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EFFECT OF UNILATERAL HYSTERECTOMY AND OVARIECTOMY ON PUBERTY, UTERINE SIZE AND EMBRYO DEVELOPMENT IN SWINE[1]

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ABSTRACT

Eighty crossbred gilts were assigned randomly to treatments: 1) removal of an ovary and ipsilateral uterine horn (UHO) at 130 d of age and removal of the remaining ovary and uterine horn 12 d post-puberty; 2) UHO at 130 d of age, mated and reproductive tracts recovered when slaughtered at 30 d of gestation; 3) UHO 12 d post-puberty, mated and slaughtered at 30 d of gestation and 4) unoperated controls that were mated and slaughtered at 30 d of gestation. Age of puberty was not affected by treatments. Gilts in treatment 1 had a mean ovulation rate at the pubertal estrus comparable to gilts in treatment 3. But, gilts in treatments 2 and 3 had 16% fewer ($P<.01$) corpora lutea at 30 d of gestation than control gilts. Length and weight of the remaining uterine horn at 12 d post-puberty for gilts treated at 130 d of age were similar to the averages of gilts left intact. Gilts with one uterine horn had 2.2 fewer live embryos at 30 d of gestation than control gilts ($P<.01$). But, the proportion of corpora lutea represented by live embryos did not differ significantly among treatments. Gilts with one uterine horn had 1.1 fewer live embryos ($P<.15$) after adjustment for number of corpora lutea, less uterine space occupied by each embryo ($P<.01$) and less total placental membrane per embryo ($P<.05$) than control gilts. Mean length of the remaining uterine horn was less for treatment 2 than for treatment 3 ($P<.01$), but time of UHO did not affect measurements of placental membranes and embryos. Number of corpora lutea and measures of uterine size explained from 25 to 67% of the variation within treatments in number of live embryos.

(Key Words: Gilts, Ovariectomy, Hysterectomy, Puberty, Uterus, Embryonic Development.)

Introduction

Uterine capacity, components of the uterus such as space, nutrients and placental surface area that are related to the number of fetuses that a uterus can support to parturition, was hypothesized to limit litter size at birth (Dziuk, 1968). Of the ova shed, 30 to 40% are not represented by piglets at birth (Pope and First, 1985). This loss explains more of the variation in litter size than ovulation rate (Johnson et al., 1984; Neal and Johnson, 1986).

In a population of gilts, ovulation rate will be less than uterine capacity in some gilts, while others will have ovulation rates that exceed uterine capacity (Leymaster et al., 1986). When ovulation rate is less than uterine capacity, variation in uterine capacity is not expressed as variation in litter size. Unilateral ovariectomy or ovariectomy and hysterectomy (UHO) resulted in ovulation rates in the remaining ovary similar to those of control females (Brinkley et al., 1964; Fenton et al., 1970). Leymaster et al. (1986) proposed that UHO produces a biological model in which ovulation rate and uterine capacity are independent. In this model, genetic variation for uterine capacity is expressed and uterine capacity can be selected for by selecting for litter size. The objectives of the present experiment were to determine the effects of UHO pre- and post-puberty in gilts on age of puberty, uterine size and embryo development to 30 d of gestation.

Experimental Procedure

Treatments. Eighty gilts from the F_6 generation of a randomly selected, randomly mated population formed by crossing British Large White and Landrace were assigned randomly to one of four treatments described in table 1. One ovary and ipsilateral uterine horn were removed from pre-pubertal gilts at 130 d of age in treatment 1; the remaining ovary and uterine horn were removed about 12 d after these gilts

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reached puberty. One ovary and ipsilateral uterine horn were removed from pre-pubertal gilts at 130 d of age in treatment 2, and at about 12 d post-puberty from gilts in treatment 3. Gilts in treatment 4 were left intact and no sham surgery was done. Gilts in treatments 2, 3 and 4 were mated at second or third estrus, and reproductive tracts were recovered at slaughter between 27 and 33 d of gestation.

Management. All gilts were born during a period of about 3 wk, weaned at 28 d of age and grown in a nursery to 56 d of age. They were then moved to a confinement building and nine to 11 gilts of about the same age were placed in each pen. From this point on, gilts were fed ad libitum a corn-soybean diet that contained 16% protein up to a weight of about 60 kg and 14% protein thereafter.

Age of puberty was defined as the first day that gilts would stand to be mounted by a boar. Exposure to boars was done once daily and began when gilts were 135 d of age. Natural mating occurred at second estrus for gilts in treatments 2, 3 and 4. They were mated each day during the estrous period that they were receptive to a boar. Gilts that did not conceive to matings during second estrus were remated on their third estrus. Forty-four of the 49 gilts in treatments 2, 3 and 4 that were mated conceived, and the distribution of conceptions to matings at second and third estrus is shown in table 1.

Surgical Procedure. Surgery was performed on all gilts within 3 d of the target age (130 d of age or 12 d post-puberty). Anesthesia was induced by thiamylal sodium (8.8 mg/kg body weight, iv) and was maintained with closed circuit inhalation of 1 to 2% halothane in combination with 11 ml of O_2 and 5 ml of $N_2O \cdot kg^{-1} \cdot min^{-1}$.

Gilts were randomly assigned for removal of the left or right ovary and ipsilateral uterine horn. Ovaries and uterus were gently exteriorized through a midventral incision, corpora lutea were counted (except for gilts in treatments 1 and 2 at 130 d of age) and length of each uterine horn was measured along the mesometrial border with a narrow, flexible tape from the external bifurcation of the uterine horn to the utero-tubal junction. Ligatures (umbilical tape) were placed on the major blood vessels in the mesovarium, mesosalpinx and mesometrium on the side designated for removal. Clamps were placed on the uterine horn (at the external bifurcation), and supporting ligaments and uterine horn and ovary were removed by electrocautery. The remaining stub of the uterine horn was closed with a purse-string suture and clamps were removed. After removal, ovaries and horns were blotted dry and weighed. Gilts were kept in post-surgery recovery rooms for 3 d and then returned to the pen from which they were removed before surgery.

Reproductive Tracts. Gilts were slaughtered between 27 and 33 d after the first day they were mated. Reproductive tracts were removed 30 to 40 min after gilts were killed, placed in thermal containers to maintain temperature and taken to a laboratory for examination. Proce-

TABLE 1. EXPERIMENTAL DESIGN AND NUMBER OF GILTS PER TREATMENT[a]

		Unilateral ovariectomy and hysterectomy at			Estrus of conception		
Treatment	No. of gilts	130 d	12-d post-puberty	No. mated	Second	Third	30 d gestation
1[b]	20	Surgery (20)	Surgery (19)				
2[c]	20	Surgery (20)		16	13	1	Slaughtered (14)
3[c]	20		Surgery (18)	16	5	9	Slaughtered (14)
4	20			17	11	5	Slaughtered (16)

[a]Numbers in parentheses are number of gilts in each treatment. Reduction in number at the different periods reflects losses from death, failure to express estrus, failure to be pregnant and loss of reproductive tracts at slaughter.

[b]Gilts were randomly assigned to unilateral hysterectomy and ovariectomy of the left or right side at 130 d of age, the other side was removed 12 d post-puberty.

[c]Gilts were randomly assigned to unilateral hysterectomy and ovariectomy of left or right side.

dures for processing tracts and data collected were similar to those described by Knight et al. (1977).

Corpora lutea on the ovaries were counted, length of each uterine horn was measured along the mesometrial border and each conceptus was carefully removed and placed on a flat surface. Length of the vascular portion and the necrotic tip of the placenta were measured without stretching the placental membrane. Volume of the placental membrane with fluid was measured by displacement of water in a graduated cylinder. Each embryo was dissected from its membranes, crown-rump length was measured and the embryo was weighed. Placental membranes, without fluid, were weighed and volume of the membranes was determined by displacement of water. Each embryo was examined and subjectively classified as alive or dead.

Statistical Analyses. Data were analyzed by Statistical Analysis System, procedure GLM (SAS, 1982). Age of puberty (all gilts) and measurements made during surgery (number of corpora lutea, uterine length and uterine weight for gilts in treatments 1 and 3) were fitted to a model including the effects of treatment and uterine side. Number of corpora lutea, number of live embryos, total number of embryos, uterine length, uterine length/live embryos and percentage live embryos of corpora lutea were fitted to this same model, and except number of corpora lutea and uterine length, were also analyzed with number of corpora lutea as a covariable to adjust treatment means for possible inherent differences in ovulation rate among gilts in each treatment. The effect of gilt (treatments 2, 3 and 4) was added to the model for analyses of measurements of the placenta and embryos; significance of treatment effects for these variables was determined with the mean square for gilts as the error variance.

Contrasts among least-squares means were made to answer specific objectives. The effect of pre-pubertal unilateral ovariectomy and hysterectomy on age of puberty was estimated by comparing the mean for gilts in treatments 1 and 2 to the mean for gilts in treatments 3 and 4. The effect of performing treatment pre-pubertally on number of corpora lutea, uterine length and uterine weight measured 12 d post-puberty was evaluated from the means for gilts on treatments 1 and 3. Two contrasts among means were made for all traits measured at 30 d of gestation. Treated gilts (mean of treatments 2 and 3) were compared with control gilts (mean of treatment 4), and the mean for gilts on treatment 2 was compared with the mean for gilts on treatment 3 to evaluate the effect of performing treatment pre- vs post-puberty.

Number of live embryos at 30 d of gestation was regressed on uterine length and weight at 130 d of age (treatment 2), uterine length and weight 12 d post-puberty (treatment 3) and uterine length and number of corpora lutea at 30 d of gestation (treatments 2, 3 and 4). Combinations of uterine length or uterine weight measured pre-breeding with uterine length and number of corpora lutea at 30 d of gestation were fitted in multiple regression models to evaluate jointly the effects of these variables on number of live embryos. Regression analyses were performed within treatments.

Results

Removal of an ovary and ipsilateral uterine horn at 130 d of age did not significantly affect age of puberty, and average length and weight of the remaining uterine horn at 12 d post-puberty were similar to the average length and weight of one horn in intact gilts (table 2). Side on which measurements were made did not significantly affect any measurement, and all means were averaged across uterine sides.

Ovulation rate at the pubertal estrus from the remaining ovary in unilaterally ovariectomized and hysterectomized gilts was similar to the total from both ovaries in control gilts (table 2). Gilts that were unilaterally ovariectomized and hysterectomized pre- and post-pubertally did not differ for number of corpora lutea at 30 d of gestation (table 3). But, the average number of corpora lutea at 30 d of gestation for these gilts was only 84% that of control gilts.

Length of the remaining uterine horn was the only uterine measurement that was affected ($P<.01$) by age at which unilateral ovariectomy and hysterectomy were performed (table 3). This measurement was 14% less for gilts treated pre-pubertally than for those treated post-pubertally.

Treated gilts had 2.2 fewer live embryos at 30 d of gestation than control gilts ($P<.01$). The proportion of corpora lutea represented by live embryos did not differ significantly among treatments; however it was highest for control gilts (table 3). The regression coefficient of number of live embryos on number of corpora

TABLE 2. EFFECT OF UNILATERAL OVARIECTOMY AND HYSTERECTOMY AT 130 D OF AGE ON AGE OF PUBERTY, NUMBER OF CORPORA LUTEA AT PUBERTAL ESTRUS AND UTERINE SIZE 12 D POST-PUBERTY

	Age of puberty (d)		No. of corpora lutea		Uterine length (cm)		Uterine weight (g)	
Treatment	n	$\bar{X}$	n	$\bar{X}$	n	$\bar{X}$	n	$\bar{X}$
Treated	36	166.1 ± 3.5[a]	19	12.0 ± .5[c]	19	102 ± 6[c]	19	274 ± 14[c]
Control	38	170.7 ± 3.4[b]	18	12.0 ± .5[d]	18	114 ± 6[d]	18	261 ± 15[d]

[a]Avg of gilts in treatments 1 and 2, see table 1 and text for description of treatments.

[b]Avg of gilts in treatments 3 and 4.

[c]Treatment 1.

[d]Treatment 3.

lutea was .54 ± .15 and the correlation between number of corpora lutea and number of live embryos was .50. Adjusting number of live embryos for possible inherent variation in ovulation rate reduced the difference between treated and control gilts to −1.1 embryos (P<.15).

Variation in number of corpora lutea did not affect the proportion of corpora lutea represented by live embryos; however the regression coefficient of length of uterus/live embryos on number of corpora lutea was −1.68 ± .67 cm. Unilateral ovariectomy and hysterectomy, as expected, reduced uterine space per live embryo measured by length of uterus/live embryos) in the remaining horn. For this variable, means

TABLE 3. EFFECT OF UNILATERAL HYSTERECTOMY AND OVARIECTOMY AT 130 D OF AGE (T2), 12 D POST-PUBERTY (T3) AND CONTROL (T4) ON NUMBER OF CORPORA LUTEA, UTERINE LENGTH, NUMBER OF EMBRYOS AND AVERAGE SPACE BETWEEN EMBRYOS AT 30 D OF GESTATION

Item	T2	T3	T4	C_1^a	C_2^a
No. of gilts	14	14	16		
No. of corpora lutea	10.8 ± .6	10.9 ± .6	12.9 ± .6	**	
Uterine length, cm	140 ± 6.5	162 ± 6.5	155 ± 4.2[b]		**
Unadjusted for no. of corpora lutea					
No. of live embryos	7.3 ± .6	7.6 ± .6	9.6 ± .6	**	
Total no. of embryos	8.4 ± .7	8.4 ± .7	9.8 ± .7		
Uterine length/live embryos, cm	21.6 ± 2.7	23.0 ± 2.7	34.3 ± 2.5	**	
Percentage live embryos of corpora lutea, %	69 ± 5	76 ± 5	75 ± 5		
Adjusted for no. of corpora lutea[c]					
No. of live embryos	7.7 ± .6	8.0 ± .6	8.9 ± .6		
Total no. of embryos	8.9 ± .6	8.9 ± .6	8.8 ± .6		
Uterine length/live embryos, cm	20.3 ± 2.6	21.9 ± 2.6	36.4 ± 2.5	**	
Percentage live embryos of corpora lutea, %	68 ± 5	70 ± 5	76 ± 5		

[a]Significant contrasts: $C_1 = 1/2\ (T2 + T3) - T4$; $C_2 = T2 - T3$.

[b]Average of left and right sides.

[c]Regression coefficients of each trait on number of corpora lutea were: .54 ± .15, .71 ± .16, −1.68 ± .67 and −.01 ± .01 for number of live embryos, total number of embryos, uterine length/live embryos and percentage live embryos of corpora lutea, respectively.

**P<.01.

for treated and control gilts differed significantly both before and after adjustment for number of corpora lutea.

Crowding of embryos caused by removal of one ovary and uterine horn resulted in less total placental membrane ($P<.05$), and particularly less support by vascularized membranes ($P<.01$), for each embryo in the remaining horn (table 4). But, this did not cause embryos to differ in length or weight at 30 d of gestation. Time of surgery did not affect means for measurements of placenta and embryos 30 d post-breeding.

Regression equations for number of live embryos at 30 d of gestation on uterine length and uterine weight at 130 d of age, 12 d post-puberty and 30 d of gestation and on number of corpora lutea at 30 d of gestation are presented in table 5 for each treatment. None of the models accounted for a significant proportion of the variation in number of live embryos among gilts unilaterally ovariectomized and hysterectomized at 130 d of age. In this group, the single variable that explained the most variation in number of embryos was uterine length at 30 d of gestation ($R^2=.19$, $P=.12$), and the most variation was explained by a model that included uterine length at 130 d of age and number of corpora lutea and uterine length at 30 d of gestation ($R^2=.26$, $P=.37$).

Neither length or weight of excised uterus in gilts unilaterally ovariectomized and hysterectomized 12 d post-puberty explained a significant proportion of the variation among gilts in number of embryos at 30 d of gestation. However, linear regression coefficients of number of embryos on uterine length and number of corpora lutea at 30 d of gestation were significant ($R^2=.37$ and .36, respectively). A model of uterine weight at 12 d post-puberty or uterine length at 30 d of gestation and number of corpora lutea at 30 d of gestation explained 52 and 53%, respectively, of the variation in number of embryos, and a model of uterine weight at 12 d post-puberty and uterine length and number of corpora lutea at 30 d of gestation explained 67% of the variation in number of live embryos.

Data for treatments 2 and 3 were combined, and regression equations of number of live embryos on number of corpora lutea and uterine length were calculated for treated and control gilts. All models explained a significant proportion of the variation in number of embryos in both treated and control groups, but for comparable models the R^2 value was higher for control gilts. The linear regression coefficient of number of embryos on number of corpora lutea was .46 ± .17 for treated gilts

TABLE 4. EFFECT OF UNILATERAL OVARIECTOMY AND HYSTERECTOMY AT 130 D OF AGE (T2), 12 D POST-PUBERTY (T3) AND CONTROL (T4) ON CHARACTERISTICS OF PLACENTA AND EMBRYOS AT 30 D OF GESTATION

Item	T2	T3	T4[a]	C_1^b	C_2^b
No. of gilts	14	14	16		
Length of placenta					
Total, cm	43.1 ± 2.1	40.4 ± 2.1	46.9 ± 1.3	*	
Anterior portion, cm	19.6 ± 1.1	19.3 ± 1.1	21.7 ± .7	*	
Vascular section, cm	14.2 ± .9	15.2 ± .9	17.4 ± .6	**	
Necrotic tip, cm	5.7 ± .7	4.1 ± .7	4.3 ± .4		
Posterior portion, cm	20.2 ± 1.0	18.5 ± 1.0	21.7 ± .7	*	
Vascular section, cm	14.8 ± .9	14.4 ± .9	17.6 ± .6	**	
Necrotic tip, cm	5.8 ± .5	4.0 ± .5	4.3 ± .4		*
Embryo length, cm	2.8 ± .1	2.9 ± .1	2.9 ± .1		
Embryo wt, g	2.2 ± .2	2.2 ± .2	2.2 ± .1		
Volume of placenta					
With fluid, ml	185 ± 12	181 ± 12	212 ± 8	*	
Without fluid, ml	24.3 ± 2.7	27.2 ± 2.7	29.0 ± 1.8		
Weight of placental membranes, g	24.3 ± 2.6	26.7 ± 2.6	29.0 ± 1.7		

[a]Average of left and right sides.

[b]Significant contrasts: $C_1 = 1/2\,(T2 + T3) - T4$; $C_2 = T2 - T3$.

*P<.05.

**P<.01.

and .79 ± .30 for control gilts. After adjusting for variation in ovulation rate, the partial regression coefficient of number of live embryos on uterine length at 30 d of gestation was still significant. Also, after adjusting for variation in uterine length, the partial regression coefficient of number of live embryos on number of corpora lutea was higher in control gilts (.59 ± .20) than in treated gilts (.33 ± .16).

Discussion

Compensation by the remaining ovary following removal of an ovary and ipsilateral uterine horn at 130 d of age resulted in the same number of ovulations 12 d post-puberty as the total from both ovaries of intact gilts. Several other researchers have reported that ovulation rate from the single ovary following unilateral ovariectomy was nearly 100% that of both ovaries in control gilts (e.g., Brinkley et al., 1964; Fenton et al., 1970; Knight et al., 1973). In our experiment, the average number of corpora lutea at 30 d of gestation for gilts with one ovary was only 84% that of control gilts. This difference was significant, but no explanation is apparent. Monk and Erb (1974) also found that weight of corpora lutea, weight

TABLE 5. REGRESSION COEFFICIENTS[a] OF NUMBER OF LIVE EMBRYOS AT 30 D OF GESTATION ON UTERINE LENGTH, UTERINE WEIGHT AND NUMBER OF CORPORA LUTEA

Independent variables	b_0	b_1	b_2	b_3	R^2	P[b]
Treatment 2						
Uterine length at 130 d, cm (X_1)	4.48	.088			.11	.26
Uterine wt at 130 d, cm (X_2)	7.39	−.008			.00	.87
No. of corpora lutea at 30 d of gestation (X_3)	4.34	.270			.07	.36
Uterine length at 30 d of gestation, cm (X_4)	.96	.046			.19	.12
$X_1 + X_3$	3.62	.069	.136		.12	.50
$X_2 + X_3$	3.9	−.033	.395		.13	.50
$X_3 + X_4$	.014	.150	.041		.21	.28
$X_1 + X_3 + X_4$	−.894	.075	−.003	.042	.26	.37
$X_2 + X_3 + X_4$	−.033	−.036	.281	.038	.25	.44
Treatment 3						
Uterine length 12 d post-puberty (X_5)	4.01	.031			.10	.26
Uterine wt 12 d post-puberty (X_6)	4.8	.011			.05	.45
X_3	1.47	.570*			.36	.02
X_4	−1.93	.059*			.37	.02
$X_5 + X_3$	−2.73	.034	.582*		.49	.02
$X_6 + X_3$	−4.99	.020†	.671**		.52	.02
$X_3 + X_4$	−3.83	.410†	.043†		.53	.02
$X_5 + X_3 + X_4$	−4.58	.017	.457†	.033	.55	.04
$X_6 + X_3 + X_4$	−9.31	.018†	.519*	.040†	.67	.01
Treatments 2 and 3						
X_3	2.46	.461*			.23	.01
X_4	.47	.047**			.27	.01
$X_3 + X_4$	−1.62	.332†	.036*		.37	.01
Treatment 4						
X_3	−.53	.789*			.33	.02
X_4	−1.01	.034*			.36	.01
$X_3 + X_4$	−6.26	.590†	.027*		.53	.01

[a] b_0, b_1, b_2 and b_3 are intercept and partial linear regression coefficients on independent variables in order of presentation.

[b] Observed level of significance for the model.

† $P<.10$.

* $P<.05$.

** $P<.01$.

of ovaries and number of corpora lutea at 30 d of gestation for unilaterally ovariectomized and hysterectomized gilts were 85, 67 and 90%, respectively, of that detected in control gilts.

The uterus imposes a limitation on fetal survival rate in the pig. Two factors seem to be involved, uterine length and spacing of the blastocysts within the lumen of the uterus (Wrathall, 1971). In the present experiment, unilateral ovariectomy and hysterectomy were used to reduce total uterine length by 50% before mating. Average length of uterus occupied by each live embryo at 30 d of gestation was reduced by about 35%. Length of the remaining uterine horn was 11% less (P>.05) at 12 d post-puberty than the mean length of both horns in intact gilts; at 30 d of gestation, gilts treated at 130 d of age had 14% shorter (P<.01) uterine horns than gilts treated 12 d post-puberty. Thus, pre-pubertal unilateral hysterectomy and ovariectomy may depress uterine length. No comparable data were found in the literature, and this experiment was not designed to investigate biological explanations for this finding. Length of the remaining uterine horn in treated gilts (average of treatments 2 and 3) was nearly the same as the average length of the two horns of intact gilts. Thus, the failure to achieve a 50% reduction in space per embryo was due almost entirely to fewer live embryos in uteri of gilts with one uterine horn.

Webel and Dzuik (1974) found that uterine space was not associated with embryonic mortality normally observed before d 30 of pregnancy. In our experiment, lower number of live emrbyos in gilts with one uterine horn was due partly to fewer ovulations for these gilts than for control gilts. The difference between treated and control gilts in total number of embryos at 30 d of gestation was 1.4 before, and −.1 after, adjusting for number of corpora lutea (table 3). Differences among treatments in total number of embryos was explained completely by variation in ovulation rate. Differences between treated and control gilts for number of live embryos, however, was 2.2 before adjustment for number of corpora lutea and 1.1 after adjustment. This comparison, and the significant regression coefficient of number of embryos 30 d post-breeding on measures of uterine size, suggest that uterine space may be important in early survival of embryos. Knight et al. (1977) suggested that placental insufficiency was the primary cause of increased fetal death and decreased fetal growth after d 35 of gestation in females that were unilaterally ovariectomized and hysterectomized. Our data support this suggestion. We found that by d 30 of gestation live embryos in uteri of gilts with one uterine horn were supported by placental membranes that were about 11% shorter than membranes supporting live embryos in uteri of control gilts. Further, there was a 16% reduction in length of the vascularized portion of placental membranes. This could have contributed to the reduction in number of live embryos at d 30 of gestation that was observed, and could very well lead to further fetal loss after d 30 in gilts with one uterine horn.

Leymaster et al. (1986) utilized unilateral ovariectomy and hysterectomy to evaluate the effect of crowding within the uterus on litter size at either 86 d of gestation or at parturition. A significant loss of fetuses occurred during the final 28 d of gestation. The distribution of ovulation rate limited the expression of uterine potential in intact gilts, but not in females with one uterine horn. They proposed that unilateral ovariectomy and hysterectomy and subsequent selection for litter size – or for ovulation rate and embryo(fetal) survival – may be more effective than direct selection for litter size in intact females. We conclude from our experiment that if such selection is done, unilateral ovariectomy and hysterectomy may be performed at 130 d of age and will not adversely affect age of puberty. Pre-pubertal treatment reduced uterine length at 30 d of gestation, but postpubertal treatment did not. Thus to achieve a normal number of ovulations with half the total uterine space, treatment 12 d post-puberty is recommended over treatment at 130 d of age.

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