Effect of empty uterine space on birth intervals and fetal and placental development in pigs

J.L. Vallet*, B.A. Freking, J.R. Miles

USDA, ARS, U.S. Meat Animal Research Center, Clay Center, NE 68933-0166, United States

Abstract

A substantial loss of embryos occurs between Days 30 and 40 of pregnancy in the pig under crowded intrauterine conditions, but it is not clear whether this loss affects the growth of adjacent conceptuses. Birth intervals are known to increase with decreasing litter size, but the factors responsible are unknown. Two possibilities are that increased birth weight associated with reduced litter size and the empty uterine space and resulting constricted uterine regions that occur in pigs with small litters may impair piglet delivery. To address these, pregnant gilts were laparotomized on Day 35 of pregnancy and one or two fetuses were manually crushed through the uterine wall on the ovarian or cervical end of each uterine horn to create an empty uterine space behind or in front of the litter of piglets, respectively, in relation to the route of delivery from the uterus. A subset of gilts was slaughtered at 105 days of gestation to confirm that the empty uterine spaces were successfully created and to determine their effects on placental and fetal weights of adjacent conceptuses. At slaughter, the lengths of all externally visible empty constricted regions of the uterus were measured. The uterine horns were opened and the lengths of each placenta were measured from the umbilicus toward the ovary and toward the cervix to assess whether placentas developed symmetrically, and then each fetus and placenta was weighed. Fetal crushing successfully created constricted empty uterine regions on the ovarian and cervical ends of the uterine horns. Ovarian-side placental lengths were greater than cervical-side for conceptuses adjacent to fetuses crushed on the ovarian end of the horn. Cervical-side placental lengths were greater than ovarian-side for conceptuses adjacent to fetuses crushed on the cervical end. Both placental and fetal weights were greater (10% and 6%, respectively, P<0.05) for conceptuses adjacent to crushed fetuses compared to nonadjacent conceptuses. Remaining gilts were farrowed to determine the effect of litter size, average birth weights, and treatment on birth intervals of piglets, which were monitored using 24-h video surveillance. The negative association between number of piglets born alive and average birth interval was confirmed and was not explained by litter size-induced reduction in litter average birth weights. Birth intervals and stillbirth rate did not differ between cervically- and ovarian-treated gilts. These results indicate that conceptus loss on Day 35 of gestation can benefit the growth of adjacent placentas and fetuses, but the benefit is small. Increased average birth weight and the presence of empty uterine space that occurs when litter size is reduced does not fully explain the effect of litter size on birth intervals.

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* Corresponding author at: USDA, ARS, U.S. Meat Animal Research Center, P.O. Box 166, Clay Center, NE 68933-0166, United States.
Tel.: +1 402 762 4187; fax: +1 402 762 4382.
E-mail address: jeff.vallet@ars.usda.gov (J.L. Vallet).

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1. Introduction

Stillbirth rate of piglets has been reported to be between 3% and 9% of piglets born, representing a significant loss to the swine industry (Fahmy et al., 1978; Tuchscherer et al., 2000; Leenhouwers et al., 2001; Mesa et al., 2006). Previous results indicated a significant association between prolonged birth intervals and stillbirth rates, indicating that stillbirth increases dramatically when individual piglet birth interval extends beyond 1 h (Randall, 1972; Sprecher et al., 1974; van Dijk et al., 2005; Vallet et al., 2010). Very little is known regarding factors that control individual piglet birth intervals, however a consistent finding has been that birth intervals are shorter in large litters compared to small litters (Canario et al., 2006; Vallet et al., 2010). Previous results suggest that this difference is not due to conceptus estrogen secretion leading up to farrowing (Vallet et al., 2010). Thus, the explanation for the increased length of birth intervals in small litters is unclear. One possibility is that reductions in birth weights known to occur when litter size increases may shorten birth intervals. Alternatively, in the course of several experiments where we collected placental and fetal samples during late gestation, we noticed that in pregnant uterine horns containing only a few conceptuses, substantial regions of the uterus appear empty and constricted compared to regions containing conceptuses. We hypothesized that constricted regions resulting from empty uterine space in small litters could impede the birth of piglets, and increase birth intervals.

It has also been consistently reported that crowded intrauterine conditions result in increased conceptus loss between Days 30 and 40 of pregnancy (Knight et al., 1977; Chen and Dziuk, 1993; Vallet and Christenson, 1993; Vonnahme et al., 2002b; Freking et al., 2007). However, pig conceptus implantation occurs between Days 12 and 18 of pregnancy (Friess et al., 1980), and it is not clear whether adjacent pig conceptuses benefit from loss of termates between Days 30 and 40 of gestation. Vonnahme et al. (2002a) reported that when every other conceptus is crushed on Day 40 of gestation in pregnant Yorkshire pigs, the remaining placentas were larger but no significant effects on the size of the remaining fetuses were observed. We sought to further test whether removal of conceptuses on Day 35 of gestation results in significant effects on placental and fetal growth in adjacent conceptuses to further explore the extent of any possible beneficial effects of embryonic loss around this time.

2. Materials and methods

2.1. Animals

All procedures involving animals were approved by the USMARC Institutional Animal Care and Use Committee. Gilts (n = 185) from the USMARC BX population (¼ Duroc, ¼ Landrace, ¼ Large White) were mated (Day 0 = day of estrus) after at least one estrous cycle of normal length to BX boars. On Day 35 of gestation, gilts were anesthetized with sodium pentobarbital, and anesthesia was maintained using fluothane. Gilts were laparotomized, the uterus withdrawn and the number of fetuses was counted by gentle palpation through the uterine wall. Number of corpora lutea (CL) was also recorded. Gilts (n = 61) were not pregnant at surgery, and were not used further. Five gilts had too few embryos in the right or left horn, and were dropped from the experiment, leaving 119 pregnant gilts. Depending on the number of conceptuses in each horn, one (two or three fetuses observed in the horn) or two (four or greater fetuses observed in the horn) fetuses on either the ovarian or the cervical ends of the uterine horns (assignment of ovarian or cervical treatment was random for each gilt) were crushed manually through the wall of the uterus. Both horns were treated similarly for each gilt. Crushing of fetuses on the ovarian end of the horn served as a control for fetal crushing for birth interval effects as the piglets do not have to pass through the ovarian end of the horn during farrowing. A subset of gilts (n = 30) were randomly assigned to be slaughtered on Day 105 of gestation to assess the effects of the treatments on empty uterine space as well as placental and fetal development. For placental and fetal changes in this design, conceptuses that are not adjacent to crushed fetuses serve as a control for conceptuses that are adjacent to crushed fetuses, regardless of whether crushing occurred on the ovarian or cervical end of the uterine horn. At slaughter, the reproductive tract was recovered and photographed. Visible regions of empty uterine space along the length of each uterine horn were measured with a measuring tape. Then, the uterine horns were opened along the antimesometrial border and each fetus was removed and weighed. Any visible remnants of the crushed fetuses were noted. The length of each placenta associated with a viable fetus was measured from the umbilical cord toward the ovarian and cervical edge using a measuring tape. Finally, each placenta was separated from the uterus and weighed. Remaining gilts (n = 89) were allowed to farrow with 24 h monitoring of the farrowing process using video cameras (Vallet et al., 2010). Each video was observed to determine the time of birth of each piglet and whether each piglet was born alive, stillborn or a mummy (farrowing records collected on the Day after farrowing were used retrospectively to help distinguish between stillborns and mummies).

2.2. Statistical methods

Ovulation rate, number of embryos before and after crushing on Day 35, number of fetuses on Day 105, number of piglets born alive and stillborn at farrowing, and litter average birth intervals (with and without log transformation) were analyzed using PROC GLM (Statistical Analysis System, SAS Institute, Cary, NC) with a model that included the effect of treatment (ovarian or cervical). The lengths of externally visible regions of constricted empty uterine space on the ovarian and cervical ends of the uterine horns measured on Day 105 were treated as separate traits and analyzed using PROC MIXED. In each case, the model included the effect of treatment (ovarian or cervical) as a fixed effect and gilt within treatment as a random effect. The number of fetuses within each uterine horn was included as a covariate. Ovarian-side and cervical-side placental lengths were also treated as separate traits and analyzed using PROC MIXED. In each case, the model included treatment (ovarian or cervical), location (whether
the conceptus was adjacent or nonadjacent to the induced empty uterine space), and the interaction between treatment and location as fixed effects and gilt within treatment as a random effect. Each model included the number of fetuses within each uterine horn as a covariate. Placental and fetal weights were analyzed using PROC MIXED with the same model as that described for ovarian-side and cervical-side placental lengths.

The effects of litter size on average birth weights and average birth intervals were examined by regression analysis. To confirm the effect of litter size on birth intervals and the contribution of birth weights to this effect, litter average birth intervals were analyzed using PROC GLM with a model that included the number of live piglets born, the effect of treatment, the interaction of treatment with the number of live piglets born, and the effect of litter average birth weight. The effect of treatment on individual piglet birth intervals was further analyzed in more detail. To standardize the known effect of the birth order of each piglet in the farrowing process on birth interval (Vallet et al., 2010), the birth order of each piglet was converted to a proportion of the litter farrowed by dividing the piglet’s position in the birth order by the total number of piglets born. Then, piglets were categorized into the following ten proportion-farrowed categories: 0–0.15 = 0.1, 0.15–0.25 = 0.2, 0.25–0.35 = 0.3, 0.35–0.45 = 0.4, 0.45–0.55 = 0.5, 0.55–0.65 = 0.6, 0.65–0.75 = 0.7, 0.75–0.85 = 0.8, 0.85–0.95 = 0.9, and greater than 0.95 = 1. Birth intervals were log transformed to reduce skewness of the data and were then analyzed using PROC MIXED with a model that included treatment, proportion of the litter farrowed category, and their interaction as fixed effects, and gilt within treatment as a random effect. PROC GLIMMIX was used to analyze the incidence of stillbirth data (0 = alive, 1 = stillborn) using a similar model to that described above for birth interval.

3. Results

Of the gilts that were pregnant on Day 35 and slaughtered on Day 105, one ovarian treated and two cervically treated gilts were not pregnant out of 30 gilts. Of the gilts that were pregnant on Day 35 and allowed to farrow, one ovarian treated and three cervically treated gilts were not pregnant out of 89 gilts. Table 1 indicates the least squares means for treatment for ovulation rate, number of embryos on Day 35 before and after crushing, number of fetuses on Day 105, number of piglets born alive and stillborn, litter average birth weight and litter average birth interval. Only the number of piglets born alive at farrowing was significantly different between treatments (P < 0.05). Nevertheless, because the treatments differed in number born alive, it was necessary to reanalyze the litter average birth interval data with litter size as a covariate because litter size influences average birth interval (see below). When this was done, litter average birth intervals still did not differ significantly between treatments.

Table 1 also indicates the effects of crushing one or two fetuses on the ovarian or cervical ends of the uterine horns on Day 35 of gestation on the incidence of empty uterine space and on placental and fetal development. Crushing fetuses in the cervical end of the uterine horn was successful in creating a significantly increased region of empty uterine space between the litter and the uterine exit. Although remnants of the crushed fetuses were observed, this did not fully prevent adjacent placenta from developing into the open space, as reflected by asymmetric placental growth in conceptuses adjacent to the empty regions. For both ovarian and cervical treatments, the side of the placenta facing the empty region was longer (P < 0.01). The side of the placenta facing away from the empty space did not differ from those of nonadjacent conceptuses. In many cases placenta appeared to adhere to the endometrium well into the regions of the uterus containing remnants of the crushed fetus.

Consistent with asymmetric development of the placenta adjacent to the induced empty uterine space, both fetal and placental weights were greater (P ≤ 0.05) for conceptuses adjacent to the induced empty uterine spaces. However, the increase in fetal and placental weights were only 6% and 10%, respectively, of the fetal and placental weights of nonadjacent conceptuses, indicating that although the benefit is statistically significant, it is nevertheless comparatively small.

Scatterplots illustrating the relationships between number born alive and average birth weight and average birth interval are shown in Fig. 1. Analyses of the effect of number born alive on litter average birth weights and litter average birth interval confirmed significant (P < 0.05 and 0.01, respectively) negative associations for each. Interestingly, the effect of the number born alive on litter average birth intervals remained (P < 0.01) even after inclusion of litter average birth weight as a covariate in the analysis.

Fig. 2 illustrates the relationships between proportion of the litter farrowed and birth intervals and stillbirth rates for the ovarian and cervically treated gilts. Differences between treatments were not statistically significant, further indicating that the presence of empty uterine space in the cervical end of the uterine horns did not influence birth intervals or stillbirth rates, even for the earliest born piglets.

4. Discussion

Although the effect of loss of an adjacent conceptus on Day 40 of gestation on placental weight has been reported (Vonnahme et al., 2002a), the current experiment demonstrates a significant beneficial effect of the loss of a conceptus on Day 35 of gestation on the weight of the immediately adjacent fetus. Results provide strong confirmatory evidence that the eventual size of the placenta during later gestation is not fixed at implantation (Days 12–18) in the pig. However, the benefit of the demise of a neighboring littermate to the remaining fetus appears to be small, arguing that although not completely fixed, most of the eventual size of the placenta and fetus is determined before Day 35 of gestation. Results of the present study confirm the effect of litter size on average birth intervals and further indicate that these effects are not explained by litter size-induced differences in average birth weights of piglets. Furthermore, this experiment provides no evidence that empty regions of the uterus interfere in the birth pro-
Table 1
Least squares means ± SEM for gilts for which one or two conceptuses were crushed on the ovarian or cervical ends of the uterine horns.

<table>
<thead>
<tr>
<th>Trait</th>
<th>Treatment</th>
<th>Ovarian</th>
<th>Cervical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovulation rate</td>
<td></td>
<td>14.9 ± 0.3 (53)</td>
<td>14.9 ± 0.3 (59)</td>
</tr>
<tr>
<td>Embryos (Day 35)</td>
<td></td>
<td>11.5 ± 0.5</td>
<td>11.9 ± 0.4</td>
</tr>
<tr>
<td>Embryos remaining (Day 35)</td>
<td></td>
<td>7.7 ± 0.4</td>
<td>8.2 ± 0.4</td>
</tr>
<tr>
<td>Fetuses alive (Day 105)</td>
<td></td>
<td>7.2 ± 0.7 (13)</td>
<td>5.7 ± 0.7 (14)</td>
</tr>
<tr>
<td>Ovarian end empty space (cm)</td>
<td></td>
<td>26.4 ± 2.4</td>
<td>4.0 ± 2.3</td>
</tr>
<tr>
<td>Cervical end empty space (cm)</td>
<td></td>
<td>7.2 ± 2.8</td>
<td>22.0 ± 2.7</td>
</tr>
<tr>
<td>Ovarian side placental length</td>
<td></td>
<td>21.4 ± 1.2</td>
<td>11.3 ± 1.2</td>
</tr>
<tr>
<td>Ovarian side placental length, adjacent (cm)</td>
<td>13.3 ± 1.1</td>
<td>13.4 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>Cervical side placental length, adjacent (cm)</td>
<td>12.5 ± 1.2</td>
<td>19.2 ± 1.2</td>
<td></td>
</tr>
<tr>
<td>Cervical side placental length, nonadjacent (cm)</td>
<td>13.7 ± 1.0</td>
<td>12.8 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>Fetal weight, adjacent (kg)</td>
<td></td>
<td>1.16 ± 0.06</td>
<td>1.10 ± 0.06</td>
</tr>
<tr>
<td>Fetal weight, nonadjacent (kg)</td>
<td></td>
<td>1.05 ± 0.06</td>
<td>1.07 ± 0.06</td>
</tr>
<tr>
<td>Placental weight, adjacent (kg)</td>
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<td>0.25 ± 0.02</td>
<td>0.25 ± 0.02</td>
</tr>
<tr>
<td>Placental weight, nonadjacent (kg)</td>
<td></td>
<td>0.22 ± 0.02</td>
<td>0.24 ± 0.02</td>
</tr>
<tr>
<td>Piglets born alive at farrowing</td>
<td></td>
<td>5.0 ± 0.5 (40)</td>
<td>6.4 ± 0.4 (45)</td>
</tr>
<tr>
<td>Average birth weight (kg)</td>
<td></td>
<td>1.5 ± 0.4</td>
<td>1.5 ± 0.4</td>
</tr>
<tr>
<td>Average birth interval (min)</td>
<td></td>
<td>41 ± 10 (31)</td>
<td>46 ± 9 (43)</td>
</tr>
<tr>
<td>Piglets stillborn at farrowing</td>
<td></td>
<td>0.6 ± 0.2 (40)</td>
<td>0.7 ± 0.1 (45)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are number of gilts.
  
* Treatment (ovarian vs. cervical; *P* < 0.01).
  
* Treatment by location (adjacent vs. nonadjacent to a crushed fetus) interaction (*P* < 0.01).
  
* Location (adjacent vs. nonadjacent to a crushed fetus; *P* ≤ 0.05).
  
* Treatment (ovarian vs. cervical; *P* < 0.05).

Fig. 1. Graphs illustrate the relationships between average birth weights and average birth intervals (top graph) and litter size and average birth intervals (bottom graph). Both relationships were statistically significant (*P* < 0.05 and 0.01, respectively).

Fig. 2. Graphs indicate least squares means for birth interval (top graph) and stillbirth rate (bottom graph) for gilts where empty uterine space was created in the ovarian or cervical ends by crushing one or two embryos in each horn on Day 35 of gestation. No significant effect of treatment on either trait was observed.
cess, and so also does not explain the negative relationship between litter size and birth intervals.

The pig conceptus undergoes a period of elongation during early pregnancy that is thought to contribute to the subsequent size of the placenta (Perry and Rowlands, 1962; Geisert et al., 1982). Some adherence of the conceptus to the endometrial epithelium begins as early as Day 13 (Keys et al., 1986), and formal implantation occurs by Day 18 (Friess et al., 1980). By Day 35 of gestation, the placenta is well adhered to the endometrium and the resulting trophoblast-endometrial epithelial bilayer begins to develop its characteristic folded appearance (Friess et al., 1980; Vallet and Freking, 2007). This adherence of fetal placenta to endometrium would be expected to limit the migration of the fetal placenta into open areas of the uterus should they become available due to the demise of neighboring conceptuses. This type of behavior is, however, actually predicted by the experiments of Wilson et al. (1998) who suggested that the fetal placentas of European breed conceptuses retain the ability to grow in size and weight late into gestation. However, other reports suggest that the growth of the placenta is limited during late gestation (Knight et al., 1977). Vonnahme et al. (2002a) reported that removal of adjacent conceptuses on Day 40 of pregnancy allowed the fetal placentas of the remaining conceptuses to grow larger, both in weight and in surface area, suggesting that placentas are capable of invading empty uterine space. Results of the present study confirm this ability, and further indicate the asymmetric growth of the placenta toward an available empty uterine space, lending further support to the idea that the fetal placenta is capable of invasion into an available space. These results confirm that the size of the placenta is not completely determined by the uterine space acquired by Day 35 of gestation. The results of Vonnahme et al. (2002a) further indicated that despite increased placental weight, there was no corresponding significant increase in fetal weight, suggesting the possibility that the increase in placentomal weight in response to adjacent conceptus loss did not represent a benefit to the fetus. Results of the present study clearly indicate increased fetal weight adjacent to an empty region of the uterus although the benefit is relatively small.

The percent increase between conceptuses that were adjacent and nonadjacent to empty uterine space in fetal (6%) and fetal placental (10%) weights suggest that despite the asymmetric growth of the fetal placenta in terms of length, this did not result in a proportional benefit in the weight of the conceptus. There is a clear discrepancy between the increase in total length of the fetal placenta (26% for ovarian treatment and 16% for cervical treatment) and the increase in weight of both the fetus and the fetal placenta. These results suggest that 90% or greater of the eventual weight of the conceptus at Day 105 of gestation is determined by relationships among conceptuses established by Day 35. The disparity between the percentage increase in fetal placentomal length and the percentage increases in fetal and fetal placental weight may suggest that the extra fetal placentomal tissue invading the available empty uterine space is only moderately functional. Several important factors, however, affect the interpretation of these results. First, crushing of fetuses bears no relationship to normal fetal loss during gestation. The damage done to the fetus or the uterus is likely to trigger a host of inflammatory reactions. It is possible that the fetal remnants after crushing or the effect of crushing on the uterus may have artifactual effects on the uterus or the remaining fetuses. Inconsistent with this is the fact that the treatment had relatively minor effects on maintenance of pregnancy in that most of the gilts remained pregnant after treatment. In addition to possible effects of tissue damage, it is unknown when the empty space truly becomes available to the adjacent conceptus once the neighboring fetus is lost. One might expect that an indeterminate amount of time would be necessary to sufficiently clear away the tissue remnants from the lost conceptus, although it would appear that the complete removal of these tissues is not necessary, because some detritus remained even by Day 105 of gestation in the present experiment. Nevertheless, these results demonstrate a clear benefit to adjacent fetuses when a neighboring littermate is lost on Day 35 of gestation and also suggests that the fetal placenta retains some ability to invade adjacent empty uterine space.

Results of the present study confirm that individual piglet birth intervals are shorter in larger litters compared to smaller litters (Canario et al., 2006; Vallet et al., 2010), but how this occurs is not known. If the underlying mechanism of this phenomenon could be exploited to reduce birth intervals during the farrowing process, it could provide an opportunity to reduce the stress of the farrowing process on the sow and reduce the incidence of stillbirth of piglets, because previous results indicated that individual birth intervals longer than 1 hour are associated with increased stillbirth rate (Vallet et al., 2010). There are several characteristics of large litters that could have an influence on the farrowing process. Pig conceptuses secrete estrogen during late gestation and it has been suggested that conceptus estrogen may participate in preparing the reproductive tract for farrowing (Guthrie, 1985), however previous results indicated that plasma estradiol concentrations leading up to farrowing did not account for the relationship between litter size and piglet birth intervals when the two variables are fitted simultaneously (Vallet et al., 2010). Large litters are also associated with reduced birth weight, which is confirmed by the current results, and it seemed possible that smaller piglets may be delivered more rapidly. However, like plasma estradiol reported in Vallet et al. (2010), litter average birth weight did not fully account for the relationship between litter size and litter average birth intervals when the two were fitted simultaneously. Consistent with this, the average birth interval found in this experiment (40–50 min) was greater than the average birth interval (15–20 min) in Vallet et al. (2010). The average birth weights (1.5 kg) of piglets in this experiment were within the normal range of BX piglets born at USMARC (1.48 kg, standard deviation 0.31 kg, n = 5883 piglets, J.L. Vallet, unpublished data). The increased birth intervals are also likely to be responsible for the somewhat increased stillbirth rate (12%) found in this experiment compared to Vallet et al. (2010). The most likely explanation for the longer average birth intervals in this experiment compared to Vallet et al. (2010) is the reduction of litter size caused by the treatments. This difference
in birth intervals is clearly predicted by the relationship between litter size and birth intervals presented in the bottom graph of Figure 1 (compare the birth interval at a litter size of six compared to a normal litter size of 10).

A third possibility for the effect of small litters on average birth interval was that the large regions of empty uterine space present during gestation of small litters might result in regions of uterine constriction that could prolong the delivery of piglets in small litters. The experimental protocol in the present study successfully created a length of empty uterine space between the litter and the uterine exit. The ovarian-treated gilts served as a control for any possible effects of the surgical procedure on the farrowing process. Thus, regardless of the average farrowing interval in the overall experiment, the treatment design was such that it allowed a valid test of the effect of empty space on birth intervals. Comparison of these two treatments indicated that there was no difference in birth intervals either overall or at any time during the farrowing process. Thus, empty regions of the uterus do not appear to impede the delivery of piglets. However, it should be recognized that the birth interval of the first piglet in the litter could not be measured, because the birth intervals of piglets are determined in relation to the birth of the previous piglet. The birth interval of the first piglet born could have been prolonged without detection. It also should be considered that piglets in each uterine horn are delivered randomly (Dziuk and Harmon, 1969), thus it is possible that the first piglet born in cervically treated pigs, which would be delivered from either horn, could have been delayed but not measured, and the delay of the first piglet born from the opposite horn could have been masked by delivery of subsequent piglets from the original horn. This scenario would likely result in an increase in the average birth intervals early in the farrowing process (because the average birth interval would originate from piglets delivered for an indeterminate amount of time from only one uterine horn instead of both uterine horns) and could also be associated with a measurable increase in stillbirth early in the process (due to delayed delivery from the opposite horn). These effects were not observed in this experiment, and the stillbirth rate of the first piglet born in each litter was not significantly different between the two treatments, again suggesting that empty uterine space did not cause significant delay in the delivery of the first piglet. Thus, it is most likely that empty uterine space did not impair farrowing, but because of the above uncertainties, the most that can be concluded is that empty uterine space did not cause any ongoing impediment to the delivery of piglets. This suggests that if uterine constriction caused by empty uterine space does influence birth intervals, passage of a single piglet through the space improves the passage of subsequent piglets. These results do not support this mechanism as the cause of increased birth intervals in small litters, which are uniformly prolonged.

These results differ dramatically from those reported by Dziuk (1979) who reported that crushing all pig fetuses except the single piglet either near the ovarian end or near the cervical end of the uterine horns resulted in stillbirth of the piglet at the ovarian end of the uterine horn, and the piglet left in the cervical end was born alive. The difference in results may be due to the greater amount of empty uterine space through which the piglet remaining at the ovarian end of the uterine horn was required to traverse. Alternatively, we and others have reported that delivery of the last piglet in a litter is significantly delayed (Randall, 1972; van Rens and van der Lende, 2004; Vallet et al., 2010), suggesting that some aspect of the delivery of a single remaining piglet from a uterus causes delivery to be more prolonged than would otherwise occur when littersmates are also present within the uterus. Thus it is possible that in the experiment by Dziuk (1979) the results obtained for single piglets left in the ovarian end of the uterine horn were due to the combined effects of excessive empty uterine space, which would not normally be encountered even in small litters, and the relative inability of a single piglet within the uterus to support the farrowing process.

These results apparently eliminate empty uterine space as a significant contributor to the prolonged birth intervals observed in small litters, and also indicate that reduced birth weights that occur as litter size increases also do not fully explain the effect of litter size on birth intervals. Previous results eliminated conceptus estrogen as a major contributing factor to this phenomenon as well. The relationship between litter size and birth intervals suggests that some additive effect of each conceptus contributes to the efficiency of the birth process. The controlling factor could be placental or fetal in origin, or due to some interaction between the conceptuses and the uterus. Fetal glucocorticoids have been suggested to be responsible for initiating the farrowing process (First and Bosc, 1979), but their effect on birth intervals is not known. Prostaglandins from the uterus and placenta have also been suggested to contribute to the control of uterine contractions during delivery (Watts et al., 1988), and it is possible that the effects of prostaglandins could be cumulative with increasing litter size. Elucidation of the mechanism responsible for the decreased birth intervals of large litters might be exploited to reduce birth intervals in all litter sizes, thereby decreasing farrowing stress on sows and stillbirth rates of piglets.

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