Interrelationships among conceptus size, uterine protein secretion, fetal erythropoiesis, and uterine capacity[1]

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ABSTRACT: The interrelationships among d-11 conceptus size, d-105 placental weight, placental efficiency (the ability of the placenta to support fetal growth and development), fetal erythropoiesis, and uterine capacity were examined in ½ Meishan, ½ White crossbred gilts that were unilaterally ovariohysterectomized at 90 to 100 d of age. In Exp. 1, gilts were mated after at least one normal estrous cycle and then slaughtered at 105 d of gestation and number of fetuses and CL, placental weights, fetal weights, hematocrits, fetal plasma iron, and fetal plasma folate were measured. In Exp. 2, gilts were mated and plasma progesterone was measured on d 2 and 3 of gestation. On d 11, the length of the remaining uterine horn was recorded and the uterine horn was flushed with minimal essential medium. Number of CL, conceptus number, conceptus diameters, and total uterine flush retinol-binding protein (tRBP), acid phosphatase (tAP), and folate-binding protein (tFBP) were measured. Gilts were mated again and slaughtered at 105 d of pregnancy and the same traits measured in Group 1 were recorded. Plasma progesterone concentrations on d 2 and 3 were correlated with average conceptus diameter on d 11 (r = 0.60, $P < 0.01$, for each day). In contrast, tRBP (r = 0.49, $P < 0.01$), tAP (r = 0.53, $P < 0.01$), and tFBP (r = 0.51, $P < 0.01$) in uterine flushings on d 11 were only correlated with d-3 plasma progesterone concentrations. No correlations between d-11 average conceptus diameter or d-11 uterine length with d-105 uterine capacity were observed. Uterine capacity was negatively correlated with placental weight, fetal weight and fetal hematocrit (r = –0.36, $P < 0.01$; r = –0.44, $P < 0.01$; r = –0.32, $P < 0.01$; respectively). Hematocrits were correlated with fetal plasma iron (r = 0.50, $P < 0.01$) and folates (r = 0.44, $P < 0.01$). Hematocrit, plasma iron, and plasma folate were each correlated with residual fetal weights after adjusting for placental weight (a measure of placental efficiency), and accounted for 11% of the variation in this trait. These data suggest that conceptus diameter and uterine protein secretion on d 11 may be influenced by the onset of progesterone secretion by the CL, but do not support an influence of conceptus growth during early pregnancy on uterine capacity. These results also suggest that reducing placental and fetal weights will likely result in increased uterine capacity.

Key Words: Fetus, Folic Acid, Iron, Placenta, Pregnancy

Introduction

Recent experiments have implicated conceptus development during early pregnancy (Youngs et al., 1994), placental efficiency (Biensen et al., 1998; Wilson et al., 1999), and fetal erythropoiesis (Pearson et al., 1998) as possible factors influencing uterine capacity of swine. In Meishan pigs, both the placenta and the fetus are smaller than in European breeds (Christenson, 1993;

Biensen et al., 1998; Wilson et al., 1998). Slower conceptus development during early pregnancy in Meishan pigs has been hypothesized to result in smaller placentas, which take up less space in the uterus, and therefore contribute to improved litter size (Youngs et al., 1994). High placental efficiency, measured as the ratio of fetal to placental weight, has been suggested to allow smaller placentas to maintain relatively larger fetuses, thereby contributing to uterine capacity and litter size (Biensen et al., 1998; Wilson et al., 1999). Finally, it has been shown that, under crowded intrauterine conditions, small fetuses have lower hematocrits, indicating that erythropoiesis is impaired in these fetuses (Pearson et al., 1998). The efficiency of fetal erythropoiesis may influence the oxygen transport capacity of the developing conceptus (Gump et al., 1968), affecting conceptus health and survival under crowded intrauterine conditions. These components are all likely to interact

with each other. For example, early conceptus development may influence placental weight during later pregnancy. In addition, the capacity of the fetal blood to transport oxygen is likely to be a component of overall placental efficiency. The objective of the following experiments was to examine the interrelationships among conceptus development, placental weight, placental efficiency, and fetal erythropoiesis and their influence on uterine capacity, defined as the number of living fetuses present per uterine horn at 105 d of gestation.

Materials and Methods

In Exp. 1, ½ Meishan, ½ White crossbred gilts were unilaterally ovariohysterectomized at 90 d of age. This was done so that subsequent litter size becomes a measure of uterine capacity (Christenson et al., 1987). At approximately 200 d of age, gilts were mated to mature boars. Gilts were slaughtered at 105 d of gestation and the reproductive tract was recovered. The broad ligament was trimmed, the uterus was opened along the antimesometrial side, and a blood sample (5 mL) from each fetus was collected from the umbilical artery into heparinized tubes. The number of fetuses, number of corpora lutea, fetal weights, and placental weights were then recorded. In Exp. 2, ½ Meishan, ½ White crossbred gilts were unilaterally ovariohysterectomized at 100 d of age. At approximately 200 d of age, gilts were observed for estrous behavior twice daily and then mated to mature boars after at least one cycle of normal length (17 to 23 d). Blood samples were collected from each gilt on d 2 and 3 (d 0 = first day of estrus; approximately 48 and 72 h after detection of estrus) by jugular venipuncture. On d 11 of pregnancy, gilts were anaesthetized and laparotomized, and the length of the remaining uterine horn was measured. Then, the uterine horn was flushed with 20 mL of minimal essential medium to recover intrauterine proteins and conceptuses and the volume recovered was recorded. The number and diameters of the conceptuses in the flushings were recorded, and then the uterine flushings were centrifuged ($1,000 \times g$) and stored at −20°C until assayed. Gilts were allowed to recover for at least one full estrous cycle and then were mated again. Gilts were slaughtered at 105 d of gestation and processed identically to those described for Exp. 1.

Maternal plasma progesterone concentrations were measured using RIA (Killen et al., 1992). The inter- and intraassay coefficients of variation were 16 and 10.9%, respectively. Limit of detection for this assay was 156 pg/mL. Fetal blood samples were measured for hematocrit and then centrifuged to collect plasma. Fetal plasma was measured for plasma iron using the method of Schade et al., (1954) and plasma folate was measured using the Quantaphase assay kit (BioRad, Hercules, CA), which we validated previously for porcine plasma (Vallet et al., 2001). The inter- and intraassay coefficients of variation for the folate assay were 12.6 and 10.6%, respectively, and the limit of detection was 1 ng/mL.

Uterine flush samples were measured for acid phosphatase (a measure of uteroferrin) using a method described previously (Vallet et al., 1994); and retinol-binding protein (**RBP**) and folate-binding protein (**FBP**) using previously validated RIA (Vallet, 1994; Vallet et al., 1999). The inter- and intraassay coefficients of variation for the RBP assay were 21 and 2.9% and for the FBP assay were 3.4 and 4.2%, respectively. Limits of detection for the RBP and FBP assays were 10 ng/mL and 1.25 ng/mL, respectively. Acid phosphatase, RBP, and FBP concentrations were multiplied by the uterine flush volume (mean = 15 mL; range 11 to 18 mL) recovered to obtain total acid phosphatase, RBP, and FBP for each gilt.

Statistical Analysis

Data from both experiments were combined, and correlation analyses were performed between all the variables measured in both experiments to determine relationships. Diameters of the conceptuses obtained from each gilt on d 11 were averaged to obtain a single average conceptus diameter for each gilt. The potential influence of placental efficiency on uterine capacity was examined in several different ways. Placental efficiency was calculated as fetal weight divided by placental weight, as has been used previously (Wilson et al., 1999). Placental efficiency values for the fetuses within each litter were then averaged to obtain a single average value for each gilt. The placental efficiency ratio is correlated with placental weight. Thus, correlations obtained using this ratio could be the result of correlations with placental weight, rather than placental efficiency. To obtain a measure of placental efficiency that was independent of placental weight, the residual fetal weight was determined for each fetus after regression analysis of fetal weight using placental weight and the square of placental weight as independent variables. The residual fetal weights within a litter were then averaged to obtain a single value for each gilt. A further hypothesis, that placental efficiency of the smallest placentas in a litter may influence uterine capacity, was tested by examining the associations between uterine capacity at d 105 for each gilt and the lowest placental weight in that litter, its corresponding placental efficiency, and its corresponding residual fetal weight.

The relative contribution of hematocrit, plasma iron and plasma folate concentrations to placental efficiency, measured as residual fetal weights after adjusting for placental weight, was determined using sequential regression analysis using the individual fetal measurements. A similar analysis was performed for factors contributing to hematocrit and included fetal plasma iron and folate.

Results

Means, SEM, and range for each trait measured are indicated in Table 1. Maternal progesterone concentra-

Table 1. Mean, number of observations (N), S.E.M., and range of values for d-2 and -3 plasma progesterone (d2P and d3P, respectively); number of corpora lutea (d11CL), number of embryos (d11EN), average conceptus diameter (d11ACD), number of uterine length (d11UL), total uterine flush acid phosphatase (tAP), total retinol binding protein (tRBP), and total folate binding protein (tFBP) measured on d 11 of pregnancy; and number of corpora lutea (d105CL), uterine capacity (d105UC), fetal plasma iron (PI), fetal plasma folate (PF), fetal hematocrit (HCT), average placental weight (PW), weight of the smallest placenta in the litter for each gilt (LOPW), fetal weight (FW), average placental efficiency (PE), placental efficiency of the smallest placenta in each litter (LOPE), average residual fetal weight after correction for placental weight using covariate analysis (FR), and the fetal residual for the smallest placenta in each litter (LOFR) measured at 105 d of gestation

Variable	N	Mean	S.E.M.	Minimum	Maximum
d2P	54	2.68	0.18	0.8	6.6
d3P	54	8.91	0.95	1.8	32.3
d11CL	55	14.02	0.42	7.0	24.0
d11EN	50	11.08	0.55	4.0	24.0
d11ACD	50	2.91	0.15	1.2	5.6
d11UL	54	163.09	5.14	76.0	260.0
tAP	54	12.71	2.89	1.3	133.6
tRBP	54	57.31	13.61	1.5	578.3
tFBP	53	6.15	1.27	0.2	42.8
d105CL	119	14.75	0.25	7.0	23.0
d105UC	114	6.36	0.22	1.0	11.0
PI	120	0.87	0.02	0.55	1.9
PF	120	16.67	0.62	3.3	44.1
HCT	121	33.81	0.35	24.0	46.5
PW	122	155.50	4.50	62.0	333.0
LOPW	121	103.73	4.26	29.0	263.0
FW	121	737.43	16.18	405.0	1,407.0
PE	121	4.92	0.07	2.7	7.5
LOPE	121	5.85	0.11	3.4	9.9
FR	121	0	9.10	−333.3	362.5
LOFR	121	19.88	11.19	−210.0	511.0

tions collected on d 2 and 3 were significantly positively correlated, and both were positively correlated with average conceptus diameter at d 11 of pregnancy (Table 2). Interestingly, intrauterine content of RBP, acid phosphatase, and FBP were correlated with average conceptus diameter but were more highly correlated with progesterone concentrations on d 3 of gestation, and were not correlated with progesterone concentrations on d 2 of gestation.

At 105 d of gestation, placental weight, fetal weight, hematocrit, plasma iron, and plasma folate were all positively correlated with each other (Figures 1, 2, and 3) and were negatively correlated with uterine capacity (Table 3). As expected, there was no correlation between number of CL at 105 d of gestation and uterine capacity, indicating that litter size in unilaterally ovariohysterectomized gilts at 105 d of gestation is independent of ovulation rate. There was a negative correlation between number of CL and fetal weight and a trend toward a negative correlation between number of CL and placental weight. Also, fetal hematocrit and fetal plasma iron were both negatively correlated with number of CL. Neither the within-litter average placental efficiency nor the placental efficiency of the smallest placenta in the litter, calculated as the weight of the

fetus divided by the weight of the placenta (Wilson et al., 1999), were correlated with uterine capacity. In contrast, placental efficiency measured as the average residual fetal weight after adjusting for placental weight, and the fetal residual corresponding to the smallest placenta in the litter, were negatively correlated with uterine capacity (Table 3).

Results of Exp. 2 allow an examination of interrelationships between variables measured at d 11 of pregnancy and variables measured at 105 d of gestation in a subsequent pregnancy in the same gilts (Table 4). Very few significant relationships were observed. Number of CL on d 11 was highly correlated with number of CL on d 105, suggesting that ovulation rate in pigs is repeatable between pregnancies. The correlation between the number of conceptuses on d 11 and uterine capacity on d 105 in a subsequent pregnancy was not significant. There was also no relationship between d-11 average conceptus diameter and d-105 placental weights in the subsequent pregnancy. Finally, no significant relationship was obtained between the length of the remaining uterine horn on d 11 (range 76 to 260 cm) and uterine capacity at 105 d of gestation.

Hematocrit, plasma iron, and plasma folate were all correlated with placental efficiency measured as resid-

Table 2. Correlations between maternal plasma progesterone on d-2 (2P), d-3 (3P), d-11 embryo numbers (d11EN), d-11 corpora lutea (d11CL), d-11 uterine length (d11UL), d-11 average conceptus diameter (d11ACD), total intrauterine acid phosphatase (tAP), retinol-binding protein (tRBP), and folate-binding protein (tFBP)

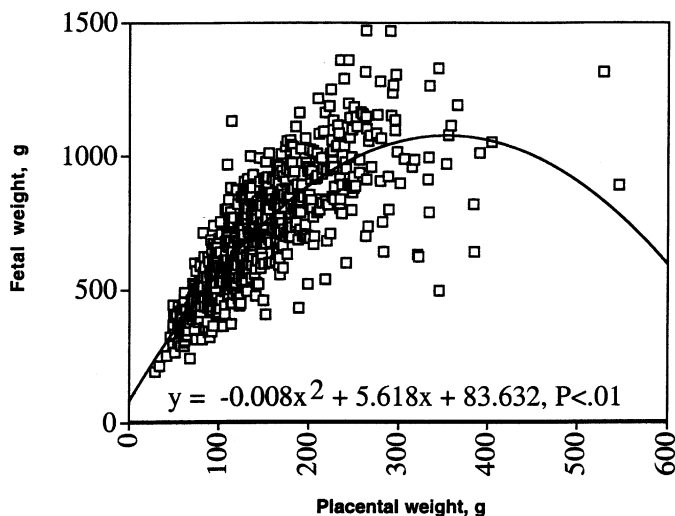| Variable	tFBP	tRBP	tAP	d11ACD	d11UL	d11CL	d11EN	3P
2P								
r	0.09	0.07	0.05	0.61	−0.18	−0.07	−0.11	0.62
P	NS	NS	NS	0.01	NS	NS	NS	0.01
N	51	52	52	48	52	53	48	54
3P								
r	0.51	0.49	0.53	0.60	−0.01	0.11	−0.07	
P	0.01	0.01	0.01	0.01	NS	NS	NS	
N	51	52	52	48	52	53	48	
d11EN								
r	0.20	0.32	0.19	0.01	0.25	0.66		
P	NS	0.03	NS	NS	0.09	0.01		
N	48	48	48	50	48	50		
d11CL								
r	0.26	0.43	0.32	−0.01	0.27			
P	0.07	0.01	0.02	NS	0.05			
N	52	53	53	50	53			
d11UL								
r	0.27	0.32	0.28	0.10				
P	0.06	0.05	0.05	NS				
N	51	52	52	48				
d11ACD								
r	0.38	0.40	0.37					
P	0.01	0.01	0.01					
N	48	48	48					
tAP								
r	0.78	0.93						
P	0.01	0.01						
N	53	54						
tRBP								
r	0.76							
P	0.01							
N	53							

Figure 1. A scatter plot showing the curvilinear ($P <$ 0.01) relationship between placental weight and fetal weight for fetuses collected in both experiments.

The equation shown in the figure:

$$y = -0.008x^2 + 5.618x + 83.632, \; P < .01$$

ual fetal weight, and they were correlated with each other. It was, therefore, of interest to determine whether hematocrit, plasma iron, and plasma folate are each related independently to placental efficiency or whether one of these variables accounts for the relationships between placental efficiency and the other two. Regression analysis indicated that hematocrit, plasma iron, and plasma folate each accounted for separate, statistically significant portions of the variability in residual fetal weight. The three variables combined account for 11% of the total variation. A similar analysis of the contribution of plasma iron and plasma folate to the variability in hematocrit indicated that both contribute significantly to hematocrit, and the two together account for 22% of the variation in hematocrit.

Discussion

The relationships obtained between the variables measured in this study support some current concepts regarding factors influencing uterine capacity, while failing to support others. The negative correlations be-
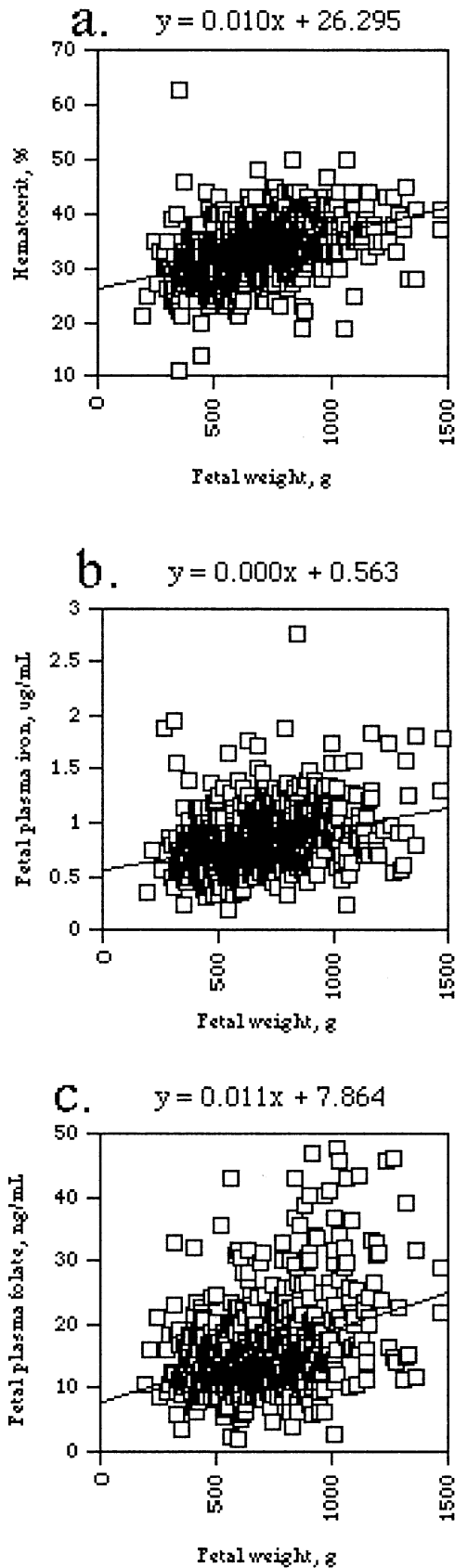
Figure 2. Scatterplots showing the relationships between fetal weight and hematocrit (a), fetal plasma iron (b), and fetal plasma folate (c).
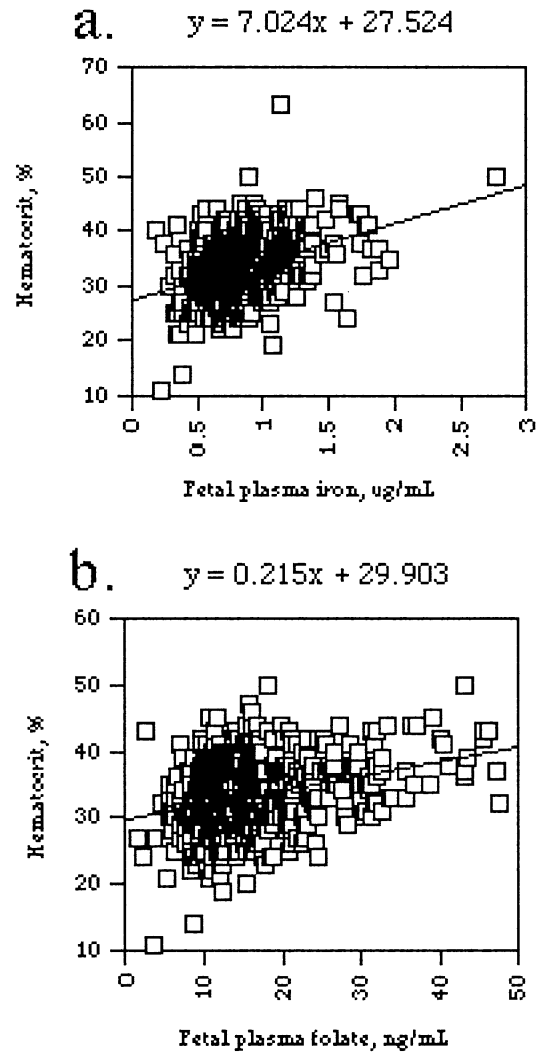

Figure 3. Scatterplots showing the relationships between hematocrit and fetal plasma iron (a) and fetal plasma folate (b).

tween uterine capacity and placental weights, fetal weights, and fetal residuals suggest that decreasing conceptus size may increase uterine capacity. The lack of correlation between placental efficiency and uterine capacity may indicate that placental efficiency, as it has been measured in previous reports, does not influence uterine capacity. The positive correlation between hematocrits and fetal weight in unilaterally ovariohysterectomized pigs confirms that uterine crowding impairs fetal erythropoiesis. Positive correlations between residual fetal weight (a measure of placental efficiency), hematocrits, plasma iron, and plasma folate suggest that improvements in iron and folate transport to the fetus during pregnancy may have beneficial effects on the efficiency of fetal erythropoiesis and may result in improvements in fetal health and survival. The correlations between plasma progesterone on d 3, d-11 uterine protein secretion, and d-11 conceptus diameters are consistent with observations that the onset of uterine protein secretion and the size of the conceptus on d 11

Table 3. Correlations between placental weight (PW), fetal weight (FW), placental efficiency (PE), fetal residual after using placental weight as covariate (FR), hematocrit (HCT), fetal plasma iron (PI), fetal plasma folate (PF), corpora lutea (d105CL), and uterine capacity (d105UC) measured on d 105 of gestation in Exp. 1 and 2 combined

Variable	d105UC	d105CL	PF	PI	HCT	LOFR	FR	LOPE	PE	FW	LOPW
PW											
r	−0.36	−0.18	0.36	0.29	0.36	0.13	0	−0.38	−0.67	0.82	0.75
P	0.01	0.05	0.01	0.01	0.01	NS	NS	0.01	0.01	0.01	0.01
N	114	119	120	120	121	121	121	0.21	121	121	121
LOPWP											
r	−0.53	−0.22	0.47	0.40	0.36	0.23	0.32	−0.46	−0.32	0.80	
P	0.01	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	
N	114		120	120	121	121	121	121	121	121	
FW											
r	−0.44	−0.24	0.45	0.38	0.42	0.42	0.56	−0.17	−0.17		
P	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.07	0.06		
N	114	118	120	120	121	121	121	121	121		
PE											
r	0.07	0	−0.01	−0.01	−0.04	0.28	0.69	0.49			
P	NS	NS	NS	NS	NS	0.01	0.01	0.01			
N	114	118	120	120	121	121	115	121			
LOPE											
r	0.16	0	−0.16	−0.16	−0.12	0.69	0.27				
P	0.09	NS	0.08	0.09	NS	0.01	0.01				
N	114	118	120	120	121	121	121				
FR											
r	−0.24	−0.14	0.30	0.25	0.28	0.55					
P	0.01	0.08	0.01	0.01	0.01	0.01					
N	114	118	120	120	121	121					
LOFR											
r	−0.23	0	0.07	0.12	0.12						
P	0.01	NS	NS	NS	NS						
N	114	118	121	120	121						
HCT											
r	−0.32	−0.22	0.44	0.50							
P	0.01	0.02	0.01	0.01							
N	114	118	120	120							
PI											
r	−0.43	−0.22	0.45								
P	0.01	0.02	0.01								
N	113	117	120								
PF											
r	−0.32	−0.02									
P	0.01	NS									
N	113	117									
D105CL											
r	0.15										
P	NS										
N	111										

of pregnancy are influenced by the timing of the onset of progesterone secretion by the CL. However, results do not support the hypothesis that small conceptuses on d 11 of pregnancy develop into conceptuses with small placentas during later pregnancy, resulting in greater uterine capacity. Furthermore, longer uterine horns were not associated with greater uterine capacity.

The idea that reduced placental and fetal weights may allow for increased uterine capacity was suggested by experiments comparing the Meishan pig to European pig breeds. A consistent finding in these experiments is that both placentas and fetuses of the Meishan are smaller than those of European breeds (Christenson, 1993; Biensen et al., 1998). The negative correlation between both placental and fetal weights and uterine capacity obtained in the current experiments is consistent with the hypothesis that reduced placental and fetal weights result in greater uterine capacity. However, it is not possible to tell whether lower conceptus weights are the cause of the greater uterine capacity or the result of it. Reliable methods to alter placental and fetal weights during pregnancy are required to test this question properly.

Table 4. Correlations between plasma progesterone concentrations on d 2 and 3, variables measured on d 11 of pregnancy and variables measured on d 105 of gestation in a subsequent pregnancy[a]

Variable	d105UC	d105CL	PF	PI	HCT	FR	LOFR	PE	LOPE	FW	PW	LOPW
2P												
r	−0.19	−0.09	−0.19	−0.16	−0.24	−0.06	−0.05	0.02	0	−0.11	−0.10	−0.14
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
N	39	46	46	46	46	46	46	46	46	46	47	46
3P												
r	−0.16	0	−0.16	−0.13	−0.09	0.02	−0.21	−0.03	0.12	0.03	−0.01	−0.03
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
N	39	46	46	46	46	46	46	46	46	46	47	46
d11EN												
r	0.20	0.43	−0.29	−0.23	−0.03	−0.01	0	0.22	0.12	−0.34	−0.35	−0.28
P	NS	0.01	0.06	NS	NS	NS	NS	NS	NS	0.03	0.02	0.07
N	37	41	43	43	43	43	43	43	43	43	44	43
d11CL												
r	0.12	0.74	−0.18	−0.27	−0.02	0.13	0.22	0.31	0.33	−0.24	−0.32	−0.24
P	NS	0.01	NS	0.06	NS	NS	NS	0.03	0.02	NS	0.02	NS
N	41	46	48	48	48	48	48	48	48	48	49	48
d11UL												
r	0.20	0.39	0.17	−0.09	−0.11	0.11	0.03	0	−0.05	0.12	0.06	0.13
P	NS	0.01	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
N	39	45	46	46	46	46	46	46	46	46	47	46
d11ACD												
r	−0.06	−0.06	0	−0.24	−0.16	0.02	−0.01	−0.09	−0.01	0.17	0.15	0.03
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
N	37	41	43	43	43	43	43	43	43	43	44	43
tAP												
r	0.20	0.19	−0.02	−0.17	0	0.04	0.32	−0.13	0.21	0.21	0.20	−0.05
P	NS	NS	NS	NS	NS	NS	0.03	NS	NS	NS	NS	NS
N	39	44	46	46	46	46	46	46	46	46	47	46
tRBP												
r	0.27	0.27	−0.05	−0.26	−0.08	0.02	0.29	−0.10	−0.21	0.13	0.13	−0.09
P	NS	0.08	NS	0.08	NS	NS	0.05	NS	NS	NS	NS	NS
N	39	44	46	46	46	46	46	46	46	46	47	46
tFBP												
r	0.29	0.17	0.08	−0.17	0.12	−0.11	0.15	−0.18	0.02	0.08	0.17	0.07
P	0.08	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
N	39	43	45	45	45	45	45	45	45	45	46	45

[a]See Table 1 for trait abbreviations.

In contrast to placental and fetal weight, no relationship was obtained between uterine capacity and either the overall average placental efficiency (measured as the ratio of fetal weight to placental weight) or the placental efficiency of the smallest placenta. Both overall average residual fetal weight, and the residual fetal weight corresponding to the smallest placenta in each litter were negatively correlated with uterine capacity. These observations are not consistent with the idea that increased placental efficiency increases uterine capacity. However, care must be taken in interpreting these results. It would seem certain that increased efficiency of the uterus and placenta in transporting nutrients to the fetus must improve the health and survival of the fetus and, therefore, influence uterine capacity. Thus, the explanation for the lack of a relationship between placental efficiency and uterine capacity may be that the measurements of placental efficiency used in this and other experiments are not a true measure of the efficiency of placental transport. The relationship between fetal weight and placental weight is not linear, indicating that the weight of the fetus is not directly proportional to the weight of the placenta over the entire range of placental weights (Figure 1). The curvilinear relationship between fetal weight and placental weight indicates that the fetal weight:placental weight ratio is inappropriate as a measure of the true efficiency of placental transport. Given a large enough placenta to meet the needs of the fetus, the weight of the fetus is no longer controlled by placental transport. In fact, for placental weights greater than 200 g, there is no relationship between fetal weight and placental weight. Under these conditions, fetal weight is more likely to be controlled, and limited by, factors that are intrinsic to the fetus. This curvilinear relationship would naturally cause the fetal weight:placental weight ratio to fall with increasing placental weight, becoming less and less a true measure of the capacity of the placenta to

transport nutrients. The use of regression analysis to account for the curvilinearity of the relationship between fetal weight and placental weight only partially corrects this problem. At high placental weights, at which the placenta no longer limits fetal weight, the variability around the curvilinear relationship between fetal weight and placental weight likely primarily reflects variability in fetal factors controlling fetal weight, not variability in placental efficiency. These fetal factors will likely only have their full influence on fetal weight when the fetus is attached to a large placenta (i.e., in a uterine environment occupied with only a few fetuses). For smaller placentas, fetal weight will be a compromise between the influence of fetal factors on growth of the fetus and the efficiency of the placenta. The negative relationship between residual fetal weights and uterine capacity for the smallest placenta in a litter suggests that when these two factors are incompatible (e.g., when fetal demands are greater than placental efficiency), conceptus loss occurs. Fetuses may only reach their true intrinsic (i.e., controlled by fetal factors) growth potential when attached to a large placenta, which occurs primarily in low-uterine capacity gilts. Thus, it is likely that neither method of calculation accurately measures the efficiency of placental transport alone. Even the calculation of residual fetal weight estimates the compromise between fetal intrinsic growth rate and placental efficiency, and a better method is needed.

As previously indicated, these results are consistent with the idea that limiting placental and fetal growth improves uterine capacity. It has been suggested that the size of the conceptus is partially controlled by the size of the blastocyst at the time of elongation (i.e., d 11 to 12 of pregnancy; Youngs et al., 1994). They hypothesized that slower growth of the blastocyst during early pregnancy results in embryos that elongate to a shorter length, interfere with each other less, take up less space in the uterus, and have smaller placentas during later pregnancy. However, there was no correlation between conceptus diameters on d 11 of pregnancy and placental weights at 105 d of gestation or uterine capacity in a subsequent pregnancy. It is possible that variability in the timing of ovulation and(or) fertilization may have contributed to the variability in conceptus diameters on d 11, decreasing the ability to detect an association between d-11 conceptus diameters and d-105 placental weights or uterine capacity. In addition, the repeatability of the average diameter of conceptuses between pregnancies in a gilt has not been measured, and could be quite low, given that the repeatability of uterine capacity between consecutive pregnancies is only moderate (r = 0.55, n = 69, $P < 0.01$; J. L. Vallet, unpublished observations). Thus, the correlation between average conceptus diameter and placental weight or uterine capacity in a subsequent pregnancy would be the product of the repeatability of conceptus diameters in subsequent pregnancies and the correlation between conceptus diameter and placental weights

or uterine capacity within a pregnancy. This combined correlation would be lower than both of the component correlations. Thus, it may be that the correlations between conceptus diameter and placental weight and uterine capacity in a subsequent pregnancy are less than our ability to detect using the number of animals in this experiment. Unfortunately, it is not possible to get this information within the same pregnancy, measurement of average conceptus diameter requires flushing the uterus, which would likely influence placental growth and uterine capacity, even if the conceptuses were returned after measurement. However, other results from this experiment suggest an alternative way of testing this hypothesis. The onset of progesterone secretion by the CL was correlated with both average conceptus diameter and uterine protein secretion. This observation confirms that uterine protein secretion can be advanced using early progesterone treatment (Vallet et al., 1998). Conceptus estrogen production was also advanced using early progesterone treatment, suggesting that conceptus development was advanced. Thus, manipulation of progesterone during the first 3 d of pregnancy offers a potential means of modifying conceptus diameters and possibly placental weights and uterine capacity. We are currently testing this idea.

Several experiments have suggested that uterine length influences uterine capacity (Wu et al., 1988; Chen and Dziuk, 1993; Wu and Dziuk, 1995). The use of the unilateral ovariohysterectomy treatment to measure uterine capacity is based on this concept. It has also been shown previously that gilts vary profoundly in the length of the uterine horns (Chen and Dziuk, 1993), an observation borne out in our experiments. However, paradoxically no correlation was obtained between uterine length and uterine capacity. One possible resolution to this paradox is that the functionality of a given length of uterus between gilts may be highly variable. Thus, uterine length may be a poor indicator of the total capacity of the uterus. This concept is supported by the low correlations between the uterine secreted proteins and uterine length. Following this logic, the unilateral ovariohysterectomy treatment may work because, regardless of the length of the uterus, one-half of the total uterine function is removed. These results also contrast the report of Wu and Dziuk (1995), in which it was shown that prepubertal uterine length was correlated with litter size on d 30 of a subsequent pregnancy. It seems likely that uterine length between subsequent estrous cycles in a gilt is repeatable; the correlation between pre- and postpubertal uterine length has been estimated to be 0.56 (Wu and Dziuk, 1995). However, the previous report (Wu and Dziuk, 1995) examined uterine capacity at d 30, so one explanation for the differences in the results obtained in our experiments vs those of Wu and Dziuk (1995) is that, under moderately crowded conditions, the limitations due to uterine capacity do not express themselves until after d 30 of gestation (Vallet, 2000). Thus, results of

the current experiment do not support the concept that gilts with longer uterine horns have greater uterine capacity, suggesting that uterine length is not a good measure of the functionality of the uterus.

Implications

These data allow an examination of the interrelationships between uterine capacity and uterine, placental, and fetal variables. Results confirm that reducing fetal and(or) placental weights during pregnancy are likely to result in improved uterine capacity. Changes in the onset of progesterone secretion by the corpus luteum may be useful in manipulating conceptus growth. In contrast, increasing uterine length is unlikely to result in greater uterine capacity. Placental efficiency measurements based on correcting fetal weights using placental weights, either by using a ratio or by covariate analysis, may not be accurate measures of true placental efficiency. Hematocrits are lower in small fetuses and this may contribute to their poor survival. Manipulation of iron and(or) folate transport may be one means to alleviate this problem. These data provide clues to potentially effective methods to improve uterine capacity and litter size of swine.

Literature Cited

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

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

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

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

Gump, F. E., H. Butler, and J. M. Dinney. 1968. Oxygen transport and consumption during acute hemodilution. Ann. Surg. 168:54–60.

Killen, J. H., R. K. Christenson, and J. J. Ford. 1992. Ovarian follicular changes after weaning in sows. J. Anim. Sci. 70:2801–2808.

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

Schade, A. L., J. Oyama, R. W. Reinhart, and J. R. Miller. 1954. Bound iron and unsaturable iron-binding capacity of serum, rapid and reliable quantitative determination. Proc. Soc. Exp. Biol. Med. 87:443–448.

Vallet, J. L. 1994. Technical Note: A radioimmunoassay for porcine retinol binding protein. J. Anim. Sci. 72:2449–2454.

Vallet, J. L., R. K. Christenson, and H. G. Klemcke. 1999. Technical Note: A radioimmunoassay for porcine intrauterine folate binding protein. J. Anim. Sci. 77:1236–1240.

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

Vallet, J. L., and R. K. Christenson. 1994. Effect of estrone treatment from day 30 to 45 of pregnancy on endometrial protein secretion and uterine capacity. J. Anim. Sci. 72:3188–3195.

Vallet, J. L., R. K. Christenson, H. G. Klemcke, and P. L. Pearson. 2001. Intravenous infusion of iron and tetrahydrofolate does not influence intrauterine uteroferrin and secreted folate binding protein content in swine. J. Anim. Sci. 79:188–192.

Vallet, J. L., R. K. Christenson, W. E. Trout, and H. G. Klemcke. 1998. Conceptus, progesterone, and breed effects on uterine protein secretion in swine. J. Anim. Sci. 76:2657–2670.

Youngs, C. R., L. K. Christenson, and S. P. Ford. 1994. Investigations into the control of litter size in swine: III. A reciprocal embryo transfer study of early conceptus development. J. Anim. Sci. 72:725–731.

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

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

Wu, M. C., and P. J. Dziuk. 1995. Relationship of length of uterus in prepubertal pigs and number of corpora lutea and fetuses at 30 days of gestation. Anim. Prod. Sci. 38:327–336.

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