 0.12	5.53 ± 0.11	5.67 ± 0.09	5.67 ± 0.13
Preweaning mortality	0.14 ± 0.02	0.15 ± 0.01	0.16 ± 0.02	0.17 ± 0.02	0.17 ± 0.02	0.20 ± 0.02	0.15 ± 0.02

[a] Contrasts indicated a progressive increase to parity 6, followed by a precipitous decrease ($P < 0.05$).

[b] Contrasts indicated no differences among parities 2 through 6, and a decrease in parities 7 and 8 ($P < 0.01$).

[c] Contrasts indicated a progressive increase from parity 2 to 8 ($P < 0.05$).

Discussion:

Despite our previous results in UHO gilts, this experiment did not confirm a beneficial effect of glucosamine supplementation on litter size in sows. There was a numerical, but nonsignificant increase in the number of piglets born, and a contributing factor to the lack of treatment effect on the number of piglets born alive was an increased number of stillborn piglets and the rate of stillbirth in late parity sows treated with glucosamine. Comparisons of total born, born alive and birth weights among parities confirmed that reductions in each occur in parity 7 and 8 sows, so it is possible that some interaction between the reproductive competence of late parity sows and glucosamine supplementation may explain the increase in stillbirth incidence and stillborn piglets.

Previous results demonstrated increased depth of the folded bilayer and a trend toward an increase in litter size in UHO gilts. The UHO surgical procedure removes one ovary and one uterine horn. The remaining ovary undergoes compensatory hypertrophy such that ovulation rate is unaffected, resulting in the same number of available embryos in half the uterine space. The UHO procedure has been shown to remove the relationship between ovulation rate and litter size, and is considered to be direct measure of uterine capacity (Christenson et al., 1987). Our previous results indicated an increase in litter size in UHO gilts after glucosamine supplementation of 1.4 live fetuses on 105 days of gestation, and because this measures the capacity of one uterine horn, it was conceivable that uterine capacity was increased by up to 3 live fetuses. The UHO measure was uncomplicated by the incidence of stillbirth, because the measure of live fetuses was made at slaughter on day 105 of gestation. Previous selection for uterine capacity using the UHO model resulted in an increase in uterine capacity of approximately 1 fetus per uterine horn, and a significant increase in litter size in intact selected gilts, albeit less of an increase due to the influence of ovulation rate on litter size in intact gilts (Christenson and Leymaster, 2002). Nevertheless, with these results in mind, it seemed likely that glucosamine would increase litter size in intact pigs, thus warranting the current experiment.

Results indicated no significant effect of glucosamine supplementation on litter size in sows ranging in parity from 2 to 8, in contrast to our previous results in gilts. In this experiment, we used the same dose of glucosamine (10 g per day) for sows as in gilts. However, the gilts in our previous work were substantially lighter than sows used here, and before this approach is abandoned it would be useful to test a comparable dose of glucosamine in sows that is adjusted for the weight of the sows. We plan to repeat this trial using a dose of 20 g per day in sows, to ensure that glucosamine dose was not a limiting factor.

An obvious complicating factor in this experiment is ovulation rate of the sows used, which we were not able to measure because of the commercial setting. Previous observations of ovulation rates in commercial sows have indicated very high ovulation rates, particularly in later parity sows (Town et al., 2005), which if they occurred in this group of sows should have been sufficient to provide a good test of uterine capacity in the intact females. The commercial farm in this experiment obtains maternal line gilts from DNA genetics (formerly Danbred USA), but we could find no published estimates of ovulation rates in these maternal line gilts. However, there are published litter size estimates for Danish maternal line gilts, demonstrating excellent genetic progress in litter size selection (Nielsen et al., 2013), and it is likely that high ovulation rates contributed to the reported increase in litter size due to selection. Thus, ovulation rates were likely to be high enough to put greater emphasis on uterine capacity as a determining factor for litter size in the sows used in this experiment. One possible exception to this may be late parity sows (parity 7 and 8). These sows clearly had reduced numbers of total born and born alive piglets, and one contributing factor to this decrease could have been reduced ovulation rates. We could not find published reports of ovulation rates specifically in sows in later parities for commercial herds, primarily because previous reports combined ovulation rate estimates of parities 4 or greater (Town et al., 2005). Thus, whether litter sizes in parity 7 and 8 sows are more affected by ovulation rate, uterine capacity or perhaps other factors, remains unknown.

The increase in the number of stillborn piglets and stillbirth rates in parity 7 and 8 sows supplemented with glucosamine was an unexpected result. Our previous results indicated that glucosamine supplementation increased the depth of the folds regardless of the size of the fetus, and because of this increased the total width of the placenta. Van Rens et al., 2004 implicated a thicker placenta in prolongation of individual piglet birth intervals, which suggests that placental thickness may contribute to stillbirth rate due to the well known relationship between piglet birth intervals and stillbirth (Vallet et al., 2010a). Van Rens et al., (2004) suggested that thicker placentas may present a greater barrier to delivery of the piglet during farrowing, increasing birth intervals. However, the effective width of the placenta is likely to be controlled by the width of the stroma above the folded bilayer, which we have reported to be reduced in small fetuses compared to large fetuses (Vallet and Freking, 2007). The incidence of larger fetuses, and therefore thicker placenta, might be expected to be reduced with increasing litter size, and it is possible that the reduced litter size in parity 7 and 8 sows observed in this experiment resulted in thicker placenta in these sows upon glucosamine supplementation, resulting in prolonged birth intervals (which we did not measure), and increased stillbirth. Whatever the mechanism for the increase in stillbirth rate, our results indicate that glucosamine supplementation may actually be detrimental in parity 7 and 8 sows due to increased stillbirth rate.

This leads one to consider the effect of parity on piglet production in general. For the sows in this experiment, clearly sows of up to sixth parity continue to improve in litter size, both in terms of total number born and born alive. Improved weaning weights also favor sows up to sixth parity. It could be argued that continued mating of sows after sixth parity results in decreased reproductive efficiency, as opposed to replacing these sows with gilts. This would depend on several factors, such as the expected farrowing rate of gilts compared to seventh parity sows, the litter size of gilts compared to seventh parity sows, and the rate at which gilts return to estrus postweaning compared to the rate at which seventh parity sows return to estrus postweaning. Results presented here suggest that gilts litter size performance will continue to improve during later parities, and seventh parity sows will not, and may actually decline further. Whether this improvement in litter size with parity for gilts offsets the differences in initial farrowing rate and postweaning return to estrus should be evaluated for each operation, to ensure optimal production.

In conclusion, although glucosamine resulted in a slight numerical increase in the number of piglets born and born alive, we cannot confirm that glucosamine supplementation increased litter size in commercial sows. It is possible that the dose of glucosamine used was not sufficient in the larger sows used compared to our previous work in gilts. Our results did indicate an increase in the number of stillborn piglets and stillbirth rate in late parity sows (parity 7 and 8), which was unexpected, but may be due to the effect of glucosamine supplementation on placental thickness, which would potentially have been exacerbated by the reduced litter sizes in these sows. Results also suggest that litter performance of these same late parity sows should be taken into account in decisions of whether and when to replace parity 7 and 8 sows with gilts.

Acknowledgements: We wish to acknowledge with thanks the efforts of the swine staff at Plymouth Ag group, without whose help this trial could not have been accomplished. In addition, we would like to acknowledge the efforts of T. De Vries on this project. Finally, we thank the Nebraska Pork Producers Council for supporting this project.

References:

Alvarenga ALN, Chiarini-Garcia H, Cardeal PC, Moreira LP, Foxcroft GR, Fontes DO, Almeida FRCL. 2013. Intra-uterine growth retardation affects birthweight and postnatal development in pigs, impairing muscle accretion, duodenal mucosa morphology and carcass traits. Reprod Fertil Dev 25(2):387-395.

Bennett GL, Leymaster KA. 1989. Integration of ovulation rate, potential embryonic viability and uterine capacity into a model of litter size in swine. J Anim Sci 67(5):1230-1241.

Christenson RK, Leymaster KA. 2002. Correlated responses in gravid uterine, farrowing and weaning traits to selection of pigs for ovulation rate or uterine capacity. World Congr Genet Appl Lvstk Prod (Proc. 7th):Comm. No. 08-25.

Christenson RK, Leymaster KA, Young LD. 1987. Justification of unilateral hysterectomy-ovariectomy as a model to evaluate uterine capacity in swine. J Anim Sci 65(3):738-744.

Flowers WL. 2013. TRIENNIAL REPRODUCTION SYMPOSIUM: Sperm characteristics that limit success of fertilization. J Anim Sci 91(7):3022-3029.

Freking BA, Leymaster KA, Vallet JL, Christenson RK. 2007. Number of fetuses and conceptus growth throughout gestation in lines of pigs selected for ovulation rate or uterine capacity. J Anim Sci 85(9):2093-2103.

Geisert RD, Ross JW, Ashworth MD, White FJ, Johnson GA, DeSilva U. 2006. Maternal recognition of pregnancy signal or endocrine disruptor: the two faces of oestrogen during establishment of pregnancy in the pig. Soc Reprod Fertil Suppl 62:131-145.

Leiser R, Dantzer V. 1988. Structural and functional aspects of porcine placental microvasculature. Anat Embryol 177(5):409-419.

Nielsen B, Su G, Lund MS, Madsen P. 2013. Selection for increased number of piglets at d 5 after farrowing has increased litter size and reduced piglet mortality. J Anim Sci 91(6):2575-2582.

Père M-C, Etienne M. 2000. Uterine blood flow in sows: Effects of pregnancy stage and litter size. Reprod Nutr Dev 40(4):369-382.

Polge C. 1978. Fertilization in the pig and horse. J Reprod Fertil 54(2):461-470.

Pope WF, Xie S, Broermann DM, Nephew KP. 1990. Causes and consequences of early embryonic diversity in pigs. J Reprod Fertil Suppl 40:251-260.

Spicer EM, Driesen SJ, Fahy VA, Horton BJ, Sims LD, Jones RT, Cutler RS, Prime RW. 1986. Causes of preweaning mortality on a large intensive piggery. Aust Vet J 63(3):71-75.

Steele VS, Froseth JA. 1980. Effect of gestational age on the biochemical composition of porcine placental glycosaminoglycans. Proc Soc Exp Biol Med 165(3):480-485.

Toole BP. 2000. Hyaluronan is not just a goo! J Clin Invest 106(3):335-336.

Town SC, Patterson JL, Pereira CZ, Gourley G, Foxcroft GR. 2005. Embryonic and fetal development in a commercial dam-line genotype. Anim Reprod Sci 85(3-4):301-316.

Uldry M, Ibberson M, Hosokawa M, Thorens B. 2002. GLUT2 is a high affinity glucosamine transporter. FEBS Lett 524(1-3):199-203.

Vallet JL, Freking BA. 2006. Changes in fetal organ weights during gestation after selection for ovulation rate and uterine capacity in swine. J Anim Sci 84(9):2338-2345.

Vallet JL, Freking BA. 2007. Differences in placental structure during gestation associated with large and small pig fetuses. J Anim Sci 85(12):3267-3275.

Vallet JL, Miles JR, Brown-Brandl TM, Nienaber JA. 2010a. Proportion of the litter farrowed, litter size, and progesterone and estradiol effects on piglet birth intervals and stillbirths. Anim Reprod Sci 119(1-2):68-75.

Vallet JL, Miles JR, Freking BA. 2010b. Effect of fetal size on fetal placental hyaluronan and hyaluronoglucosaminidases throughout gestation in the pig. Anim Reprod Sci 118(2-4):297-309.

Vallet JL, Freking BA, Miles JR. 2011. Effect of empty uterine space on birth intervals and fetal and placental development in pigs. Anim Reprod Sci 125(1-4):158-164.

Vallet JL, McNeel AK, Johnson G, Bazer FW. 2013. TRIENNIAL REPRODUCTION SYMPOSIUM: Limitations in uterine and conceptus physiology that lead to fetal losses. J Anim Sci 91(7):3030-3040.

van Rens BTTM, van der Lende T. 2004. Parturition in gilts: duration of farrowing, birth intervals and placenta expulsion in relation to maternal, piglet and placental traits. Theriogenology 62(1-2):331-352.

Wood IS, Trayhurn P. 2003. Glucose transporters (GLUT and SGLT): expanded families of sugar transport proteins. British Journal of Nutrition 89(01):3-9.

Zijlstra C, Kidson A, Schoevers EJ, Daemen AJJM, Tharasanit T, Kuijk EW, Hazeleger W, Ducro-Steverink DWB, Colenbrander B, Roelen BAJ. 2008. Blastocyst morphology, actin cytoskeleton quality and chromosome content are correlated with embryo quality in the pig. Theriogenology 70(6):923-935.