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THE LIFESPAN OF CORPORA LUTEA INDUCED DURING THE LUTEAL PHASE OF THE ESTROUS CYCLE IN SWINE.¹

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A more complete understanding of the mechanisms involved in the function and maintenance of the corpus luteum would be very useful in developing more effective methods of controlling the estrous cycle in farm animals. Various types and classes of experimental animals have been utilized in an effort to define the factors causing the persistence of the corpus luteum. In swine, several different experimental approaches have been made in an attempt to extend, experimentally, the functional lifespan of the corpus luteum in non-pregnant animals. Less frequently, attempts have been made to induce premature regression. In general, the procedures used to induce premature regression have not been effective when applied to the corpora lutea of cycling swine. For example, Sammelwitz *et al.* (7) reported that injected progesterone would cause luteal regression in pregnant swine but not in cycling swine.

The experiment to be discussed here was conducted with non-pregnant gilts. The experimental design included an attempt to cause premature regression by inducing ovulation during the latter part of the luteal phase so that corpora lutea of two different ages would be present on the 14th to 16th day of the estrous cycle. By this procedure, it was possible to determine if the simultaneous regression of the two groups of corpora lutea would occur without respect to age of the luteal tissue. In addition, observations were made on the effectiveness of factors responsible for the development and function of induced corpora lutea in causing the persistence of older corpora lutea present in the same ovary.

Figure 1 presents a summary of the experimental results. In general, when corpora lutea were induced during the luteal phase of the estrous cycle, regression of the spontaneous and induced corpora lutea was not simultaneous. Instead, the induced corpora lutea were maintained for one cycle length following formation, even though regression of the spontaneous corpora lutea occurred without any apparent change in lifespan.

Two separate means of inducing ovulation was used. In one group of animals, ovulation was induced with a single injection of a pituitary FSH preparation. In six of nine animals, the regression and maintenance pattern stated above was exhibited. In two animals having a limited number of induced

ovulations and in 1 additional gilt, the induced corpora lutea regressed prior to autopsy. The second method involved the injection of PMS and HCG to induce ovulation. Thirteen animals were examined. Eighty-seven percent of the induced corpora lutea marked during the luteal phase were still present in the ovary in an apparently functional condition at autopsy 20 to 25 days following estrus. These results are presented in more detail by Neill and Day (6).

Figure 1 also presents a summary of the results obtained when corpora lutea were induced in cycling gilts that were subsequently hysterectomized. In these animals, both the spontaneous and induced corpora lutea were maintained for an extended period of time.

Observations were made to determine the functional abilities of the persistent induced corpora lutea. At autopsy, the gross appearance of the induced corpora lutea was not different from that of spontaneous corpora lutea of a comparable age. It was also observed that estrus was not exhibited following regression of spontaneous corpora lutea when induced corpora lutea were present in the ovaries. Studies were made on the progesterone concentration of the induced corpora lutea and, as shown in table 1, the results indicate that the functional abilities of the two sets of corpora lutea were not different prior to regression. The data presented in table 2 represents the progesterone concentration of induced corpora lutea on days 19 to 23 of the estrous cycle or approximately 8 to 10 days following formation. These levels appear to be normal. Progesterone determinations were also made on spontaneous and induced luteal tissue present in one ovary that was surgically removed during the luteal phase of the estrous cycle and these levels were then compared to the progesterone concentration of the corpora lutea present in the opposite ovary of the same animal 3 to 4 days later, which was after regression of the spontaneous corpora lutea. This comparison also suggests that the functional abilities of the spontaneous and induced corpora lutea were not different.

The results presented in tables 2 and 3 provide evidence that the lifespan of the spontaneous corpora lutea was not altered by inducing ovulation. This conclusion is also supported by the findings that both groups of corpora lutea persisted in hysterectomized

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animals, regressed spontaneous corpora lutea were observed as early as the 18th day of the estrous cycle, and at the time of laparotomy, which was 2 days after the administration of HCG, the spontaneous corpora lutea appeared normal. In contrast to these findings for the pig, Mayer and Klein (4) reported that in rabbits exhibiting 2 superimposed pseudo-pregnancies, and consequently the ovaries contained 2 sets of corpora lutea, the first generation of corpora lutea involuted rapidly following the formation of the second generation of corpora lutea. However, both generations of corpora lutea were maintained for at least 11 days when estrogen injections were continued following the second mating.

In many respects, the results obtained in the present study indicate that the lifespan of corpora lutea in cycling swine is determined by a factor intrinsic to the individual gland. However, this does not mean that systemic factors can not also be involved in the regression of cyclic corpora lutea since changes in the receptivity of the corpora lutea to the action of extrinsic luteotrophic or luteolytic factors may be an important part of the complete mechanism. In fact, the maintenance of both spontaneous and induced corpora lutea observed in hysterectomized animals included in the present study suggests the existence of such a mechanism.

If it is assumed that a hypophysial luteotrophic factor is in fact required before persistence of corpora lutea will occur in cycling swine, the results presented here are in agreement with the hypothesis presented by Sammelwitz *et al.*, (7) that the luteotrophic factor in pigs is not released continuously during the luteal phase. Also, by considering that a progestational type of hypophysial blockage normally exists during the luteal phase of the estrous cycle, the results reported here may be compared to those reported by Brinkley *et al.*, (1) on the function of corpora lutea in gilts fed a progestogen to obtain hypophysial blockage. In both experiments it was observed that follicles ovulated by injecting gonadotrophin formed functional corpora lutea. It is felt that these results coupled with those observed in hypophysectomized pigs (du Mesnil du Buisson and Léglise, 5) ascertain that - in contrast to findings in the rat - a continual supply of hypophysial luteotrophic substance is not required for the function of corpora lutea in cycling swine. Similar results have been found in hypophysectomized ewes (Denamur and Mauleon, 2). However, in intact ewes, the lifespan of induced corpora lutea has been reported to be considerably different from that observed in swine. Inskeep *et al.* (3) found that corpora lutea added to the ovaries as a result of gonadotrophin treatment did not persist after the naturally-formed glands regressed.

In conclusion, it is thought that increased consideration should be given to the possibility

that separate - but perhaps related - mechanisms are involved in the persistence of corpora lutea in swine during the luteal phase of the cycle and during pregnancy. Although there is a considerable amount of evidence to support the hypothesis that formation is the only prerequisite to persistence during the luteal phase in swine, there are perhaps not sufficient findings to conclude that a luteotrophic factor is definitely not involved. On the other hand, the available evidence does indicate that a luteotrophic substance of hypophysial origin - or lack of a uterine luteolytic factor that may in fact act through the pituitary gland - does control persistence of the corpus luteum during pregnancy. On this premise, the present approach toward the control of the estrous cycle in swine of extending the luteal phase with orally effective progestogens - or by other designs - does appear to have more likelihood of success than the possible alternative of attempting to decrease the length of the luteal phase with a luteolytic substance in order to synchronize matings.

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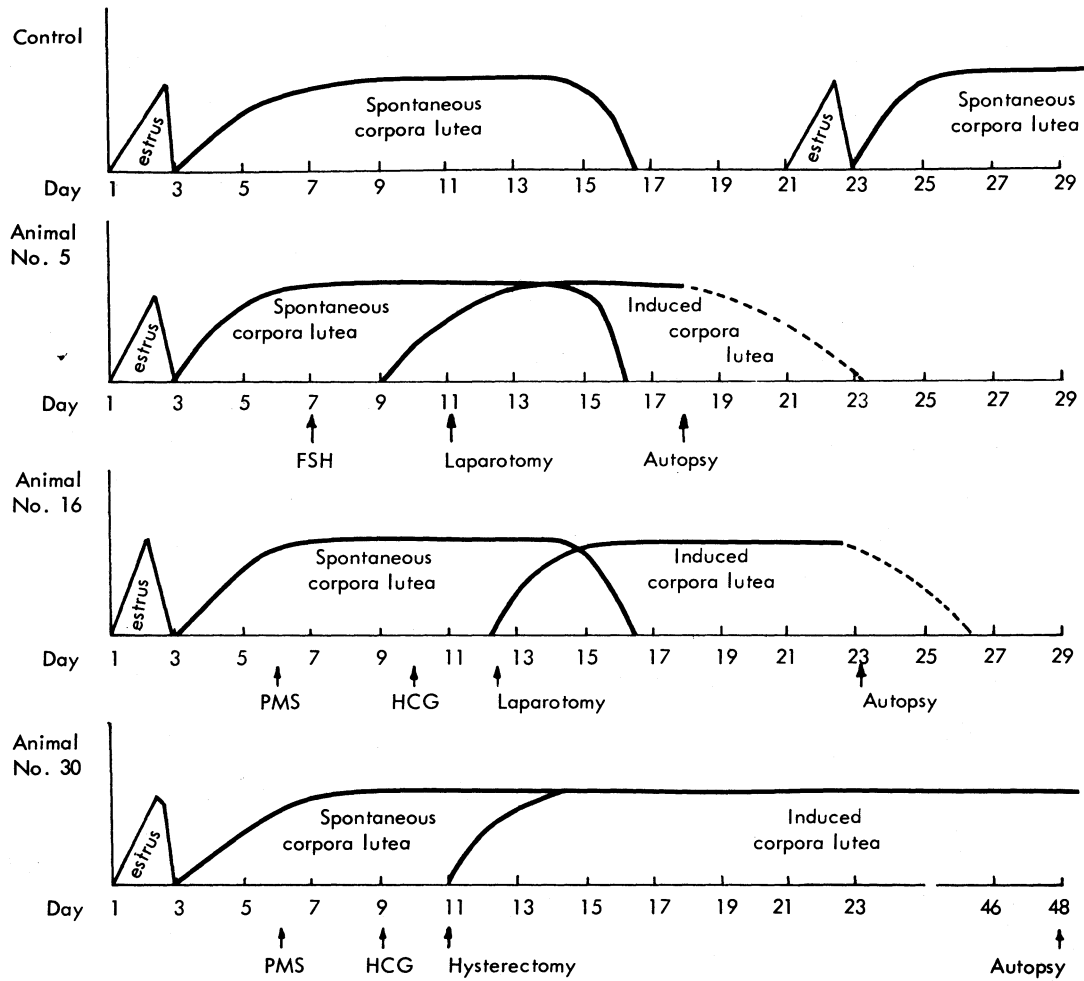


Figure 1. A selected example of each treatment series is depicted for comparison of results with the normal female reproductive pattern of swine. (From Neill and Day, 1964)

Table 1. --Progesterone concentration of spontaneous and induced corpora lutea prior to regression of the spontaneous corpora lutea

Animal Number	Day of Cycle Ovulation Induced	Autopsy	No. of Corpora Lutea		Progesterone, $\mu\text{g}/\text{gm}$	
			Spontaneous	Induced	Spontaneous Corpora Lutea	Induced Corpora Lutea
41-6	11	14	9	13	44	35
38-2	12	16	11	13	36	38

Table 2. --Progesterone concentration of induced corpora lutea following regression of the spontaneous corpora lutea

Animal Number	Day of Cycle Ovulation Induced	Autopsy	Number of Induced Corpora Lutea	Progesterone, $\mu\text{g}/\text{gm}$
				of luteal tissue
42-3	11	19	11	30
8-2	13	21	14	38
8-1	13	23	14	41

Table 3.--Within animal comparison of the progesterone concentration of spontaneous and induced corpora lutea before and after regression of the spontaneous corpora lutea

	<u>Animal Number</u>	
	1-5	1-3
Ovulation induced, day	11	12
Number of corpora lutea		
Day 15 or 16		
Spontaneous	5	5
Induced	8	5
Day 19		
Spontaneous	6	10
Induced	9	6
Progesterone, ug/gm of luteal tissue		
Day 15 or 16		
Spontaneous	63	45
Induced	59	63
Day 19		
Spontaneous	9	0
Induced	42	71