Reproductive Function in the Gilt as Affected by Level of Feeding and Treatment with Altrenogest

by

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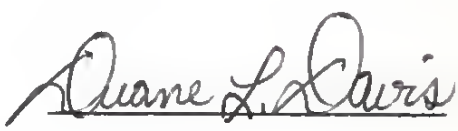

Major Professor

Dedication

I would like to dedicate my first reaserch project to Melvin and Charollette Rhodes, my Mom and Dad, without whose emotional and financial assistance completion of this degree and project would not have been possible. I would also like to dedicate this work to my fiance'e, Sandy Grebe, whose patience and willingness to plan our wedding has allowed me to give my full time and attention to the completion of this thesis. Without the love and support of these three people, neither this project or my future would be complete.

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Introduction

Swine producers face increasing economic pressures and their survival often depends upon the utilization of management tools that increase the efficiency of production. One such tool is feeding gilts high levels of energy during the period just prior to breeding (flushing) which may increase the number of pigs farrowed. Another such tool is the synchronization of estrus for gilts entering the breeding herd.

During the last 25 years, results of flushing experiments have been inconsistent. Some of this inconsistency may be attributable to varying amounts of "control" and "flushing" diets, length of flushing and time that flushing was discontinued relative to the onset of estrus. Synchronization of estrus may allow more precise timing of flushing treatments and thereby produce more consistent responses to flushing.

Although flushing and estrus synchronization have been studied individually, their combined effects have received little attention. The availability of altrenogest, a synthetic progestogen currently being investigated for use in estrus synchronization in swine, afforded the opportunity to evaluate the combined action of flushing and altrenogest. Hence, the objective of this thesis is to consider the current understanding of flushing and synchronization with altrenogest and to report the results of a study designed to elucidate their potential modes of action.

Effects of Flushing on Ovulation Rate and Litter Size

Pigs. The initial determinant of litter size is ovulation rate. Increasing ovulation rate will increase the number of pigs farrowed up to at least 23 eggs shed for sows mated after weaning of their first litter (King and Williams, 1984). However, maximum litter size for gilts may be obtained with 18 ovulations (Blichfeldt and Almlib, 1982) and therefore fewer ovulations may be required to maximize litter size at term. For the latter estimate, litter size was determined at day 28 to 34 of gestation and therefore the number of ovulations required to maximize litter size for gilts remains in question. The relationship between ovulation rate and litter size can be expressed as either a curvlinear or linear (Blichfeldt and Almlib, 1982 ; King and Williams, 1985) effect when either number of viable embryos, or pigs farrowed are considered, respectively. This relationship will be discussed in further detail in later sections of this review. Anderson and Melampy (1971) reviewed studies of factors affecting ovulation rate in the pig. The conclusions of their review and results of more recent studies will be discussed in this report.

Level of feeding has repeatedly been shown to affect ovulation rate. The term level of feeding may encompass changes in the total diet but usually only protein and energy levels are considered when data from several studies are compiled. The component(s) of the diet responsible for the flushing effect are unknown but there are indications that energy alone can increase ovulation rates. Rats fed

50% of ad libitum intake and supplemented with free choice glucose had similar body weight, anterior pituitary weight, ovarian weight and plasma LH as compared to full fed rats whereas those restricted to 50% ad libitum intake and not provided supplemental glucose showed decreased values for the same variables (Howland, 1972). These results indicate that in the rat glucose, or perhaps more generally energy, is an important nutrient required for full reproductive performance and that low energy intake may inhibit ovarian activity. The combined data of Kirkpatrick et al. (1967b), Rigor et al. (1963) and Zimmerman et al. (1960) provides evidence that increasing energy intake in the form of either glucose, animal fat or vegetable fat for a period of 6 to 13 days prior to estrus is adequate stimulus to increase the ovulation rate in gilts. Aherne and Kirkwood (1985) reported that levels of crude protein (CP) between 12.5 and 16%, regardless of source, and short term, one cycle, protein deprivation have little effect on ovulation rate. However, Jones and Maxwell (1974) found that restriction of CP to 8% or 14% of the total diet from 146 days of age to the third estrus resulted in decreased ovulation rates when compared to 20% CP. However, the number of live embryos, embryo survival rate and embryo length were unaffected. The 14% CP treatment is borderline to the minimum requirement of growing-finishing swine as established by the National Research Council (NRC, 1979). Therefore, the possibility exists that increasing protein intake will produce an increase in the ovulation rate of gilts.

Gilts fed high-energy diets prebreeding generally have higher ovulation rates (Anderson and Melampy, 1971). Experiments attempting to characterize the effects of energy intake on ovulation rate are difficult to compare due to differences in amounts of energy fed, duration of increased energy feeding, when increased energy was fed relative to estrus and management of animals prior to treatment.

An increase of 1.57 eggs ovulated due to flushing is a realistic expectation for flushing treatments (Anderson and Melampy, 1971). In a summary of 40 experiments (Anderson and Melampy, 1971), gilts fed restricted diets were fed an average of 5370 kcal/day (range 0 to 7170) and gilts fed high-energy diets received about 10030 kcal/day (range 6000 to 12830) with an average difference between full and restricted energy treatments of 4650 kcal/day (range 1700 to 10960 kcal). Six of the forty experiments, using a difference between full and restricted energy levels ranging from 5800 to 7700 kcal/day, yielded an increase in ovulation rate of 2.15 eggs. Lesser increases in ovulation rate were reported when differences in flushing and restricted diets were smaller. The duration of flushing is also important and should be considered when the practice of flushing is utilized. Anderson and Melampy (1971), in reviewing the duration of flushing in 40 experiments, concluded that the optimum duration was 11 to 14 days before the expected estrus of mating.

Feeding high levels of energy prior to estrus will result in increased numbers of ovulations as estimated by the number of corpora lutea (CL). For this increase in ovulation rate to be expressed as

litter size at farrowing, the flushing treatment must be removed at estrus (or breeding) or shortly thereafter. High-energy diets fed 25 to 43 days postmating decreased embryonic survival by 3 to 11% in an average of 30 experiments (Anderson and Melampy, 1971). This decrease in embryonic survival negated the increased ovulation rate attributable to flushing. Other work (Maxwell et al., 1976), indicates the detrimental effects of a high feed intake may occur if high energy is provided for as few as 2 days after mating.

Ewes. The ewe is generally said to require increased energy feeding for at least the length of one estrous cycle, or about 17 days, to produce an increase in ovulation rate (Haresign, 1981). However, increased numbers of multiple ovulations have been reported when feeding lupin grain supplement for as few as 6 days prior to estrus (review by Scaramuzzi and Radford, 1983).

The majority of the research (Findlay and Cumming, 1976; Haresign, 1981; Rhind et al., 1984; Smith, 1985) theorizes that body condition prior to and during flushing has an important role in determining the effects of flushing. Ewes with less condition tend to respond more favorably to flushing than those with greater stores of body fat on a good quality basal diet providing approximately 200 g protein/day (Scaramuzzi and Radford, 1983). Morely et al. (1978), from analysis of previous research, calculated that each additional kg of live weight is generally associated with a 2 to 2.5% increase in ovulation rate at fall mating in the ewe. This relationship of body condition and ovulation rate is not evident in the pig. In addition to energy,

sheep also show an increased number of multiple ovulators in response to increased protein intake (Smith, 1985).

Physiological Events of the Estrous Cycle of Gilts

The mechanisms of actions which lead to increased ovulation rates in the pig and ewe have been the subject of several studies. Lamming (1969) surmised that any influence(s) of nutrition on the activity of the gonads is either directly or indirectly mediated by the pituitary gland. However, before discussing the effects of nutrition on reproductive activity, the stages and hormonal patterns during the estrous cycle of the pig will be described.

Endocrine Aspects. The estrous cycle of the pig has a duration of about 21 days with a normal range of 18 to 24 days. Numerous reviews exist which give detailed accounts of the physiological events throughout the estrous cycle of swine and other species (Hafez, 1980; Richards, 1980; Brinkley, 1981; Hansel and Convey, 1983; Foxcroft and Hunter, 1985), thus only the general patterns will be emphasized here. The luteal phase of the cycle follows ovulation, lasts approximately 15 days and is characterized by: 1) secretion of progesterone (P) and formation of functional CL with maximum CL weight and P secretion occurring about day 10 (first day of estrus = day 0) and maximum P secretion being maintained until about day 15 of the cycle (Brinkley,

1981); 2) an increase in estradiol (E) concentration during the early portion of the phase (Hendricks et al., 1972) which is most likely resultant from large estrogen active follicles on the ovary as has been shown in the cow (Hansel and Convey, 1983); 3) secretion of luteinizing hormone (LH) in low frequency-high amplitude pulses under the predominant influence of P (Brinkley, 1981) and 4) two increases in follicle stimulating hormone (FSH) concentration, the first beginning shortly after ovulation, plateauing at about day 2 and beginning to decline at about day 4 to reach basal levels at about day 7 and the second being of shorter duration (about 1 d) at about day 9 of the cycle (Brinkley, 1981). The follicular phase follows the luteal phase, usually has a duration of 3 to 4 days and is characterized by: 1) the demise of the CL beginning at about day 15 and the return of P concentrations to basal levels by about day 16 (Brinkley, 1981); 2) increasing E concentrations beginning on about d 16 with sporadic pulses until a maximum level is reached on about day 20 (Brinkley, 1981); 3) secretion of LH in high frequency-low amplitude pulses under the predominant influence of E (Van de Wiel et al., 1981) and 4) concentrations of FSH at or below basal levels relative to the rest of the pig's estrous cycle (Brinkley, 1981). The estrous cycle culminates at estrus and the most distinguishing characteristic of this phase of the cycle is ovulation. The estrus phase of the pig's cycle lasts 2 to 3 days and is further characterized by: 1) maintenance of P concentrations at the basal level for the cycle (Hansel and Convey, 1983); 2) decline of E

concentrations to minimum levels on about day 1 (the day of ovulation and the second day of estrus) after reaching a maximum concentration 1 day prior to estrus (Brinkley, 1981); 3) the preovulatory LH surge which begins about 1 day prior to estrus, reaches a maximum concentration on the first day of estrus (d 0) and then declines to basal levels between day 1 and day 2 of the ensuing cycle (Brinkley, 1981) and 4) maintenance of FSH concentrations at or below levels at the end of follicular phase (Brinkley, 1981).

Follicular Aspects. According to the review of follicular maturation in the pig by Foxcroft and Hunter (1985), except during the follicular phase, continual development and sequential atresia provide a proliferating pool of 1 to 6 mm follicles which number approximately 50 follicles, 2 to 5 mm in diameter. Recruitment occurs from this pool between day 14 and 16 of the cycle to provide the follicles destined to ovulate. Growth of selected follicles is accompanied by rapid atresia of nonselected follicles and a block to their replacement in the proliferating pool. Recruitment may occur at one time, in which case selected follicles must be in different stages of development, or recruitment may continue into the follicular phase whereby the stimulus or partial stimulus (circulating gonadotropins and steroids) for recruitment would change as recruitment proceeds. An increase in FSH is not a mandatory prerequisite for follicular recruitment in either the gilt or weaned sow; however, Foxcroft and Hunter (1985) contend that plasma FSH levels are consistently elevated at the time of follicular recruitment. Assuming that an interaction

exists between the gonadotropic effects of FSH and LH, changes in LH with either stable or declining concentrations of FSH constitute an adequate stimulus for follicular maturation.

As reviewed by Foxcroft and Hunter (1985), biochemical development of follicles follows a consistent pattern of events. The biochemical changes that take place as follicles progress from small (< 2 mm) to large (≥ 7 mm) diameters may be summarized as follows: 1) thecal tissue binds more LH; 2) the number of LH binding sites/granulosa cell increases but there is not an increased number of FSH receptors and 3) an increased concentration of E in follicular fluid from day 17 to day 20 as the follicles become more steroidogenic. Estradiol may play a role in the formation of LH receptors as follicles mature because high concentrations of E are present just prior to high LH binding by the granulosa cells.

Effects of Flushing on Endocrine Secretions

Pigs. Cox et al. (1984) studied the effects of intravenous insulin (.1 IU/kg body weight every 6 h) and flushing (9600 vs 5700 kcal metabolizable energy (ME)/day) on concentrations of FSH and E in serum after withdrawal of altrenogest. Both flushing and insulin increased ovulation rate and FSH was elevated 12 to 30 h after last altrenogest treatment for gilts receiving both flushing and insulin as compared to controls. Flushing without insulin did not increase FSH

and levels of E were unaffected by treatment. Jones et al. (1983), after applying the same treatments, found that the number of LH pulses/4 h on day 3 after last altrenogest treatment were greater in gilts receiving 9600 kcal ME/day than those receiving 5700 kcal ME/day. Basal concentrations of LH, LH pulse amplitude (maximum concentration minus basal concentration) and concentrations of LH in serum taken at 6 h intervals starting 12 h after last progestogen feeding did not differ between treatments. Flowers et al. (1986) examined the effects of feeding 4400 kcal ME/day versus flushing with 11000 kcal ME/day from day 8 of the cycle to estrus and reported that the average concentration of FSH on days -5, -4 and -3 before estrus was increased by flushing. The number of LH pulses/6 h period were also increased on days -4, -3 and -2 before estrus while average daily concentration of LH and LH pulse amplitude were not affected. Gilts fed two different energy intakes showed no difference in anterior pituitary content of LH (measured by the ovarian ascorbic acid depletion test), FSH (measured by the HCG-synergism test) or in anterior pituitary dry weight (Kirkpatrick et al., 1967a). The assays of pituitary LH and FSH content had heterogeneous regressions of response on dose between days and therefore are open to question. Thus, the gonadotropin content of the pituitaries of flushed gilts remains uncertain.

Ewes. Several experiments and reviews have been published on the effects of varying nutrient intake on hormonal correlates of reproduction in the ewe. Five studies, reviewed by Scaramuzzi and

Radford (1983) and Smith (1985), found no differences in FSH, LH or E between ewes fed varying amounts of energy and protein, but did show differences in ovulation rates between treatments. Ewes were bled once every 15 min for 6 h and thus, it seems likely that had there been differences, sufficient samples were taken to detect them. Increasing the protein intake has been shown to increase the circulating concentration of FSH in three experiments (Knight et al., 1981; Smith, 1985) and E in one experiment (Knight et al., 1981). Earlier work by Howland et al. (1966) and Memon et al. (1969) indicated that ewes with greater intakes of both protein and energy had heavier pituitaries but were not different in either FSH or LH concentration within the gland. These results were interpreted to indicate that increased nutrient intake resulted in higher production of both gonadotropins. With the inconsistency between experiments for both gilts and ewes, it is evident that the interactions between nutrition and the hypothalamo-pituitary-ovarian axis are not fully understood.

Effects of Flushing on Ovarian Follicle Populations

Dailey et al. (1975) determined that gilts fed ad libitum for 7 d (d 15 through estrus) had a larger average diameter of the four largest follicles, a greater number of large (7 to 10 mm) follicles per gilt and a greater percentage of gilts with hemorrhagic follicles

on the first day of estrus. No treatment effects were found for the number of milky follicles; however, the proportion of milky follicles varied as percent of total follicles. Ad libitum feeding the last 4 to 6 days of the estrous cycle resulted in a decreased ratio of the number of small to the mean number of medium and large sized follicles (Dailey et al., 1972) and a similar length of flushing resulted in a negative regression (-0.26) of the average number of large follicles on the average percent milky (Dailey et al., 1975). These results were interpreted to indicate that flushing increases the number of preovulatory follicles by salvaging follicles destined for atresia. Kirkpatrick et al. (1967a) and Dailey et al. (1972) have reported losses of the total number of follicles in the range of 40 and 50%, respectively, while showing increases in the number of large follicles, indicating that the larger follicles are the ones being salvaged. Similar relationships between ovulation rate and follicular atresia exist in Booroola Merino ewes, a highly prolific breed, (Scaramuzzi and Radford, 1983). Experiments to determine possible differences in ovarian follicle populations between flushed and non-flushed ewes are, to my knowledge, unavailable but similar relationships also may exist.

Effects of Exogenous Hormones on Ovulation Rate and Litter Size

Phillippo (1968) presented a detailed review of the effects, including embryonic survival, of exogenous hormones on superovulation in the pig. Very little research on superovulation has been conducted in the 18 years since Phillippo's review.

Insulin. Recently, Cox et al. (1984) and Jones et al. (1983) reported increased ovulation rates when .1 IU insulin/kg of body weight was injected every 6 h beginning on the last day of altrenogest treatment and ending 24 h after estrus. However, Kirkpatrick et al. (1967b) were unable to show differences in either ovulation rate or blood glucose concentrations when gilts were given 25 IU insulin twice daily at feeding from day 4 through day 2 to 4 of the following cycle. The less frequent treatment schedule may account for the failure of Kirkpatrick et al. (1967b) to demonstrate effects of insulin since the daily dose was similar for both experiments and insulin has such a short half-life (3 to 5 min in humans, Karam et al., 1983).

Pregnant Mares' Serum Gonadotropin (PMSG). Pregnant mares' serum gonadotropin given during the follicular phase consistently increased the mean ovulation rate in a dose-dependent manner (Anderson and Melampy, 1971; Phillippo, 1968). Hunter (1964) calculated a regression coefficient of 1.89 $\pm$ .5 CL for each 100 IU PMSG. Day 15 or 16 of the estrous cycle seems to be the optimal time for PMSG treatment for the induction of superovulation (Anderson and Melampy,

1971; Phillippo, 1968). Treatment with PMSG on these days of the cycle has been shown to reduce the duration of the estrous cycle and also the duration of estrus. The latter effect decreases the maturation time of the oocyte and the shortened maturation time might lead to defects within the zygote and account for the increased embryo mortality resulting from superovulation (Phillippo, 1968; Day and Longnecker, 1968). Pregnant mares' serum gonadotropin (1200 or 1500 IU) increased ovulation rates when it was administered 24 h after the last I.C.I. 33828 treatment (Pope et al., 1968; Day and Longnecker, 1968) or on the day of weaning for sows (Longnecker and Day, 1968). Mean number of CL for the three experiments was 12.5 for controls and 21.9 for those receiving PMSG treatment. Day and Longnecker (1968) reported an increase of 11.2 embryos at day 25 of gestation for gilts treated with PMSG after the feeding of I.C.I. 33828 for 20 days. The combined data of Longnecker and Day (1968), Pope et al. (1968) and Baker et al. (1970), when a 1000 to 1500 IU dose of PMSG was injected 24 h after the last I.C.I. 33828 treatment, demonstrate an increase in the total number of pigs farrowed of approximately 1.3 pigs per litter. However, the difference in number of pigs farrowed was not statistically significant in all of the experiments.

FSH. Treatment with FSH has been given between day 14 and day 20 of the estrous cycle as either 3 injections on consecutive days or as a single injection close to estrus. With these injection schemes, the researchers were unable to show markedly increased ovulation rates (Phillippo, 1968). Day et al. (1959) presented data to give an

average ovulation rate of 19, calculated from 3 of 4 gilts which ovulated, when a single injection of FSH (40 Armour Units) was given on day 15 or 16 of the cycle. Control gilts were not utilized in this study so it is impossible to say whether or not this increase was significant. Effects of PMSG may surpass those of FSH due to the combined FSH and LH activities of the former or the sustained gonadotropic actions due to the long half-life of PMSG.

Therefore, although some results are suggestive of benefits, regimens for increasing litter size at farrowing are not available. This is not due to an inability to stimulate additional ovulations since PMSG is highly effective for this purpose. It is also possible to stimulate markedly larger litters at day 25 of gestation. However, most of the benefit is lost when comparisons of litter size are made at term. In all likelihood, this embryonic loss is due to the restriction imposed by uterine capacity after day 25 of pregnancy.

Effects of Reproductive Experience on Ovulation Rate and Litter Size

Pubertal Gilts. As the number of estrous cycles completed increases so does the ovulation rate. An average increase of .8 eggs has been observed from the first to the second estrus in inbred lines of gilts and another increase was realized from the second to the third ovulation of 1.1 eggs. However, little if any increase is seen

beyond the fourth postpubertal estrus (Anderson and Melampy, 1971). The general recommendation for age at first breeding is to wait until the third estrus to breed replacement gilts so that one may take advantage of increased ovulation rates without sacrificing too much in increased cost of maintenance for replacement females (Diehl et al., 1982).

Several studies have attempted to determine the relationship between age and the number of estruses on reproductive performance of gilts. The combined data of MacPhearson et al. (1977), Warnick et al. (1951) and Young and King (1981) illustrate that delaying breeding until the third estrus vs pubertal estrus increases or tends to increase the total number of pigs born in the first parity by 1.7 pigs/litter. Differences shown in breeding at the first estrus were lost by the third parity with the exception of litter weight which differed in only one study (MacPhearson et al., 1977). Adam and Shearer (1977) and Brooks and Smith (1980) determined the effects of age at breeding, disregarding the number of estrous cycles experienced, on reproductive performance. They found no differences in number of pigs born or reared when gilts were first bred from 160 to 233 days of age.

Parous Sows. Ovulation rate increases with each succeeding ovulation as parity increases to seven or more litters (Anderson and Melampy, 1971). However, the number of pigs farrowed peaks by the fourth or fifth parity or by an approximate age of 4.5 years of age (Anderson, 1980). This increase in litter size results from age

rather than pregnancy associated effects (French et al., 1979). By the eighth parity number of pigs born alive begins to decline while number of stillbirths begins to increase (Anderson, 1980).

Effects of the Synthetic Progestogen, Altrenogest, on Reproductive Functions of the Gilt

In the past 15 years, numerous experiments have been conducted to determine the effects of feeding the orally active progestogen, altrenogest, on estrous synchronization during the cycle and preceding puberty in gilts and after weaning the litter in sows. These experiments entail seventeen reports and the use of over 3000 animals in attempts to determine the optimal feeding level and duration of feeding required to effectively suppress follicular development, ovulation and estrus. In addition to dose and duration, researchers also have studied its effects on fecundity of the gilt and various breeding schemes following altrenogest treatment. Unless otherwise stated, the subsequent discussion pertains to use and effects altrenogest in the gilt rather than in the sow.

Level of Feeding. The daily dose of altrenogest has ranged from 2.5 to 40 $mg \cdot gilt^{-1} \cdot day^{-1}$ in group or individual feeding systems. Six experiments (Boland and Gordon, 1981; Kraeling et al., 1981; Redmer and Day, 1981a; Varley, 1983; Webel, 1976; Webel, 1978), in attempts to determine the minimum feeding level, have fed altrenogest for 18 d

the following mg·gilt^{-1}·day^{-1} (number of experiments); 2.5 (2), 5 (3), 10 (4), 12.5 (3), 15 (4), 16 (1), 17.5 (1), 20 (5) and 40 (3). Summarization of these studies led to the conclusions that; 1) the percentage of treated gilts showing follicular and (or) luteal cysts increased as feeding level decreased from 67% for gilts fed 2.5 mg/day to 0% for those receiving 40 mg/day and its incidence was most frequent at lower levels when gilts were group fed; 2) altrenogest effectively suppressed estrus, regardless of dose, because no gilts were detected in estrus during treatment; 3) percentage of gilts expressing estrus after withdrawal of altrenogest increased as level of feeding increased from 17% for 2.5 mg·gilt^{-1}·day^{-1} to 100% for gilts treated with 40 mg/day (these results were presumably due to development of cystic follicles in gilts receiving the lower doses) and 4) the mean interval from treatment withdrawal to estrus increased with the daily dose from 4 days for gilts fed the 2.5 mg/day to 7.8 days for those receiving 40 mg/day. The minimal dose required to prevent cystic follicle formation and yet provide the earliest possible return to a synchronized estrus seems to be 12.5 or 15 mg·gilt^{-1}·day^{-1} and 15 mg·gilt^{-1}·day^{-1} tends to produce the most consistent results. The 12.5 mg dose appears to be the minimal effective dose for producing acceptable results but if a gilt should not receive the full dose, as is the potential with group feeding, then results of altrenogest treatment are less desirable in terms of ovarian cyst formation and synchrony of estrus. Cystic follicles were reported for gilts receiving 2.5 to 20 mg altrenogest/day; however,

the number of cysts generally was not sufficient to prevent expression of estrus in gilts fed 12.5, 15 or 20 mg of altrenogest/day but were of sufficient number and (or) size to suppress estrus after altrenogest withdrawal in some gilts fed lower doses.

Duration of Feeding. The pig's luteal phase lasts until day 14 or 16 of the estrous cycle. Theoretically this should be the minimum treatment duration for controlling the time of estrus. Davis et al. (1979) and O'Reilly et al. (1979) fed altrenogest for 19 to 21 days at a level of 12.5 $mg \cdot gilt^{-1} \cdot day^{-1}$ and reported a closer synchrony of estrus when compared to controls. The treated gilts had a mean interval from altrenogest withdrawal to estrus of 5.1 days.

An 18-day feeding period of 12.5 or 15 $mg \cdot gilt^{-1} \cdot day^{-1}$ has been shown to synchronize estrous effectively in about 95% of the treated gilts to within a 10-day period. The data of Knight et al. (1976), Redmer and Day (1981a), Redmer et al. (1976) and Webel (1978) collectively show that about 99% of the gilts show first estrus within 10 days of altrenogest withdrawal and express a mean interval to estrus from this time of 5 days when 12.5 mg/day are fed for 18 days. Similar values for percentage of gilts showing estrus within 10 days and mean interval to estrus have been reported when feeding 15 mg/day (96% and 5.6 days, respectively) (Boland and Gordon, 1981; Davis et al., 1979; Stevenson and Davis, 1982; Webel, 1978).

Several researchers have investigated the effectiveness of a 14-day treatment. The combined data of Stevenson and Davis (1982) and Webel (1978), who fed 15 and 12.5 $mg \cdot gilt^{-1} \cdot day^{-1}$, respectively,

showed that about 97% of the gilts come into estrus within 10 days after altrenogest withdrawal with a mean interval to estrus of 5.4 days. The 18-day treatment tended to improve the synchrony of estrus but treatment for 14 days has the advantage of decreased time and expense.

Fecundity and Fertility. As stated previously, with an adequate dose and duration of altrenogest treatment there are no adverse effects on percent of gilts showing estrus. When researchers have examined the effects of prebreeding altrenogest treatment on fertility and fecundity some rather surprising results have been obtained. Table 1 lists the results of 11 experiments which have examined various reproductive traits performance after feeding zero to 20 $mg \cdot animal^{-1} \cdot day^{-}$ for 7 to 21 days. Average differences for the combined data presented in Table 1 indicate that altrenogest treatment increased ovulation rate by 1.7 eggs, total pigs born by .7 pigs and pigs born alive by .6 pigs/litter. This summary also suggests that there was no adverse effect on farrowing rate. Although all experiments did not show significant treatment differences, only two experiments reported differences in favor of controls (Redmer and Day, 1981b; Davis et al., submitted). O'Reilly et al. (1979) and Pursel et al. (1981) conducted experiments to measure the effects of altrenogest on reproductive performance of gilts after insemination with different types of semen or natural service. Pursel et al. (1981) reported that average total pigs, pigs born alive and litter size at weaning were smaller for control gilts inseminated with frozen-thawed semen than

Table 1. Experiments Reporting Ovulation Rate or Fecundity after Treatment with Altrenogest

	Control					Altrenogest Treated						
Reference	OR[a]	TPB[b]	PBA[c]	FR[d]	n[e]	OR	TPB	PBA	FR	n	Dose[f] / Duration	P[g]
Boland and Gordan (1981)	14.1	---	---	--	20	14.6	---	---	--	17	15 or 20 / 18	N.S.
Davis et al. (1979)												
Trial 1	11.4	---	---	--	24	15.6	---	---	--	16	12.5 / 19	.01
Trial 2	15.0	---	---	--	11	18.5	---	---	--	10	12.5 / 18	.10
Davis et al. (submitted)												
Farm A	----	8.9	8.4	83	33	----	8.7	8.5	78	29	15 / 14	N.S.
Farm B	----	8.7	8.4	54	55	----	9.9	9.2	64	64	15 / 14	.06
O' Reilly et al. (1979)	11.2	---	---	--	16	12.7	---	---	--	32	12.5 or 15 / 19 - 21	N.A.
Pursel et al. (1981)	----	9.1	8.8	74	68	----	10.5	9.9	71	58	15 / 18	.01
Redmer and Day (1981a)	12.8	---	---	--	10	13.6	---	---	--	48	10 - 20 / 18	N.S.
Redmer and Day (1981b)	12.1	---	---	--	9	11.4	---	---	--	8	15 / 18	N.S.
Stevenson et al. (1985)[h]	----	8.9	8.4	46	78	----	9.4	8.6	64	7	20 / 7	.06
Varley (1983)	----	10.0	9.3	100	20	----	10.6	10.3	88	40	16 or 20 / 18	.05

(continued on next page)

Table 1. (cont'd) Experiments Reporting Ovulation Rate or Fecundity after Treatment with Altrenogest

	Control					Altrenogest Treated						
Reference	OR[a]	TPB[b]	PBA[c]	FR[d]	n[e]	OR	TPB	PBA	FR	n	Dose[f] / Duration	P[g]
Webel (1978)	----	10.0	---	66	70	----	11.3	---	75	68	? / ?	.05
Webel (1982)	----	8.7	---	92	95	----	9.2	---	85	230	15 / 7 or 14	N.S.
average	12.8	9.2	8.7	74	---	14.5	9.9	9.3	75	---	----------	----
total	----	---	---	---	509	----	----	---	---	627	----------	----

[a] Average ovulation rate.
[b] Average total number of fully formed pigs born/litter excluding mummified fetuses.
[c] Average number of pigs born alive/litter.
[d] Farrowing rate as a percentage of the animals bred or artificially inseminated.
[e] Number of animals.
[f] Daily dose and duration of days of altrenogest treatment.
[g] Probability that altrenogest treatment differed from control. N.A. = not available.
[h] N.S. = nonsignificant.
This study utilized primiparous sows following weaning of their litters.

for altrenogest treated gilts inseminated with frozen-thawed semen. However, average litter size of gilts bred by natural service was not increased over insemination with frozen-thawed semen when all gilts were treated with altrenogest. Altrenogest might improve litter size in gilts inseminated with frozen-thawed semen by increasing ovulation rate. The resulting increase in fertilized eggs would be beneficial since fertilization rate is low after insemination with boar semen that has been subjected to frozen storage. Alternatively, these results may indicate that altrenogest, through either enhanced sperm transport or possibly by progestin priming of the uterus, increases the number of eggs fertilized and (or) embryo (fetal) survival. The work of O'Reilly et al. (1979) appears to give support to the hypothesis that altrenogest increases the proportion of eggs fertilized after insemination with either fresh or frozen-thawed semen. The proportion of cleaved eggs after insemination with fresh semen was 30% vs 80% and frozen-thawed semen was 19% vs 80% for control and treated gilts, respectively. However, the differences were nonsignificant.

Mechanism of Action. Although the number of experiments dealing with the effects of altrenogest is quite large, relatively few studies address its mechanism of action. Follicular development is inhibited during the time which would have been the follicular phase in gilts treated with altrenogest (Guthrie and Bolt, 1985; Redmer and Day, 1981b). The feeding of altrenogest at a rate of 2.5 $mg \cdot gilt^{-1} \cdot day^{-1}$ did not suppress follicular development but did inhibit the

pre-ovulatory LH surge, and consequently estrus. Thus follicles were not ovulated and cysts were formed (Redmer and Day, 1981b).

The two experiments previously cited and that of Patterson and Day (1984) investigated hormonal patterns resulting from altrenogest treatment and reached the following conclusions. Concentrations of P in plasma were elevated for treated and control gilts and similar in both groups during the luteal phase of the cycle. These levels began to decline at the end of the luteal phase and remained at basal levels (< 1 ng/ml) until day 1 to 2 of the following cycle. However, gilts treated with altrenogest for 18 days had an extended period of basal P as the period from luteal regression to the pre-ovulatory LH surge was longer than in control gilts (Redmer and Day, 1981b). Plasma E was low during the luteal phase of control gilts and during the altrenogest feeding period in treated gilts. These levels began to increase after luteolysis or withdrawal of altrenogest feeding for control and treated gilts, respectively, and were similar for control and treated gilts on day -4 through day 4. The secretion pattern of LH (Patterson and Day, 1984) was similar among treated and control groups as was the average concentration of LH. Average concentrations of LH remained at basal levels during the luteal phase and during altrenogest treatment. Average FSH in daily samples began to increase in apparent synchrony with the LH surge and a maximal concentration of 63.8 ng/ml occurred 2 to 3 days after the maximal concentration of LH (4.4 ng/ml) of the LH surge (Guthrie and Bolt, 1985).

Effects of Progesterone on the Ovary

Progesterone has been shown to have other effects on the ovary besides its well documented effect of delaying estrus. Dufour et al. (1972) noted that in ewes with only one CL, more follicles greater than or equal to 1 mm in diameter were present in the ovary containing the CL than on the contralateral ovary on day 8 of the cycle. They also determined that electrocoagulation of all surface follicles and removal of the CL from one ovary, when both had a CL, resulted in greater follicular development after 4 days in the ovary in which the CL was left intact. One possible explanation for these effects is that follicles responded to local P production by the CL. Harned and Casida (1971) tested the hypothesis that local administration of P would increase follicular development and their results supported this hypothesis. Anestrous ewes pretreated with FSH and receiving an 11 mg injection of P in one ovary had greater follicular fluid weights 4 days after treatment than the contralateral ovary which received only vehicle. Number of CL and developing follicles were also greater in the previously P treated ovary after ovulation.

Studies similar to those discussed for the ewe have not been carried out in the pig. However, Baker et al. (1954) studied the effects of 14 daily injections of P on subsequent fertility in gilts. These researchers concluded that injections of 100 mg $P \cdot gilt^{-1} \cdot day^{-1}$ for 14 days resulted in 1) an increased number of follicular cysts and 2) an increased ovulation rate in gilts which ovulated; however, the

number of viable embryos and unfertilized eggs were adversely affected by P treatment.

Conceptus Survival in the Pig

Pope and First (1985) and Wrathall (1971) have presented detailed reviews of embryonic and fetal survival in the pig. Relevant discussions from these reviews and other literature will be presented in an attempt to explain why increased ovulation rates from flushing and exogenous hormones does not always result in increased numbers of pigs farrowed.

Embryonic Survival and Ovulation Rate. Increases in ovulation rate beyond the normal physiological range, such as those brought about by PMSG-induced superovulation, show a depressed percentage of eggs normally fertilized. This depression in fertilization rate may result, in part, from the proportion of eggs which were ovulated with vesicular nuclei and thus were too immature for fertilization. Wrathall (1971) concluded that increases in ovulation rate from 35 to 40 eggs greatly increases the chances of total litter loss very early in gestation. Postulated causes for this total loss of potential litters were that a very large number of developing eggs may severely tax the limited essential nutrients in the uterus and (or) normal embryonic development may be precluded by possible excessive or imbalanced hormone production from multiple CL.

The mechanisms controlling embryonic survival in swine, when ovulation rates are within the normal physiological range, are not clear. However, a great deal of information exists from which general conclusions can be drawn. Wrathall (1971) points out that there is a basal embryonic loss of 30% by day 25 of gestation when the number of viable embryos recovered is compared with the number of CL. Basal embryonic loss is that loss associated with gilts and sows under optimal environmental conditions. Wrathall (1971) stated that basal losses were correlated positively with ovulation rate and published studies estimated a 1.24% increase in embryonic loss for each additional egg ovulated. Most embryo counts were made from 20 to 40 days of gestation. In attempting to account for this decreasing survival rate with increases in ovulation rate, Wrathall (1971) concluded that between day 2 and 4 of gestation a loss of .63% is expected for each additional ovum shed above 13. He suggested this loss was due to incomplete fertilization. The second major part of embryonic loss is seen between day 25 and the early post-attachment stage and is reported as .45% for each additional egg shed. This leaves only about .16% loss that perhaps could be accounted for in the variability of regressions.

Losses associated with fertilization failure were categorized as; 1) zygotes showing signs of fragmentation, 2) polyspermic eggs, 3) unpenetrated secondary oocytes and 4) ovulation of primary oocytes. Ovulation rate-dependent losses during the embryonic stage after fertilization may be accounted for in a number of ways. The simplest

of these explanations is the combination of two factors; embryo spacing and size of the uterus. Wrathall (1971) stated that an overcrowding effect results from increased ovulation rates causing competition between embryos for attachment to available endometrial space. Insufficient placental attachment area may lead to inadequate nutrition for normal embryonic development. Spacing of embryos is not entirely random but rather can be an effect of embryos exerting a repelling action on one another. Dziuk (1985) reviewed the literature and reported that an embryo may create space for itself by fostering uterine contractility originating from its location which would tend to oppose contractions in adjacent parts of the uterus and thus prevent the migration of one embryo into another embryo's space. Whether or not embyros have a direct effect on their spacing, a larger number of embryos/uterus increases the probability that some will acquire inadequate attachment areas and fail to develop normally in the immediate post-attachment period (Wrathall, 1971). All studies do not agree that over-crowding affects embryo survival at less than 20 d of gestation; however, there is a general consensus that spacing will affect survival from day 25 to 30 through term (Dziuk, 1985; Pope and First, 1985; Wrathall, 1971). Embryos have a direct effect on the length of the uterus by causing it to elongate and grow locally before day 30. After attachment, the growth is directly proportional to the number of embryos in each horn when individual horn lengths are considered separately (Dziuk, 1985) and is not affected by the number of embryos prior to this period (d 14 to 18) (Wrathall, 1971).

Wrathall (1971) presented a second possible explanation for increased ovulation rate resulting in decreased survivability during early gestation. Namely, the presence of an essential biochemical factor for which embryos must compete if normal development is to proceed. This compound might be similar to blastokinin. If such a compound exists, competition for it during the early blastocyst stage might result in only the more viable embryos obtaining enough space for continued growth.

Wilmut et al. (1985) proposed an alternative theory for embryo mortality in the ewe which is also a tenable explanation in the pig. Asynchrony between the dam and the embryo seems to be a likely cause of mortality in both species, especially since morphological variation between littermate embryos is common (Pope and First, 1985). The timing of changes in uterine function is determined by the timing of the increase in progesterone after ovulation in the ewe. Progesterone priming of the uterus advanced uterine function by exactly the interval that the schedule of P injections was advanced and priming with 5 or 10 mg/day resulted in lower embryo survival than priming with 20 or 25 mg P/day. Completion of ovulation from start to finish in the pig requires 1 to over 6.5 h (Wrathall, 1971). If fertilized, those eggs ovulated near the end of ovulation may have a decreased chance of survivability due to a suboptimal uterine environment. Eggs ovulated near the beginning of ovulation probably have a better chance of surviving than those ovulated near the end due to the former embryos advancing the uterine stage by their secretion of estrogens

and other hormones. Also, since luteinization of granulosa and theca cells occurs just prior to, or during, ovulation and thus the start of P production, the uterine development may be most synchronized with eggs ovulated near the beginning of the ovulatory period. The relationship between the stage of the uterus and embryo survival may be exemplified as follows: In both the pig and ewe, embryos transferred into a younger uterus (a day 7 embryo transferred into a day 6 uterus) have a better chance of survival than embryos transferred to an older uterus (a day 6 embryo into a day 7 uterus) (Pope and First, 1985).

Fetal Survival and Ovulation Rate. An additional increase of 1.45% in mortality occurs during the fetal stage (d 40 to term) of development for each additional egg ovulated (Wrathall, 1971). The relationship between embryonic and fetal survival may be summarized by stating that low embryonic mortality is usually followed by higher fetal mortality and visa versa. The over-crowding theory more clearly fits fetal survival data than the observations on embryonic survival. Wrathall (1971) presented the following supportive evidence: A higher percentage of fetuses die and a higher percentage of "runted" fetuses are present when the average number of fetuses in an individual uterine horn is 5 or more than when the number is less than 5, irrespective of stage of gestation. At 105 days of gestation, as fetal number increases per horn, a tendency exists for fetal weight to decrease. Wrathall suggests that this relationship is in direct response to available space for placental development. Dziuk (1985)

reported, that at day 30 of gestation, the fetus requires about 20 cm of uterine space and if this area is restricted to less than 20 cm the fetus may die and be resorbed prenatally or be smaller than littermates (runts) at farrowing. Wrathall (1971) summarized the effect of the size of the uterus on piglet survival in the following manner: ". . . uterine length is an important primary factor in the determination of litter size; this it brings about by a limitation of the number of embryos or fetuses when the uterus is short or allows more to survive when it is long."

Effects of Flushing. As reviewed above, flushing increases the ovulation rate; however, continuation of flushing after breeding causes greater loss of embryos. Anderson and Melampy (1971) summarized 30 experiments which determined embryo survival from day 25 to day 43 of gestation. In 22 of these experiments, the proportion of CL represented by viable embryos was lower for animals receiving high-energy diets than for those receiving restricted diets. While percentage embryo survival was lower irrespective of day of gestation, the actual number of embryos present was higher for the high energy diets at day 25 to 31 of gestation and lower for this same group on day 37 to 43. Most of these experiments also showed an increased ovulation rate due to elevated feeding levels. Thus, it is not known whether this decreased survival resulted indirectly from increased ovulation rate or if the increased energy directly increased mortality.

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Reproductive Endocrine Function in Gilts as Affected by Level of Feeding and Treatment with Altrenogest

ABSTRACT

Twenty-nine nulliparous gilts were assigned to receive either 0 or 15 mg altrenogest/day for 14 consecutive days. From the ninth day of altrenogest treatment until estrus, one-half of each altrenogest group was offered an additional 1.54 kg of ground sorghum grain (flush). Serial blood samples were collected daily for 4 h from day 1 through day 4 and analyzed for estradiol-17β (E), progesterone (P), follicle stimulating hormone (FSH) and luteinizing hormone (LH). Flushing resulted in an increased ovulation rate (16.3 $\pm$ 1 vs 13 $\pm$ 1.2 corpora lutea, $P=0.06$) and a shorter interval to estrus (5 $\pm$ 0.2 vs 5.9 $\pm$ 0.2 days, $P<0.01$). Altrenogest treatment resulted in an increased interval to estrus (5.8 $\pm$ 0.2 vs 5.1 $\pm$ 0.2 days, $P<0.01$). Flushing increased the average concentration of LH ($P<0.05$) by 0.2 ng/ml and the LH baseline concentration ($P<0.02$) by 0.3 ng/ml. The data also were analyzed relative to estrus using days -5, -4, -3 and -2. Altrenogest increased E (1.6 pg/ml, $P<0.05$) and decreased P (0.6 ng/ml, $P<0.05$), whereas flushing increased P by 0.8 ng/ml ($P<0.01$) and the concentration of FSH 1.6 ng/ml ($P=0.07$). These data point to changes in FSH and (or) P as likely hormonal causes for increased ovulation rates in flushed gilts.

INTRODUCTION

It is well established that an increased level of feeding prior to breeding (flushing) will increase the succeeding ovulation rate (Anderson and Melampy, 1971). Review of the literature also suggests that altrenogest treatment may increase ovulation rate (Davis et al., 1979; O'Reilly et al., 1979). Several studies have addressed the effects of flushing (Cox et al., 1984; Flowers et al., 1986; Jones et al., 1983; Kirkpatrick et al., 1967) or altrenogest (Guthrie and Bolt, 1985; Patterson and Day, 1981; Redmer and Day, 1981) on gonadotropin and steroid secretion of gilts. Flushing either increased (Flowers et al., 1986) or failed to change (Cox et al., 1984) circulating concentrations of FSH during the follicular phase. However, several differences existed in the experimental designs utilized in these studies. A major difference being the treatment of all gilts with altrenogest by Cox et al. (1984) whereas no altrenogest was used by Flowers et al. (1986). Both Jones et al. (1983) and Flowers et al. (1986) reported that the number of pulses of luteinizing hormone (LH) was increased but no effect was seen on the concentration of estradiol-17β (E) in peripheral circulation (Cox et al., 1984). Studies with altrenogest have demonstrated few differences between treated and nontreated gilts but there was an increase in the concentration of FSH following withdrawal of the altrenogest treatment (Guthrie and Bolt, 1985).

Therefore, the effects of flushing have not been resolved and no information is available on the combined effects of altrenogest and flushing. The objective of the present study was to determine the effects of treatment with altrenogest and flushing on the concentrations of E, progesterone (P), FSH, and LH in serum and the pulsatile characteristics of LH. To this end a factorial design was employed which allowed the evaluation of the individual effects of altrenogest or flushing alone or in combination.

MATERIALS AND METHODS

Animals. Twenty-nine Yorkshire x Chester White x Duroc gilts averaging 193 ± 0.7 days of age and 112 ± 0.9 kg body weight were utilized for this experiment. Gilts were housed in a modified open front building and fed ad libitum from approximately 34 kg body weight to the start of the experiment.

Experimental Design. Gilts were moved to outside pens and given fence line contact with two mature boars approximately 19 days before the start of breeding. Checks of estrus were conducted twice daily from the third to the fifth day of boar exposure. Gilts detected in estrus were weighed, ear tagged, moved to a confinement breeding barn where they were placed in 1.54 m x 0.52 m individual stalls, and allotted to treatments according to dam, weight and date of estrus. Beginning on day 2 to 4 of their estous cycle (estrus = day 0), gilts

were fed either 0 or 15 mg altrenogest·gilt^{-1}·day^{-1} for 14 consecutive days in 1.81 kg of a diet (Table 1) formulated to meet or exceed all nutrient requirements (NRC, 1979). Altrenogest was provided in the first 0.454 kg of the diet fed each day. One-half of the gilts receiving each altrenogest treatment were fed an additional 1.54 kg of ground sorghum grain (flushing) beginning on the ninth day of altrenogest treatment. This resulted in the following four treatment groups; 1) control (n = 7), 2) altrenogest, (n = 7) 3) flush (n = 7) and 4) altrenogest plus flush (n = 8). Before feeding each day (1000 h), feed not consumed the previous day was collected and weighed. Control and flush gilts were given 15 mg prostaglandin $F_2\alpha$ (PGF) at 0700 h on day 14 of their estrous cycle, followed by an additional 10 mg at 1900 h to insure luteolysis. Ovulation rates of all gilts were determined by midventral laporotomy under general anesthesia (thymylal sodium and methoxyflurane) at 11 to 15 days after first detected estrus.

Cannulation Procedures. Gilts were fitted with indwelling anterior vena cava catheters on either the 11th or 12th day of altrenogest treatment. Gilts were anesthetized (thymylal sodium and methoxyflurane) and an incision approximately 8 cm long and 1.5 cm deep was made in the jugular groove of the neck to the right of the esophagus and centered on the point of an imaginary isosceles triangle whose base was defined by the points of the shoulder and the sternum. The incision site was closely clipped, washed and swabbed with 70% ethanol and iodine. A 12 gauge x 8.9 cm needle was then

used to locate the anterior vena cava and insert 30.5 cm of Tygon[1] tubing (1.02 mm I.D. x 1.78 mm O.D.) tubing which had been coated with heparin[2] solution. The catheter was passed subcutaneously from the incision site dorsally to a point about 13 cm posterior to the base of the ear using a modified French straw insemination pipette which had been sharpened and served as a trocar and cannula. The catheter was sutured to nearby fascia in the throat incision and the incision closed. Next, a 3.8 cm collar (3.18 mm I.D. x 4.76 mm O.D. silicone rubber tubing) was placed over the catheter near the point of exteriorization and glued to the catheter with silicone adhesive. The collar was then sutured to the skin. A 2.5 mm 18 gauge luer adapter was placed in the free end of the catheter and capped with a plastic plug. Then the catheter was passed through a hole in the center of a zippered denim pouch (9 cm x 9 cm) and the pouch, containing the catheter, glued to the skin. The pouch was further secured by elastic tape loosely wrapped around the gilt's neck and then with "duct" tape. Following cannulation, all gilts were injected intramuscularly with 3×10^6 U procaine penicillian G. Patency of the cannula was maintained with a sodium citrate (3.5g/100 ml) solution containing 600 U/ml procaine penicillin G.

Blood Sampling. Samples were collected every 15 min from 1200 h to 1600 h on day 1 through day 4 after last altrenogest treatment or

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[1] Tygon is a registered trade mark of U.S. Stoneware Co., Arkon, OH.

[2] TDMAC heparin complex (2%), Polysciences, Inc., Warrington,PA.

first PGF injection for estimation of progesterone (P), estradiol (E), luteinizing hormone (LH) and follicle stimulating hormone (FSH) secretion and the characteristics of LH secretion during the follicular phase after treatment. Checks for estrus (0800 and 1600 h daily) were initiated on day 3 after PGF or last altrenogest and continued until all gilts were in estrus (day 8).

Luteinizing Hormone. Concentrations of LH in porcine serum (pLH) were determined by a double-antibody RIA similar to that described by Kraeling et al. (1982) with modifications. Purified pLH (USDA-pLH-I-1, 2.5 ug) was reacted with 15 ug chloramine-T and 500 uCi ^{125}I. The reaction was stopped with 60 ug of sodium metabisulfite and ^{125}I-pLH was separated from free ^{125}I by anion exchange (AG 2 x 8, chloride form, 100 to 200 mesh, BioRad Laboratories, Richmond, CA) and gel filtration chromatography (Bio-Gel P-60, 100 to 200 mesh, BioRad Laboratories, Richmond, CA). For the assay, a large pool of porcine serum was filtered through a hollow fiber filter system (Amicon Corp., Danvers, MA) to remove pituitary hormones (exclusion limit = 10,000 molecular weight). Albumin from chicken eggs (Sigma Chemical Co., St. Louis, MO) was added to the pool of filtered serum to give a 5 mg/100 ml solution (EA-FPS). Standard curves were prepared in EA-FPS to give between 0.05 and 10 ng USDA-pLH-I-1/200 ul EA-FPS. Binding of ^{125}I-pLH to antisera was similar for tubes containing 200 ul EA-FPS plus 300 ul assay buffer (0.1 M phosphate buffered saline with 1 mg/100 ml bovine serum albumin, pH 7.5) and for tubes with 500 ul assay buffer. The

antiserum (Chemicon International, Inc., El Segundo, CA) did not crossreact significantly with USDA-pGH-B-1 (2.1%), USDA-pFSH-B-1 (.2%) or USDA-pPRL-B-1 (<.06%). Increasing volumes of sow serum displaced ^{125}I-pLH from the antisera to produce a binding curve that was parallel to the standard curve. When 0.3, 0.6, 1.2, 2.5, 5.0 and 10.0 ng USDA-pLH-B-1/ml were added to EA-FPS, 0.3, 0.4, 1.2, 2.4, 5.9 and 12.4 ng were recovered, respectively (average 99.2% recovery). Sensitivity of the assay was 0.1 ng/assay tube. All samples were quantified in six assays and the intra- and inter-assay coefficients of variation were 12.2% and 16.9%, respectively.

Follicle Stimulating Hormone. Concentrations of FSH in porcine serum (pFSH) were determined by a double-antibody RIA similar to that described by Kraeling et al. (1982) for pLH. Purified pFSH (LER-1419-3, 2.5 ug) was reacted with 10 ug chloramine-T and 500 uCi ^{125}I. The reaction was stopped with 40 ug of sodium metabisulfite and ^{125}I-pFSH was separated from free ^{125}I as previously described for pLH. Albumin from bovine serum (Sigma Chemical Co., St. Louis, MO) was added to the pool of filtered serum to give a 5 mg/100 ml solution (BSA-FPS). Standard curves were prepared in BSA-FPS to give between .128 and 32 ng LER-1419-3/200 ul BSA-FPS. Binding of ^{125}I-pFSH to antisera was similar for tubes containing 200 ul BSA-FPS plus 300 ul assay buffer (0.1 M phosphate buffered saline with 1% bovine serum albumin, pH 7.5) and for tubes with 500 ul assay buffer. The antiserum (Chemicon International, Inc., El Segundo, CA) did not crossreact significantly (< 0.1%) with USDA-pLH-I-1, USDA-pGH-B-1 or

USDA-pPRL-B-1. Increasing volumes of sow serum displaced ^{125}I-pFSH from the antisera to produce a binding curve that was parallel to the standard curve. When 1, 2, 4, 8, 16 and 32 ng LER-1419-3/ml were added to BSA-FPS, 0.8, 1.6, 4.3, 9.6, 18.4 and 34.2 ng were recovered, respectively (average 101.6% recovery). Sensitivity of the assay was 0.1 ng/assay tube. All samples were quantified in four assays and the intra- and inter-assay coefficients of variation were 5.3% and 8.5%, respectively.

Estradiol and Progesterone. One sample taken at the same time from all gilts during each day of frequent sampling was analyzed for P. After quantifying the concentrations of FSH, LH and P, approximately 400 1 serum was taken from each 15 min sample and combined to form a pool to determine of daily average concentration of E. Concentrations of E (Kluber et al., 1985) and P (Davis et al., 1985) in porcine serum were quantified by previously described methods. All samples were quantified for E and P in three assays for each hormone. Assay sensitivities and inter- and intra-assay coefficients of variation were 3.9 pg/tube, 11.1% and 6.2% for E and 0.6 ng/tube, 10.7% and 13.3% for P, respectively.

Pulsatile Characteristics of LH. The pattern of LH secretion was described as average concentration, number of pulses, baseline concentration, pulse amplitude, pulse magnitude and pulse duration. Average concentration was determined to be the mean of all concentrations during the 4-h period (window) on a given day. A pulse was defined as a pattern of concentrations with 1) at least one

concentration 50% above the previous nadir or greater and 2) sufficient time must have lapsed between the pulse magnitude and following nadir to allow for the circulating half-life of LH (30 min, Esbenshade, et al., 1986). If the highest concentration of a series that started at the beginning of a window met the requirement of being 50% above the following nadir, then that series was also determined to be a pulse. If the series met the first requirement and it appeared to be a pulse beginning as the window was stopped, then it too was determined to be a pulse. Neither of the latter cases were required to meet the second requirement nor could pulse amplitude, magnitude or duration be determined in these cases. Pulse duration was the interval from the previous nadir to following nadir. After all concentrations associated with the pulse were identified and deleted, the remaining concentrations were once again averaged and this value was defined as the baseline concentration. Pulse magnitude was the greatest concentration in a pulse and pulse amplitude was the magnitude minus the base concentration.

Statistical Analysis. Data were subjected to analysis of variance using General Linear Model procedures of the Statistical Analysis System (SAS, 1982). Dependent variables were analyzed using a split-plot analysis with repeated measures (Gill, 1978). Treatment, day of blood sampling and treatment x day were included in the model. Treatment was tested using the gilt within treatment variance (whole-plot error). When treatment means were significant, they were seperated using the Duncan's procedure of SAS (1982).

Treatment effects were further partitioned into orthogonal contrasts for estimation of altrenogest (0 vs 15 mg) and flushing (0 vs 1.54 kg additional grain) effects. Amplitude of peaks of LH and duration were analyzed only for days 1, 2 and 3 because of the infrequency of LH pulses on day 4. After initial analyses, data were standardized to the onset of estrus by subtracting the day of first detected estrus from the day of sampling and reanalyzed. Due to limited data, only days -2, -3, -4 and -5 relative to estrus were included in these analyses.

RESULTS

Data from seven gilts were deleted from the analyses because their catheters did not remain patent during the periods of blood collection. Data for two other gilts in the flush and altrenogest plus flush treatments were deleted because they failed to consume their allotted feed. All other gilts consumed their alloted feed by 1000 h on the following day. Number of gilts providing data is presented in Table 2.

Ovulation rate was higher ($P=0.06$) in flushed than in nonflushed groups (16.3 ± 1.0 vs 13.0 ± 1.2, respectively; Table 2). Altrenogest treatment had no effect on ovulation rate. Gilts treated with altrenogest but not flushed had longer ($P<0.05$) intervals to estrus than gilts in the other treatment groups. When treatment was partitioned into the main effects for altrenogest and flushing, gilts

fed altrenogest had longer ($P<0.01$) intervals to estrus than gilts not fed altrenogest (5.8 $\pm$ 0.2 days vs 5.1 $\pm$ 0.2 days) and flushed gilts had shorter ($P<0.01$) intervals to estrus than gilts not receiving flushing (5.0 $\pm$ 0.2 days and 5.9 $\pm$ 0.2 days).

All gilts not fed altrenogest (control and flush treatments) had functional corpora lutea (CL) before the first PGF injection as indicated by concentrations of P in serum of from 11 to 30 ng/ml at 0700 h on day 0. Progesterone declined after PGF for all gilts to 2 to 6 ng/ml of serum before the second PGF injection (1900 h).

Hormone Profiles After Treatment. Concentration of P in serum after last altrenogest or PGF injection (day 0) was affected by day ($P<0.001$) but not by treatment (Fig. 1). Concentration of E in serum was not affected by treatment but day ($P<0.001$) and treatment by day of sampling ($P<0.02$) effects were observed (Fig. 1). This interaction appeared to be due to elevated concentrations of E in serum on day 2 for altrenogest plus flush gilts and on day 3 for flush gilts. By day 4, E had increased for all treatments but was higher for controls than other treatment groups.

Average concentration of FSH in serum was unaffected by treatment (Table 3) but decreased with increasing days after treatment ($P<0.001$) and showed a tendency for a treatment by day interaction ($P=0.14$; Fig. 2). Altrenogest-treated and flushed gilts, whether or not they received altrenogest, had higher FSH concentrations on day 1 than control gilts. Gilts flushed, with or without altrenogest

treatment, also had higher FSH concentrations than control and altrenogest gilts on day 4.

Orthogonal contrasts revealed that flushing increased ($P<0.05$) LH in serum by 0.2 ng/ml (Table 3). The treatment by day of sampling interaction ($P<0.1$; Fig. 2) and day ($P<0.01$) also affected LH concentrations. Concentrations of LH on day 4 for gilts receiving flush or altrenogest plus flush were higher than for control and altrenogest gilts. Flushing resulted in one less (orthogonal contrast, $P<0.01$, Table 4) pulse of LH/4 h and the number of pulses of LH decreased ($P<0.001$) with increasing days after treatment.

The ratio of FSH to LH was unaffected by treatment (Table 3) but showed a day ($P<0.001$) effect with decreasing ratios as day of sampling increased and a day by treatment interaction ($P<0.05$; Fig. 3). Higher FSH/LH ratios were observed on day 1 for altrenogest and for flush gilts than for control or altrenogest plus flush gilts and higher ratios on day 2 for control and altrenogest gilts than for flush or altrenogest plus flush gilts. On subsequent days the FSH/LH ratio was similar for all treatments.

Flushing (flush and altrenogest plus flush) resulted in a 0.3 ng/ml increase ($P<0.02$) in the baseline concentration of LH in serum compared with nonflushed (control and altrenogest) gilts (Table 4). There was also a day effect ($P<0.001$) and a treatment by day interaction ($P<0.1$) which appeared to result from elevated baseline levels of LH on day 4 for both flushed treatments but not for control and altrenogest gilts.

Average duration of pulses of LH was unaffected by treatment or the day by treatment interaction (Table 4). However, duration decreased ($P<0.1$) with increasing days after treatment (Table 4).

Amplitude of pulses of LH decreased with day ($P<0.01$) and showed a treatment by day interaction ($P=0.08$; Table 4). This interaction resulted from declining amplitudes of pulses of LH for altrenogest, flush and altrenogest plus flush gilts but relatively constant, low amplitude pulses for controls. Altrenogest-treated gilts appeared to have higher amplitude LH pulses on day 1 than nonaltrenogest-treated gilts.

Hormone Profiles Before Estrus. When the data were analyzed retrospectively relative to estrus, circulating E increased ($P<0.05$) from -5 to -2 days before estrus (Fig. 4). Treatment tended ($P=0.12$) to affect concentrations of E in serum and orthogonal contrasts revealed that altrenogest increased E ($P<0.05$) by 1.6 pg/ml but that flushing was without effect on E concentrations. Concentrations of P in serum were affected by day before estrus ($P<0.001$), treatment ($P<0.01$) and the treatment by day interaction ($P<0.05$, Fig. 4). Concentrations of P in serum decreased as gilts approached estrus but were greater on day -5 relative to estrus for flush and altrenogest plus flush gilts than for control and altrenogest gilts (Fig. 4). Orthogonal contrasts revealed both altrenogest ($P<0.05$) and flushing ($P<0.01$) effects. Altrenogest decreased (0.6 ng/ml) P and flushing increased (0.8 ng/ml) concentrations of P in serum (Table 3).

Average concentrations of FSH in serum were increased (P=0.07) by flush and altrenogest plus flush treatments (4.6 and 4.3 ng/ml) as compared to control and altrenogest gilts (2.9 and 2.8 ng/ml; Table 3) and decreased (P<0.001) as the gilts reached estrus (Fig. 5). However, the FSH/LH ratio was affected (P<0.001) only by day relative to estrus as the ratio decreased for days nearer estrus (Fig. 6). Number of pulses of LH decreased (P<0.001), LH baseline increased (P<0.05) and the amplitude of pulses of LH decreased (P<0.05) as estrus approached (Table 5). The amplitude of pulses of LH showed a tendency for a treatment by day relative to estrus interaction (P<0.1, Table 5) because pulse amplitude decreased from -5 to -2 days before estrus for all except altrenogest gilts. The LH pulse amplitudes for these gilts decreased to day -3 but then increased on day -2 to day -5 levels.

DISCUSSION

Differences in mean ovulation rate were within the expected range as reported previously (Anderson and Melampy, 1971) and are consistent with our own observations for these same treatments (Rhodes, Davis and Stevenson; unpublished observations). Luteolysis for control and flush gilts was induced by PGF injections. Therefore, the increased interval to estrus resulting from altrenogest treatment is probably a function of altrenogest delaying

the start of follicular maturation leading to ovulation (Guthrie and Bolt, 1985; Redmer and Day, 1981). Perhaps this delay resulted from a longer interval required for clearance of the progestational effects of altrenogest as compared to that occurring during luteolysis in nonaltrenogest (PGF) treated gilts. This possibility could not be evaluated because no assay is available for the biologically active form of altrenogest (Roussel - UCLAF, personal communication). The reason for the shortened interval to estrus for flush and altrenogest plus flush gilts may be the altered patterns of gonadotropin secretion in flushed gilts (see below).

Hormone Profiles After Treatment. Higher concentrations of E in serum of altrenogest plus flush gilts on day 2 after altrenogest is probably a result of increased steroidogenic activity of ovarian follicles which are perhaps more physiologically mature. This is consistent with the relatively early return to estrus by these gilts. Flush gilts also returned quickly to estrus and their somewhat elevated E concentrations on day 3 after PGF may also reflect earlier maturation of their ovarian follicles. By day 4 after PGF, control gilts also had elevated E concentrations which tended to be higher than other groups. These patterns of E secretion are consistent with the pattern of E secretion in normally cycling sows and gilts during the follicular phase (Brinkley, 1981). Therefore, gilts in treatment groups having similar average intervals to estrus (4.8 to 5.3 days, Table 2) had evidence of increased follicular steroidogenesis during the 4 day sampling period compared to altrenogest gilts. In addition

to lower circulating E, these latter gilts also had the longest average interval to estrus (Table 2).

Concentrations of both FSH and LH in serum were higher for flushed than for nonflushed gilts on day 4. This may reflect direct effects of flushing on gonadotropin secretion. Alternatively, day 4 samples for these gilts may have included a portion of the preovulatory gonadotropin surge since many of these gilts were in estrus on day 4 or 5.

The suppression of the number of pulses of LH and the increase in the baseline concentration of LH in serum for flushed vs nonflushed gilts suggests that flushing alters the secretion pattern of LH. These changes may have been brought about by the flushing treatment acting directly on the hypothalamic pulse generator. However, since flushed gilts also came into estrus earlier than nonflushed gilts it is possible the differences in the secretory pattern of LH represent the secretory characteristics normally encountered prior to estrus. These events were advanced for flushed gilts, possibly by elevated FSH on day 1 after treatment.

The effects of altrenogest on the LH secretory pattern were to increase the number of pulses on day 2 and increase the pulse amplitude on day 1. These alterations of LH secretion may be explained by lingering progestational effects of altrenogest since they are more like the pattern found in the luteal phase (Brinkley, 1981). This interpretation is consistent with the delayed interval to estrus for altrenogest and altrenogest plus flush gilts (Table 2).

Hormone Profiles Before Estrus. The reason for increased E concentration in the serum of altrenogest treated gilts (Fig. 4) is unknown. Since altrenogest did not affect ovulation rate in our study, we have no evidence that increased E concentrations reflect increased numbers of maturing follicles. A similar trend is apparent in the data of Redmer and Day (1981) but is not discussed by the authors. Treatment with altrenogest has been associated with increased ovulation rate in some studies (Davis et al., 1979; O'Reilly et al., 1979) but if follicular development was affected by altrenogest in our study it was not reflected in ovulation rate (Table 2). In contrast, altrenogest-treated gilts had lower P than nonaltrenogest-treated gilts and flushing increased concentrations of P in serum (Fig. 4 and Table 3). We can not explain these treatment effects but they apparently indicate treatment induced changes in ovarian steroidogenesis.

When data were analyzed relative to estrus (day -5 to day -2), LH pulse duration, the number of pulses of LH, and average and baseline concentrations of LH were unaffected by treatment. Therefore, these characteristics may have been altered by treatment-induced changes in the interval to estrus that were only apparent when data were analyzed according to day after treatment. However, the amplitude of pulses of LH had a more rapid decline with approaching estrus for flushed as compared to nonflushed gilts and may be representative of the earlier return to estrus in flushed gilts.

Higher concentration of FSH in serum of flush and altrenogest plus flush gilts was observed with differences in FSH being most apparent on day -5. These day -5 concentrations most closely correspond to day 1 after treatment when FSH concentrations were also increased for flush and altrenogest plus flush gilts. Therefore, our data point consistently to increased concentrations of FSH in the serum of flushed gilts. In contrast, FSH concentrations were elevated for altrenogest versus control gilts on day 1 after treatment but no altrenogest effects were observed when data were analyzed relative to estrus. Therefore, of the treatment effects on FSH, only the effect of flushing is free of the potentially confounding influence of stage of the cycle relative to estrus. Because altrenogest lengthened the interval from treatment to estrus (Table 2), it is likely its progestational influence continued into day 1 of sampling making this day more similar to the luteal phase than the early follicular phase which nonaltrenogest-treated gilts were experiencing. Follicle stimulating hormone is known to decrease during the early follicular phase (Guthrie and Bolt, 1985). Therefore, clearance of altrenogest may explain its elevating effects on concentrations of FSH in serum on day 1 after treatment and the absence of this effect when the data were analyzed relative to estrus.

General Discussion. Several recent studies can be compared with our study. Increased FSH in the present study, particularly during the early to mid-follicular phase, agrees well with the results of

Flowers et al. (1986) who reported increased concentrations of FSH in flushed gilts on days -5, -4 and -3 relative to estrus. In contrast, Cox et al. (1984) compared flushed to nonflushed gilts after altrenogest treatment and found no differences in FSH. However, Cox et al. (1984) did not report FSH values after 30 h post-altrenogest treatment. Therefore, their data correspond to our observations on day 1 after treatment when we also observed no differences for FSH after treatment between altrenogest and altrenogest plus flush gilts. Therefore, experimental design considerations may explain why Cox et al. (1984) failed to detect effects of flushing on FSH concentrations.

The data of Flowers et al. (1986) and Jones et al. (1983) show an increased number of pulses of LH in flushed gilts on days -4, -3 and -2 relative to estrus, or on day 2 following last altrenogest treatment, respectively. However, our data indicate a decrease in the number of pulses of LH after treatment and no effect when the data were analyzed relative to estrus. Perhaps this contradiction is explained by different definitions of a secretory pulse of LH in our study versus others (Flowers et al., 1986; and Jones et al., 1983). Alternatively, similar contradictions exist between studies attempting to define the hormonal correlates associated with flushing in the ewe (Knight et al., 1981; Memon et al., 1969; Scaramuzzi and Radford, 1983; Smith, 1985) and the cause(s) for the discrepencies in these studies is not resolved.

Concentrations of FSH in serum were affected by treatment in the present study regardless of the statistical analysis used. We postulate that the higher concentration of FSH during the early follicular phase of flushed gilts is the predominant factor accounting for the increased ovulation rate and for initiating the other hormonal changes resulting in a decreased interval to estrus. A higher concentration of FSH during the period of follicular recruitment may allow selection of a larger number of follicles (Foxcroft and Hunter, 1985) or provide support for follicles which would otherwise become atretic (Daily et al., 1972; 1975). Circulating P was also elevated in flushed gilts and increased concentrations of intraovarian P have been shown to increase ovulation rate in ewes (Dufour et al., 1972; Harned and Casida, 1971). Therefore, both FSH and P may have contributed to the increase of 3.3 CL for flushed versus nonflushed gilts in the present study.

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Table 1. Diet Composition

Ingredient	Percentage of diet	kcal of ME[a] per kg
Sorghum grain	80.85	3229
Soybean meal[b]	15.00	3090
Dicalcium phosphate	2.20	0
Limestone	1.10	0
Salt	0.50	0
Trace minerals[c]	0.10	0
Vitamin Premix[d]	0.25	0
Total	100.00	3067

[a] Calculated metabolizable energy.

[b] Crude protein = 44%.

[c] Provided the following in mg/kg of complete diet: Mn, 50; Zn, 100; Fe, 100; Cu, 10; I, 3; and Co, 1.

[d] Contributed the following per kg of diet: vitamin A, 8,800 USP; vitamin D_3, 660 USP; vitamin E, 44 IU; riboflavin, 9.9 mg; menadione, 3.4 mg; d-pantothenic acid, 26.4 mg; niacin, 55 mg; choline chloride, 1014.2 mg; vitamin B_{12}, 48.4g.

Table 2. Number of Corpora Lutea (CL) and Interval to Estrus after Altrenogest Treatment or Prostaglandin $F_{2\alpha}$[a]

	Treatment				Orhtogonal Comparison	
Variable	Control	Altrenogest	Flush	Altrenogest + Flush	Flush - no Flush	Altrenogest - no Altrenogest
No. Gilts	4	4	5	6	---	---
No. CL	12.5 ± 1.7	13.5 ± 1.7	16.8 ± 1.5	15.8 ± 1.4	3.3[b]	.02
Interval to estrus (d)	5.3 ± .3	6.5 ± .3	4.8 ± .3	5.2 ± .2	- .9[c]	.8[c]

[a] Least squares means ± S.E.
[b] P = .06.
[c] P < .01.

Table 3. Concentration of FSH, LH, P and E and the Ratio of FSH to LH in Serum of Gilts as Affected by Treatment with Altrenogest or Flushing[a]

Item	Treatment[b] C	A	F	A+F	Orthogonal Comparison: Flush - No Flush	Altren. - No Altern.
Following Treatment						
Average FSH (ng/ml)	2.6 ± 0.3	3.4 ± 0.3	3.5 ± 0.3	3.1 ± 0.3	0.3	0.2
Average LH (ng/ml)	0.7 ± 0.1	0.7 ± 0.1	1 ± 0.1	0.9 ± 0.1	0.2[c]	-0.1
FSH / LH Ratio	4.2 ± 0.4	5.5 ± 0.4	4.8 ± 0.4	4.1 ± 0.4	-0.4	0.4
E (pg/ml)	5 ± 0.5	4.6 ± 0.6	4.4 ± 0.5	4.6 ± 0.5	-0.3	-0.1
P (ng/ml)	0.8 ± 0.2	1.1 ± 0.2	1 ± 0.2	0.5 ± 0.2	-0.1	-0.1
Before Estrus						
Average FSH (ng/ml)	2.9 ± 0.4	2.8 ± 0.3	4.6 ± 0.4	4.3 ± 0.4	1.6[d]	-0.2
Average LH (ng/ml)	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.1	0.1	0.1
FSH / LH Ratio	5.2 ± 0.7	4.7 ± 0.6	7.6 ± 0.8	5.2 ± 0.7	1.4	-1.5
E (pg/ml)	3.3 ± 0.7	5.2 ± 0.6	3.2 ± 0.8	4.6 ± 0.7	-0.3	1.6[c]
P (ng/ml)	0.9 ± 0.2[e,f]	0.6 ± 0.2[e,f]	2.1 ± 0.2[e]	1.2 ± 0.2[e,f]	0.8[g]	-0.6[c]

[a] Least squares means ± S.E.

[b] C = control, A = altrenogest, F = flush and A + F = altrenogest plus flush.

[c] Comparison differs $P<0.05$.

[d] Comparison differs $P<0.07$.

[e,f] Means within the same row with different superscripts differ $P<0.05$.

[g] Comparison differs $P<0.01$.

Table 4. Characteristics of LH Secretion in Gilts as Analyzed by Day of Sampling[a]

Item	Day 1	2	3	4	Trt Mean
Number of Pulses					
Control	3.0 ± 0.4(5)	2.4 ± 0.4(5)	1.2 ± 0.4(5)	0.6 ± 0.4(5)	1.8[b] ± 0.2
Altrenogest	2.8 ± 0.5(4)	2.5 ± 0.5(4)	1.3 ± 0.5(4)	1.3 ± 0.5(4)	1.9[b,c] ± 0.2
Flush	2 ± 0.4(5)	0.8 ± 0.4(5)	0.2 ± 0.4(5)	0.4 ± 0.4(5)	0.9[c,d] ± 0.2
Altrenogest + Flush	2.5 ± 0.4(6)	1.2 ± 0.4(6)	0.2 ± 0.4(6)	0 ± 0.4(6)	1.0[d] ± 0.2
Baseline Concen.[e] (ng/ml)					
Control	0.4 ± 0.2(5)	0.5 ± 0.2(5)	0.6 ± 0.2(5)	0.7 ± 0.2(5)	0.6 ± 0.1
Altrenogest	0.4 ± 0.2(4)	0.5 ± 0.2(4)	0.6 ± 0.2(4)	0.5 ± 0.2(4)	0.5 ± 0.1
Flush	0.5 ± 0.2(5)	0.7 ± 0.2(5)	0.6 ± 0.2(5)	1.8 ± 0.2(5)	0.9 ± 0.1
Altrenogest + Flush	0.5 ± 0.2(6)	0.4 ± 0.2(6)	0.8 ± 0.2(6)	1.4 ± 0.2(6)	0.8 ± 0.1
Pulse Duration (min)					
Control	24 ± 6(5)	20 ± 7(4)	37 ± 9(3)		27 ± 5
Altrenogest	60 ± 7(4)	40 ± 8(3)	19 ± 11(2)		40 ± 5
Flush	24 ± 6(5)	24 ± 12(2)	19 ± 17(1)		22 ± 8
Altrenogest + Flush	38 ± 6(6)	20 ± 10(4)	6 ± 17(1)		21 ± 7
Pulse Amplitude[e] (ng/ml)					
Control	0.4 ± 0.1(5)	0.3 ± 0.1(3)	0.4 ± 0.1(3)		0.3 ± 0.1
Altrenogest	1.1 ± 0.1(4)	0.6 ± 0.1(4)	0.2 ± 0.2(4)		0.6 ± 0.1
Flush	0.3 ± 0.1(5)	0.4 ± 0.2(2)	0.1 ± 0.2(1)		0.3 ± 0.1
Altrenogest + Flush	0.7 ± 0.1(6)	0.2 ± 0.1(4)	0.1 ± 0.2(1)		0.3 ± 0.1
Pulse Magnitude[f] (ng/ml)					
Control	0.8 ± 0.1(5)	0.8 ± 0.1(4)	0.9 ± 0.1(3)		0.8 ± 0.1
Altrenogest	1.5 ± 0.1(4)	1 ± 0.1(4)	0.8 ± 0.1(2)		1.1 ± 0.1
Flush	0.8 ± 0.1(5)	1.1 ± 0.2(2)	0.8 ± 0.2(1)		0.9 ± 0.1
Altrenogest ± Flush	1.2 ± 0.1(6)	0.7 ± 0.1(4)	0.9 ± 0.2(1)		0.9 ± 0.1

[a] Least squares means ± S.E.(n).

[b,c,d] Means within respective characteristic with different superscripts differ P<0.05.

[f] Treatment x day interaction P<0.1.

[d] Treatment x day interaction P<0.05.

Table 5. Characteristics of LH Secretion as Analyzed Relative to Estrus (day 0)[a]

Item	Day -5	-4	-3	-2	Trt Mean
Number of Pulses					
Control	2.7 ± 1(1)	4 ± 0.4(5)	1.6 ± 0.4(5)	1.4 ± 0.4(5)	2.4 ± 0.3
Altrenogest	2.5 ± 0.4(4)	2.3 ± 0.4(4)	1.3 ± 0.4(4)	0.7 ± 0.6(2)	1.7 ± 0.2
Flush	2.5 ± 1(1)	2.2 ± 0.5(3)	1.2 ± 0.4(5)	0.2 ± 0.4(5)	1.5 ± 0.3
Altrenogest + Flush	4.4 ± 1(1)	2.2 ± 0.3(6)	0.8 ± 0.3(6)	0.2 ± 0.3(6)	1.9 ± 0.3
Baseline Concen. (ng/ml)					
Control	0.4 ± 0.2(1)	0.4 ± 0.1(5)	0.5 ± 0.1(5)	0.6 ± 0.1(5)	0.5 ± 0.1
Altrenogest	0.4 ± 0.1(4)	0.5 ± 0.1(4)	0.6 ± 0.1(4)	0.5 ± 0.1(2)	0.5 ± 0.1
Flush	0.5 ± 0.2(1)	0.5 ± 0.1(3)	0.6 ± 0.1(5)	0.7 ± 0.1(5)	0.6 ± 0.1
Altrenogest + Flush	0.2 ± 0.2(1)	0.5 ± 0.1(6)	0.6 ± 0.1(6)	0.7 ± 0.1(6)	0.5 ± 0.1
Pulse Magnitude[b] (ng/ml)					
Control	0.6 ± 0.2(1)	0.9 ± 0.1(5)	0.8 ± 0.1(4)	0.8 ± 0.1(3)	0.8 ± 0.1
Altrenogest	1.2 ± 0.1(4)	0.9 ± 0.1(3)	0.5 ± 0.1(2)	1.5 ± 0.2(1)	1 ± 0.1
Flush	0.8 ± 0.2(1)	0.8 ± 0.1(3)	0.9 ± 0.1(4)	---------(0)	---------
Altrenogest + Flush	1.7 ± 0.2(1)	1 ± 0.1(6)	0.6 ± 0.2(3)	0.8 ± 0.2(1)	1 ± 0.1
Pulse Amplitude[b] (ng/ml)					
Control	0.2 ± 0.2(1)	0.5 ± 0.1(5)	0.3 ± 0.1(3)	0.2 ± 0.1(3)	0.3 ± 0.1
Altrenogest	0.8 ± 0.1(4)	0.4 ± 0.1(3)	0 ± 0.2(2)	0.8 ± 0.2(1)	0.5 ± 0.1
Flush	0.4 ± 0.3(1)	0.3 ± 0.1(3)	0.3 ± 0.1(4)	---------(0)	---------
Altrenogest + Flush	1.2 ± 0.3(1)	0.3 ± 0.1(6)	0.2 ± 0.2(3)	0.1 ± 0.3(1)	0.5 ± 0.1
Pulse Duration (min)					
Control	28 ± 20(1)	21 ± 9(5)	27 ± 9(4)	29 ± 11(3)	26 ± 7
Altrenogest	50 ± 11(3)	28 ± 11(3)	14 ± 15(2)	1 ± 20(1)	23 ± 7
Flush	26 ± 21(1)	25 ± 12(3)	22 ± 10(4)	-------(0)	------
Altrenogest ± Flush	57 ± 23(1)	34 ± 7(6)	19 ± 16(3)	4 ± 21(1)	28 ± 7

[a] Least squares means ± S.E.(n).
[b] Treatment by day interaction $P<0.1$.

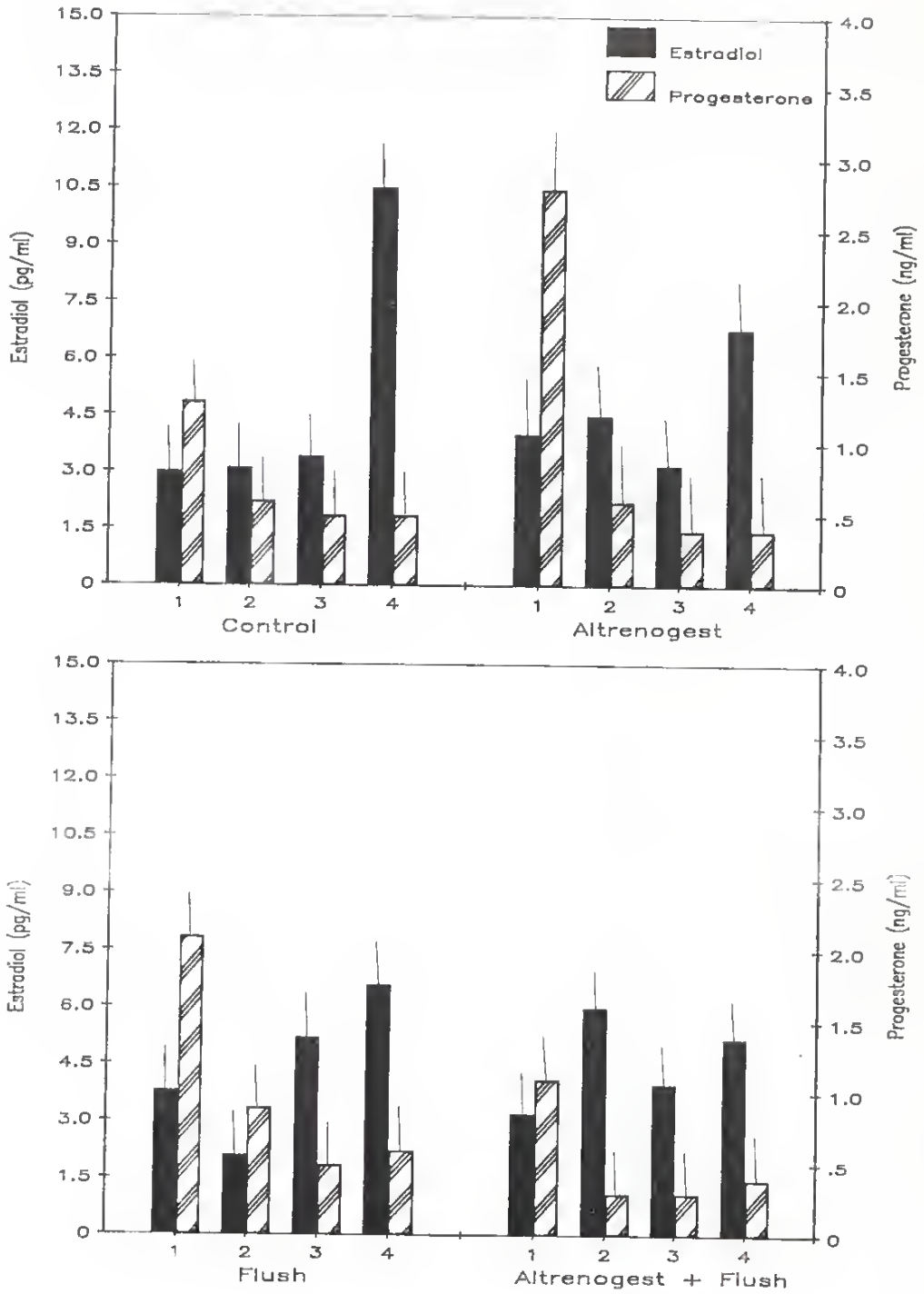


FIG. 1. Concentrations of estradiol-17B and progesterone on day 1, 2, 3, and 4 after altrenogest or PGF.

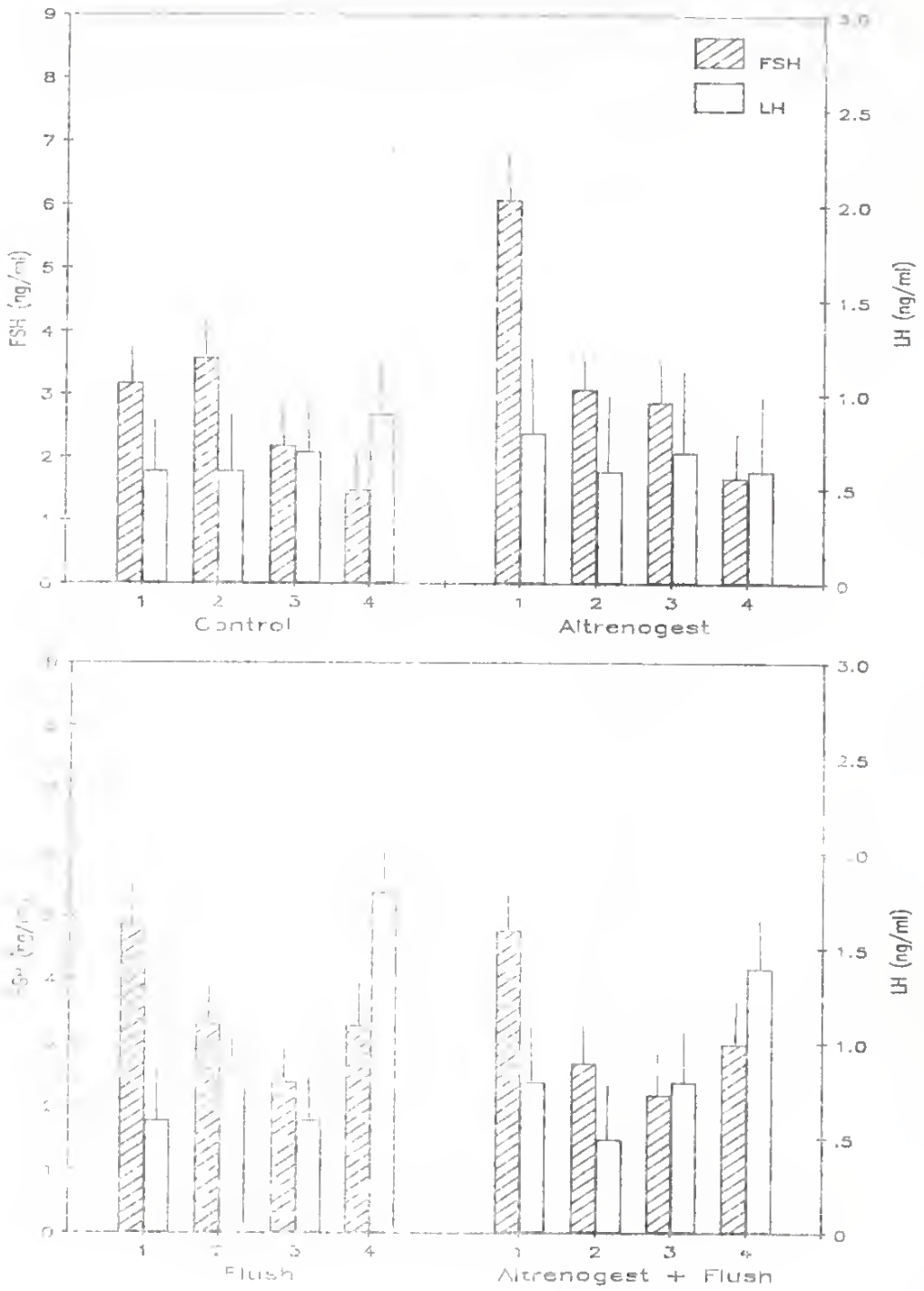


Fig. 2. Concentrations of FSH and LH on day 1, 2, 3, and 4 after Altrenogest or PGF

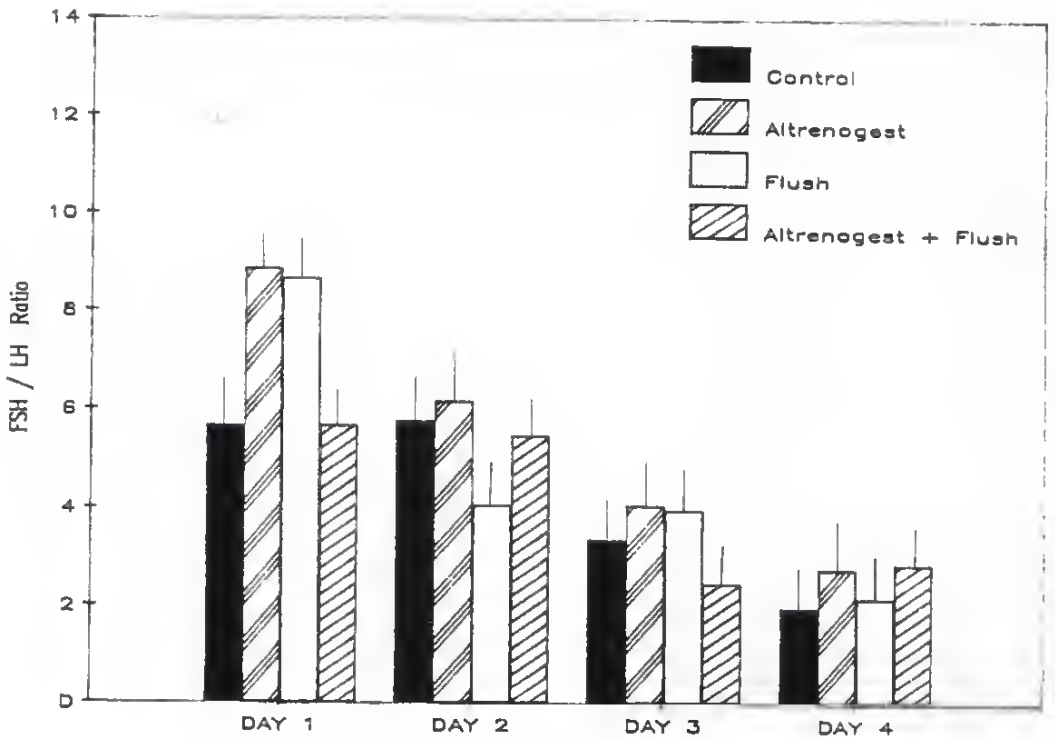


FIG. 3. Ratios of FSH to LH after last altrenogest treatment or PGF.

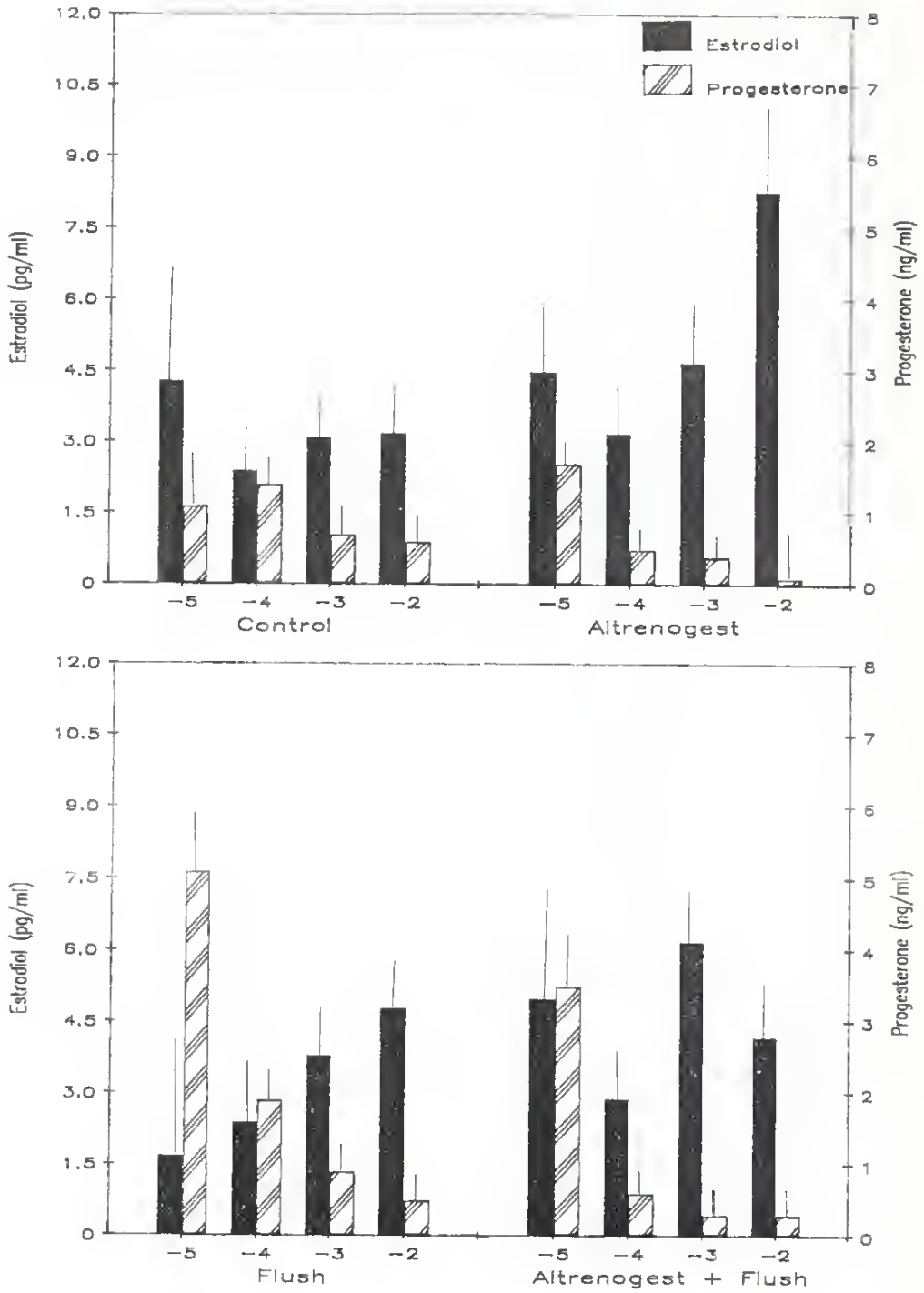


FIG. 4. Concentrations of estradiol-17B and progesterone on days -5, -4, -3, and -2 before estrus (day 0) following altrenogest treatment or PGF.

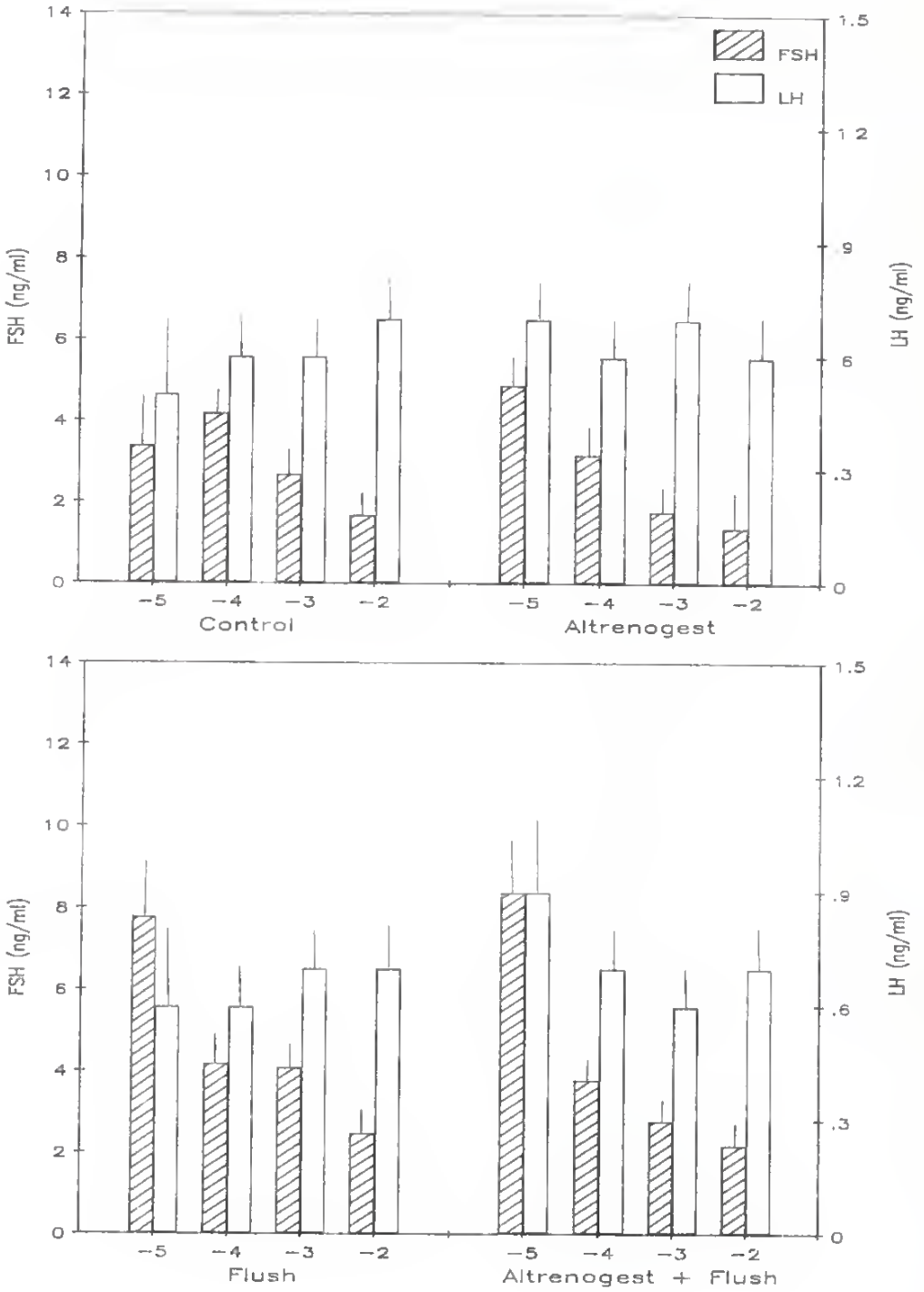


FIG. 5. Concentrations of FSH and LH on days -5, -4, -3, and -2 before estrus (day 0) following altrenogest treatment or PGF.

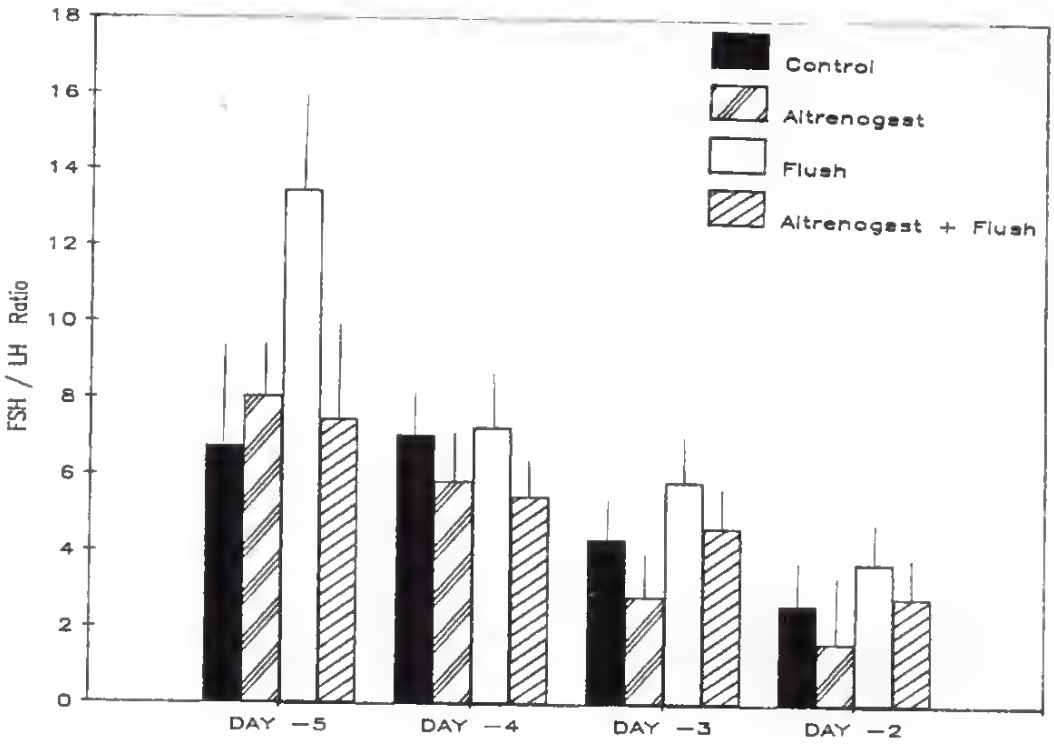


FIG. 6. Ratios of FSH to LH on days -5, -4, -3, and -2 before estrus (day 0).

Appendix Table 1. Concentrations of E and P in Serum of Gilts Following Treatment with Altrenogest or Prostaglandin $F_{2\alpha}$

		Day of Sampling									
		1		2		3		4			
Gilt	Trt[a]	E[b]	P[c]	E	P	E	P	E	P	Day of Estrus[d]	Analyzed[e]
G82	C	2.4	1.3	3.1	0.5	5.1	0.6	17.7	0.5	5	YES
G85	C	3.4	0.7	1.9	0.4	1.0	0.5	3.2	0.4	6	YES
G86	C	3.5	2.3	3.9	0.8	3.6	0.6	14.3	0.7	5	YES
G87	C	2.9	1.3	4.9	0.7	2.6	0.5	8.9	0.6	5	YES
G88	C	2.8	1.0	1.5	0.7	4.5	0.5	8.2	0.5	5.5	YES
Y75	C	1.5	6.4	---	6.7	3.2	0.9	2.7	0.5	6	NO
Y94	C	---	1.2	8.8	0.5	6.4	0.3	4.9	0.5	7	NO
G61	A	1.8	1.4	---	---	---	---	---	---	7	NO
G62	A	2.1	5.0	2.7	1.0	1.0	0.5	2.6	0.3	7	YES
G63	A	---	5.0	6.7	0.9	4.3	0.6	8.5	0.5	6	YES
G64	A	5.4	0.9	7.0	0.3	3.4	0.4	7.7	0.4	7	YES
G66	A	2.8	1.4	3.2	0.4	2.4	0.6	---	---	6	NO
Y95	A	1.5	10.0	1.5	2.3	2.6	0.9	---	0.5	7.5	NO
Y99	A	2.7	0.3	1.5	0.2	4.0	0.2	8.2	0.3	6	YES
G90	F	1.4	5.0	1.5	1.7	3.5	0.7	5.2	0.5	6	YES
G91	F	2.9	1.6	2.2	0.7	5.1	0.5	8.8	0.5	5	YES
G93	F	4.6	0.9	2.8	0.5	5.0	0.3	2.3	0.5	4	YES
G94	F	7.3	1.0	3.0	0.6	4.7	0.4	12.6	0.7	4	YES
G95	F	2.6	2.2	1.2	1.0	7.9	0.5	3.9	0.6	5	YES
Y93	F	2.2	1.1	6.7	0.8	7.5	0.9	---	---	3.5	NO

Continued on Next Page

Appendix Table 1 (Cont'd). Concentrations of E and P in Serum of Gilts Following Treatment with Altrenogest or Prostaglandin $F_2\alpha$

		Day of Sampling									
		1		2		3		4			
Gilt	Trt[a]	E[b]	P[c]	E	P	E	P	E	P	Day of Estrus[d]	Analyzed[e]
G68	A+F	1.6	0.6	6.4	0.3	5.5	0.3	5.3	0.3	5	YES
G69	A+F	2.0	0.5	9.9	0.2	3.4	0.3	1.9	0.4	5	YES
G70	A+F	2.9	0.9	10.5	0.3	3.3	0.4	5.0	0.4	5	YES
G71	A+F	6.2	0.4	5.5	0.4	4.6	0.3	5.8	0.6	5	YES
G72	A+F	2.1	1.0	1.8	0.5	2.4	0.3	---	0.4	5	NO
G73	A+F	3.6	3.6	1.8	0.5	2.8	0.5	4.4	0.5	6	YES
Y96	A+F	2.6	0.4	1.9	0.3	4.1	0.2	8.5	0.3	5	YES

[a] Treatment: C = neither altrenogest or flushing.
A = altrenogest.
F = flushing.
A+F = altrenogest plus flush.

[b] Estradiol-17 concentration (pg/ml serum).

[c] Progesterone concentration (ng/ml serum).

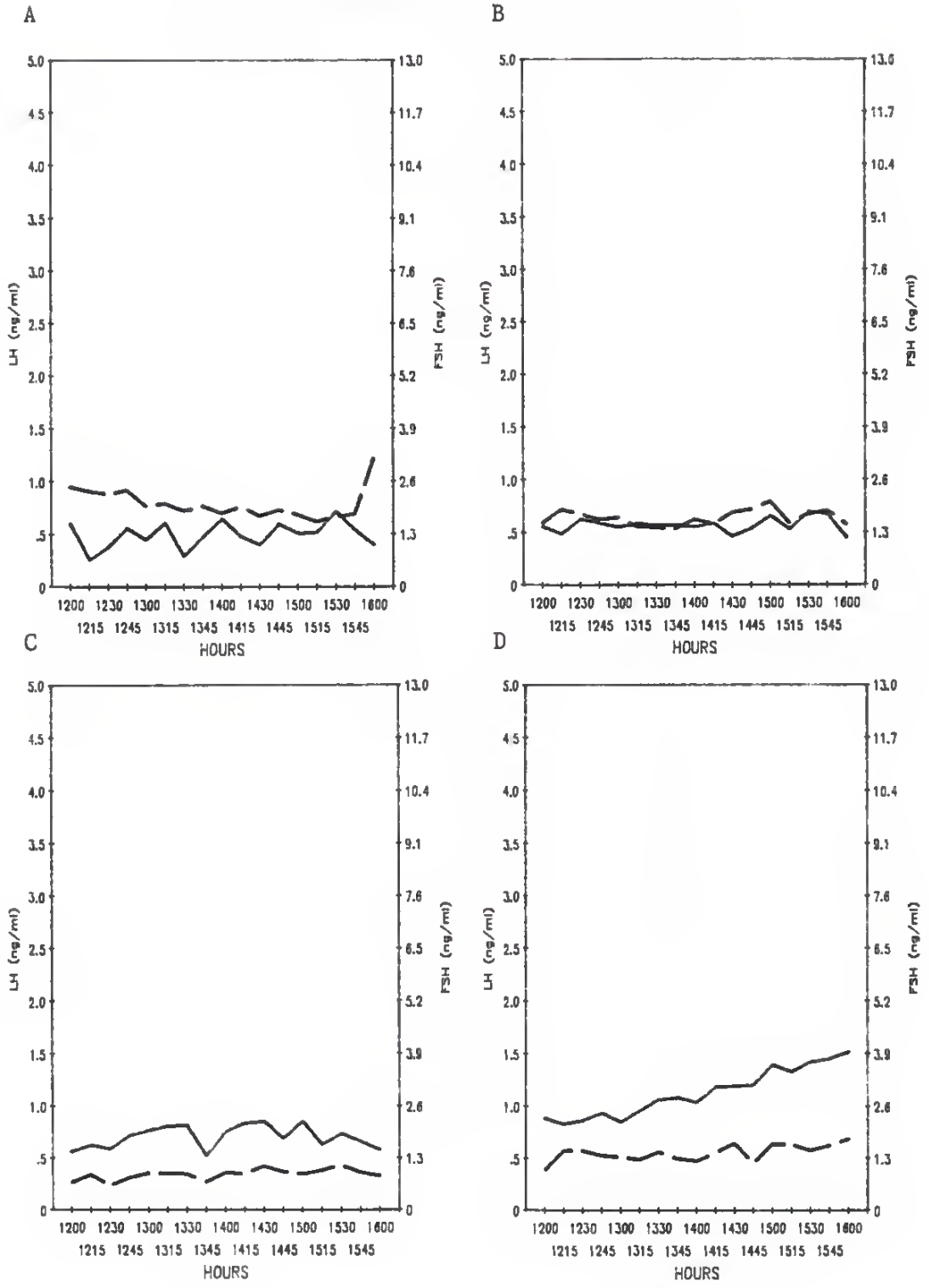
[d] Following last altrenogest treatment or first PGF injection.

[e] Whether or not gilts were included in statistical analysis.

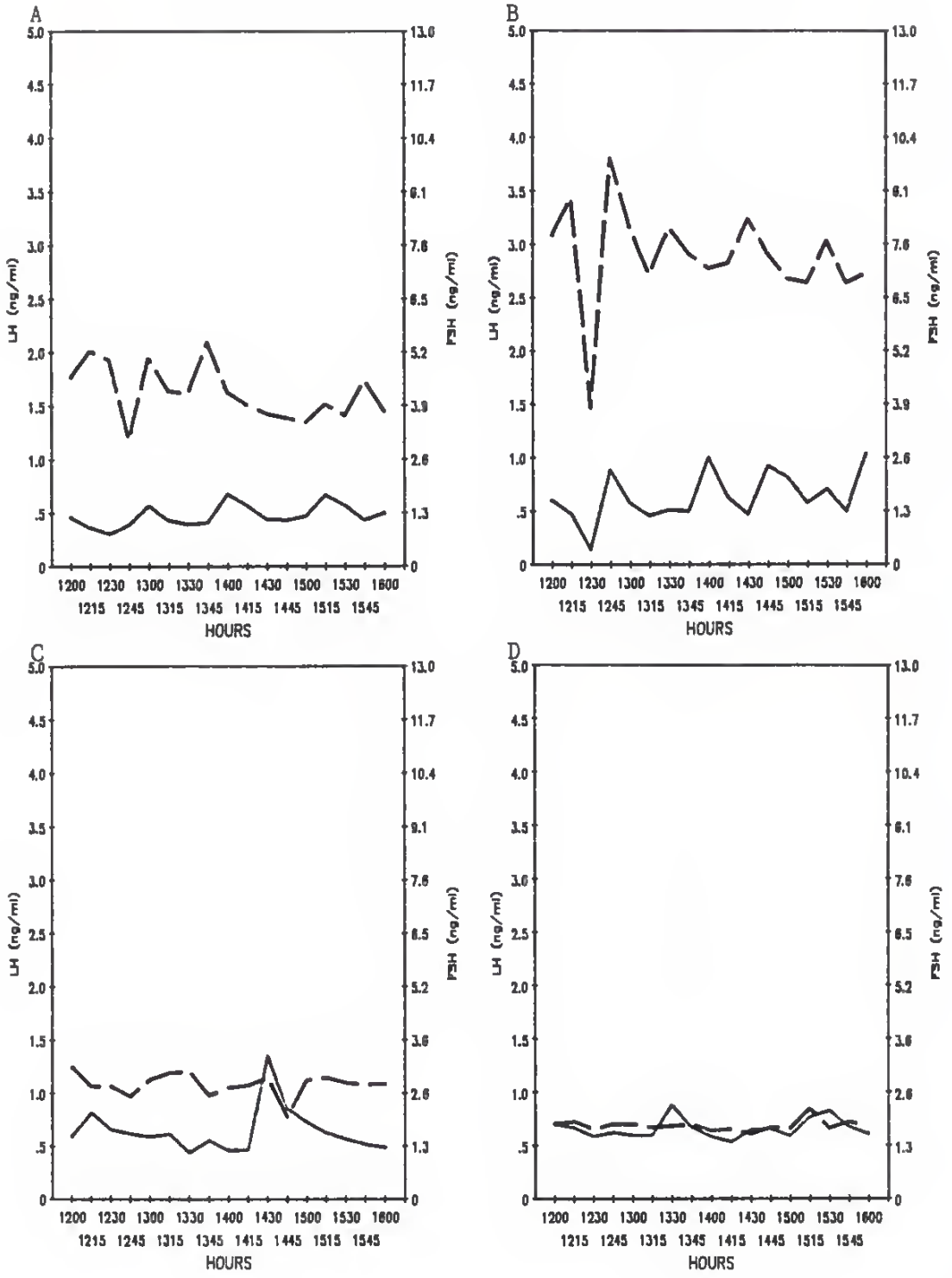
Appendix Figures 1 through 27.

FSH (dashed lines) and LH (solid lines) profiles for d 1 (A), d 2 (B), d 3 (C) and d 4 (D). Treatments: C = neither altrenogest or flushing, A = altrenogest, F = flush and A+F = altrenogest plus flush. Profiles which are not present or are incomplete represent missing data due to catheter failure. Estrus represents number of days from last altrenogest treatment or from first PGF injection to estrus. Values for LH were drawn at points below the sensitivity of the assay (0.3 ng/ml) in some cases.

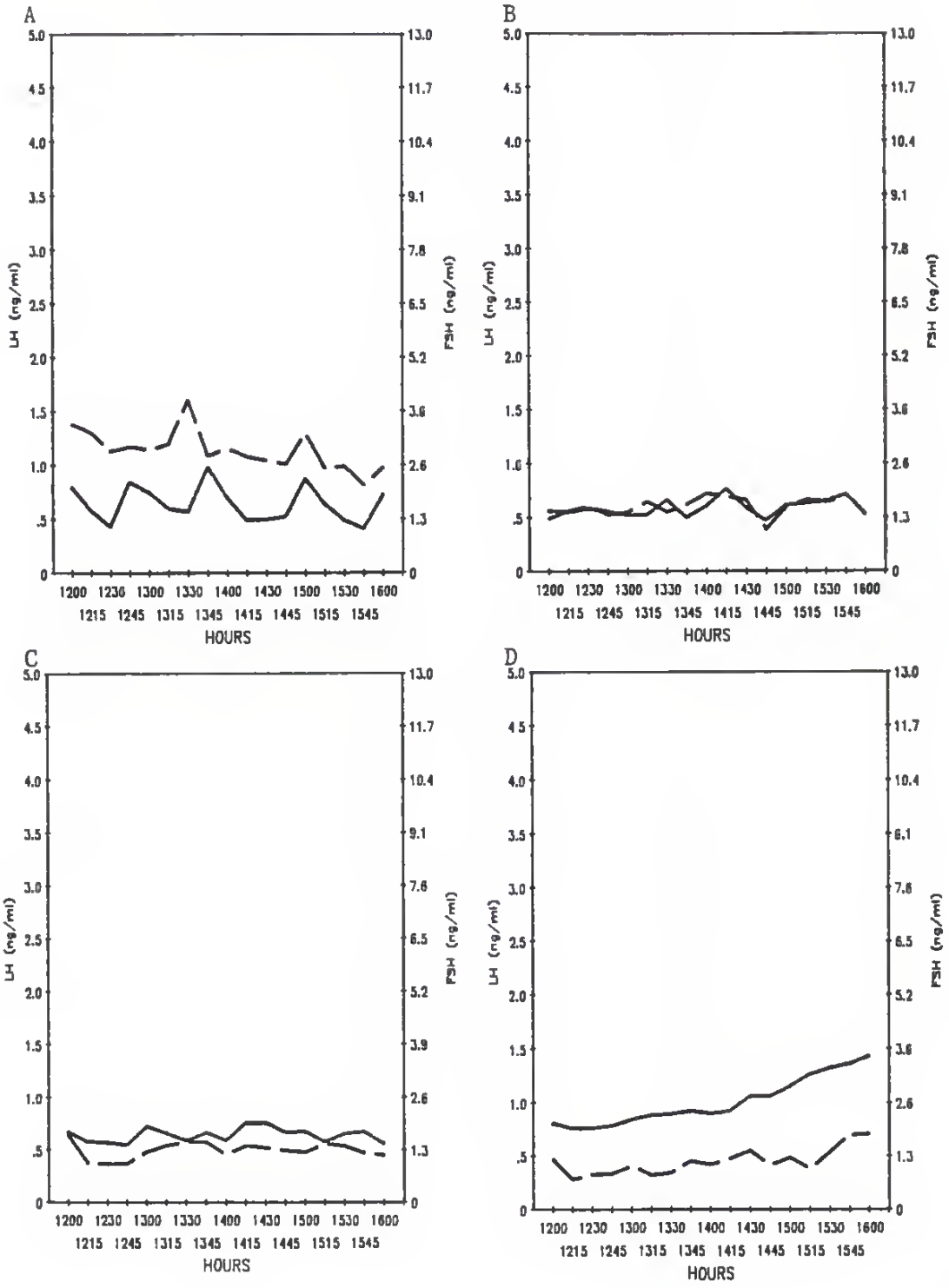
Appendix Figure 1.
Gilt G82, Treatment = C and Estrus = d 5.



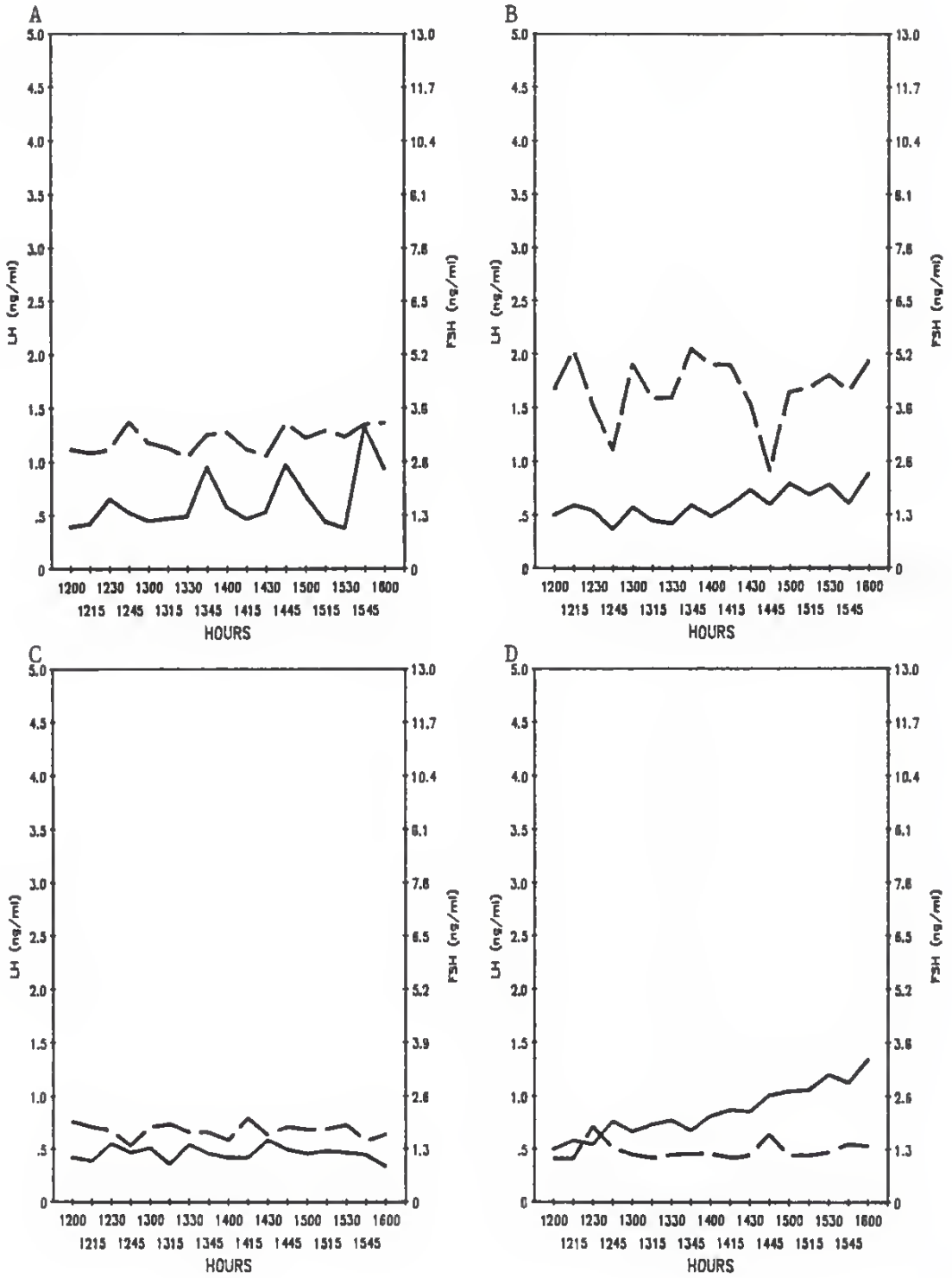
Appendix Figure 2.
Gilt G85, Treatment = C and Estrus = d 6.



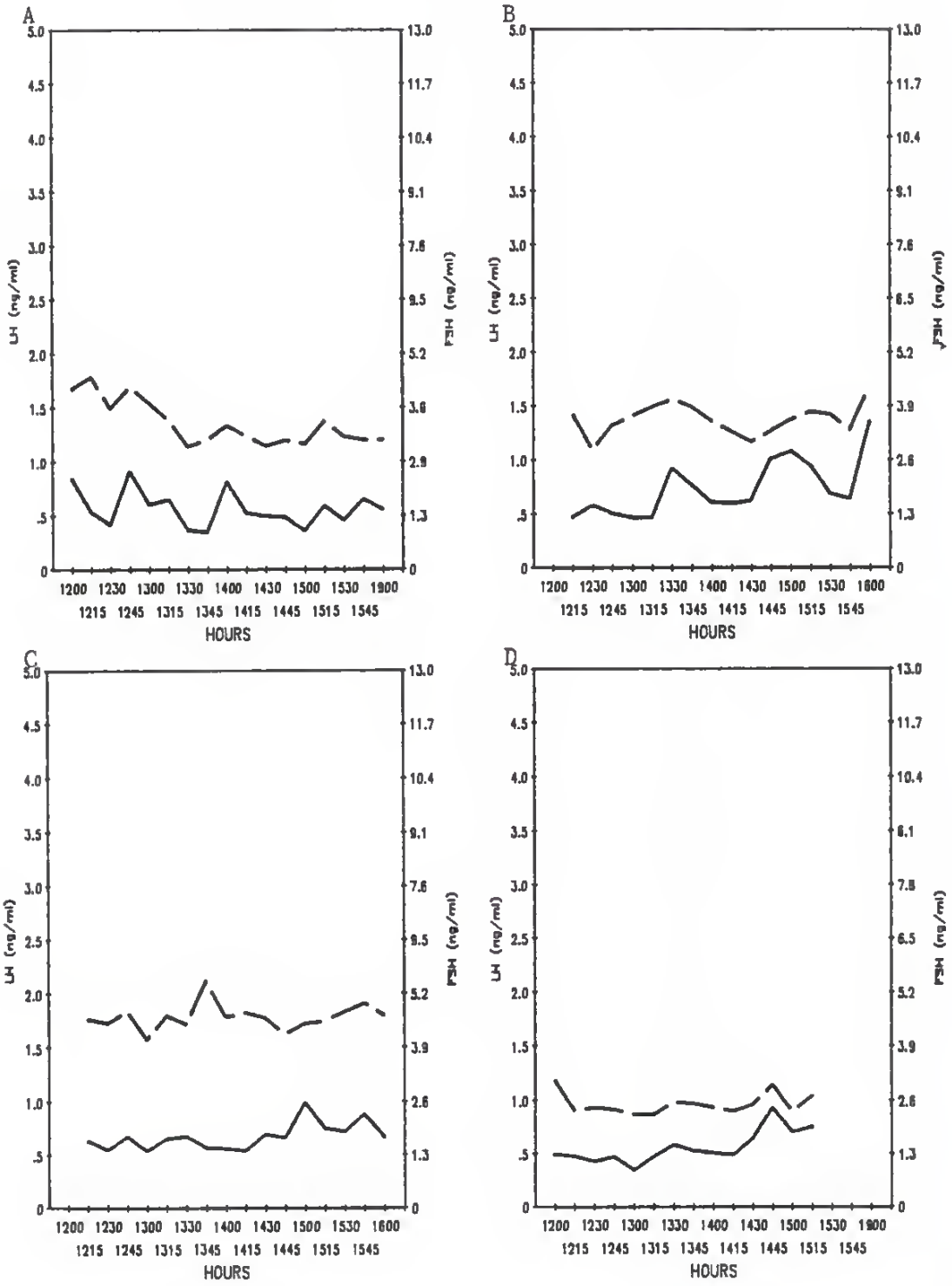
Appendix Figure 3.
Gilt G86, Treatment = C and Estrus = d 5.



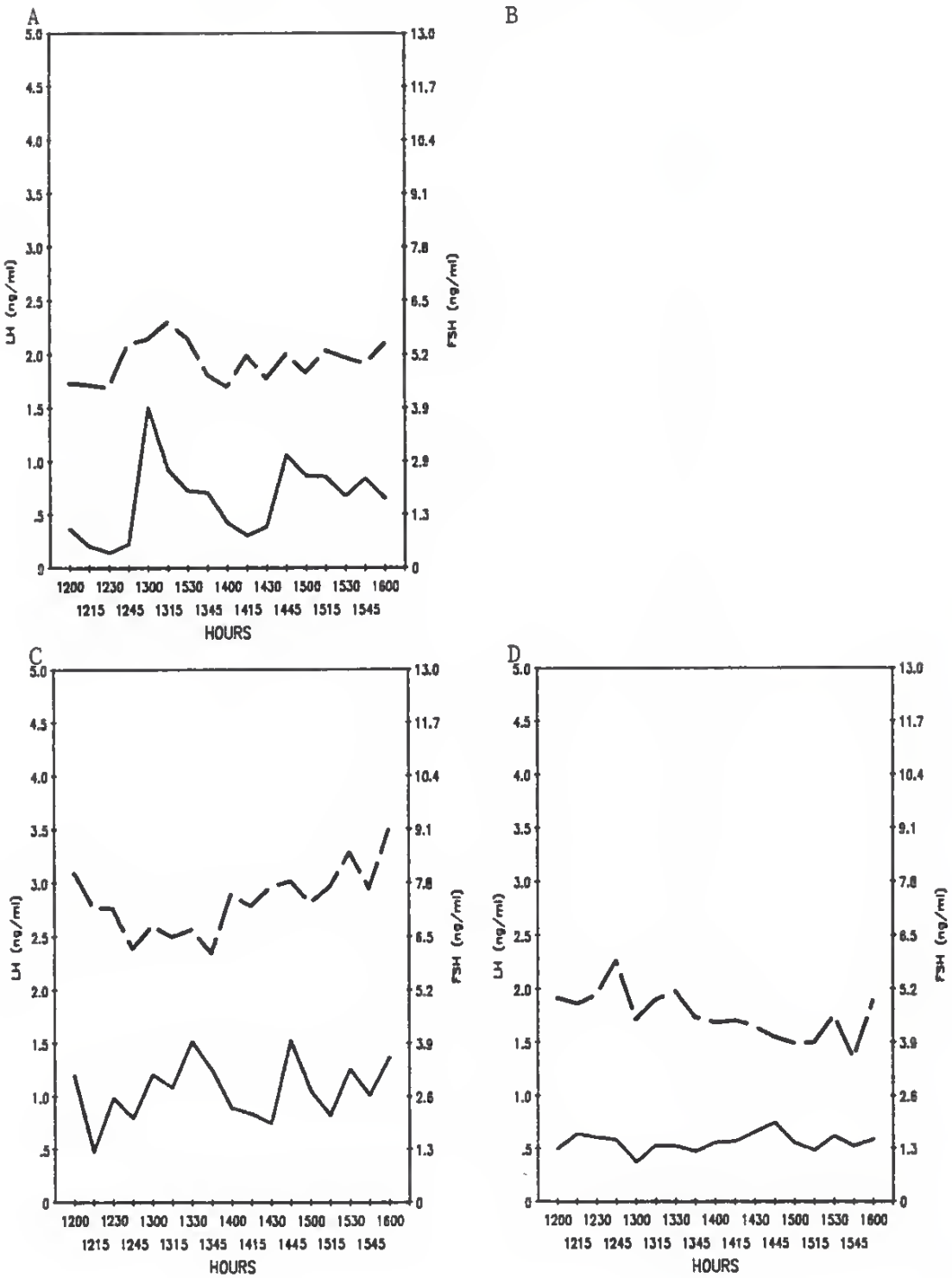
Appendix Figure 4.
Gilt G87, Treatment = C and Estrus = d 5.



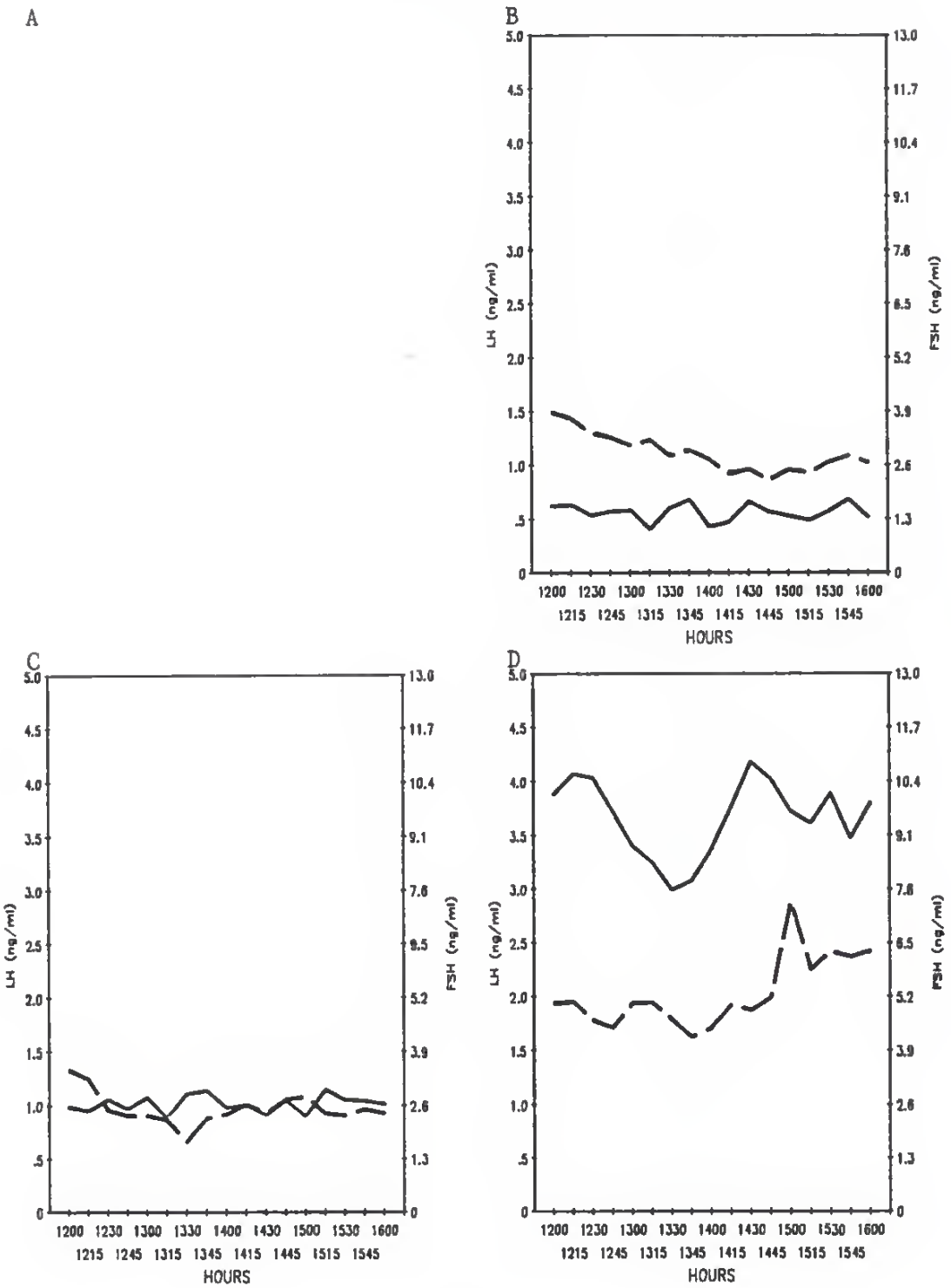
Appendix Figure 5.
Gilt G88, Treatment = C and Estrus = d 5.5



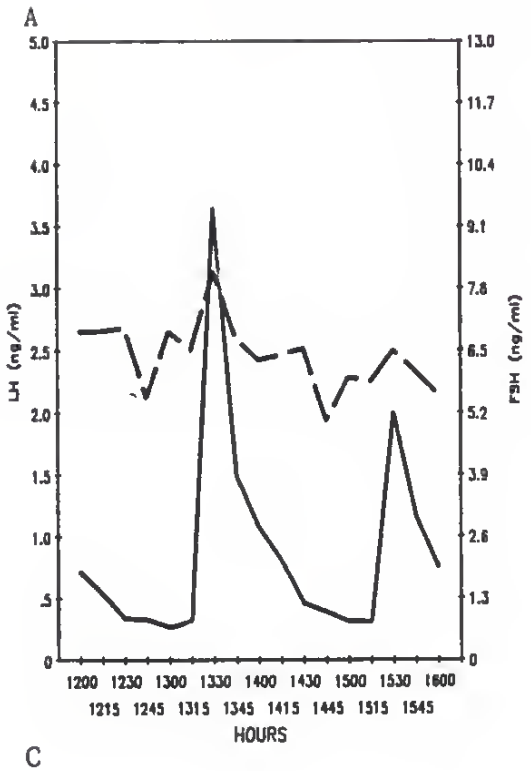
Appendix Figure 6.
Gilt Y75, Treatment = C and Estrus = d 6.



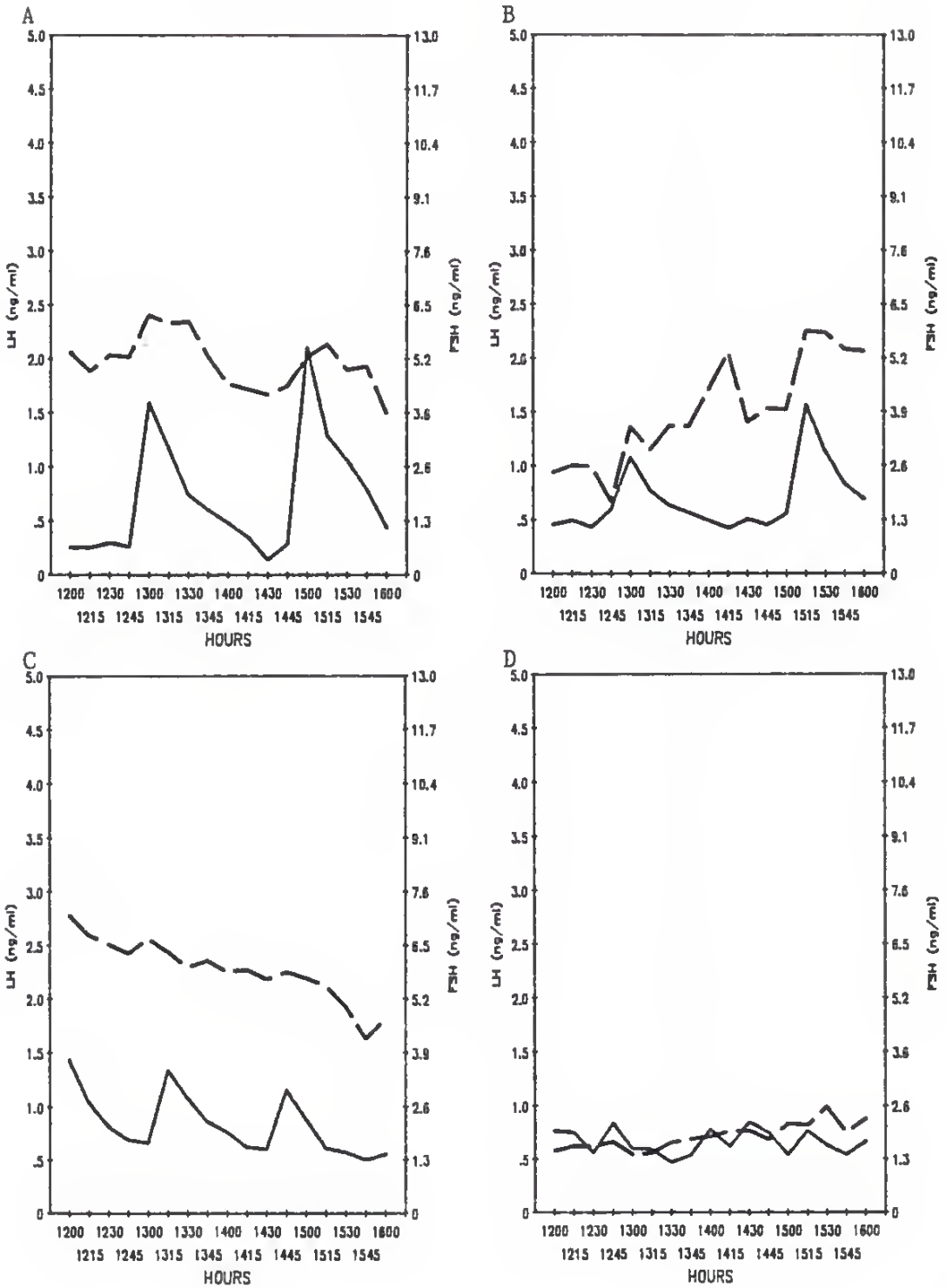
Appendix Figure 7.
Gilt Y94, Treatment = C and Estrus = d 7.



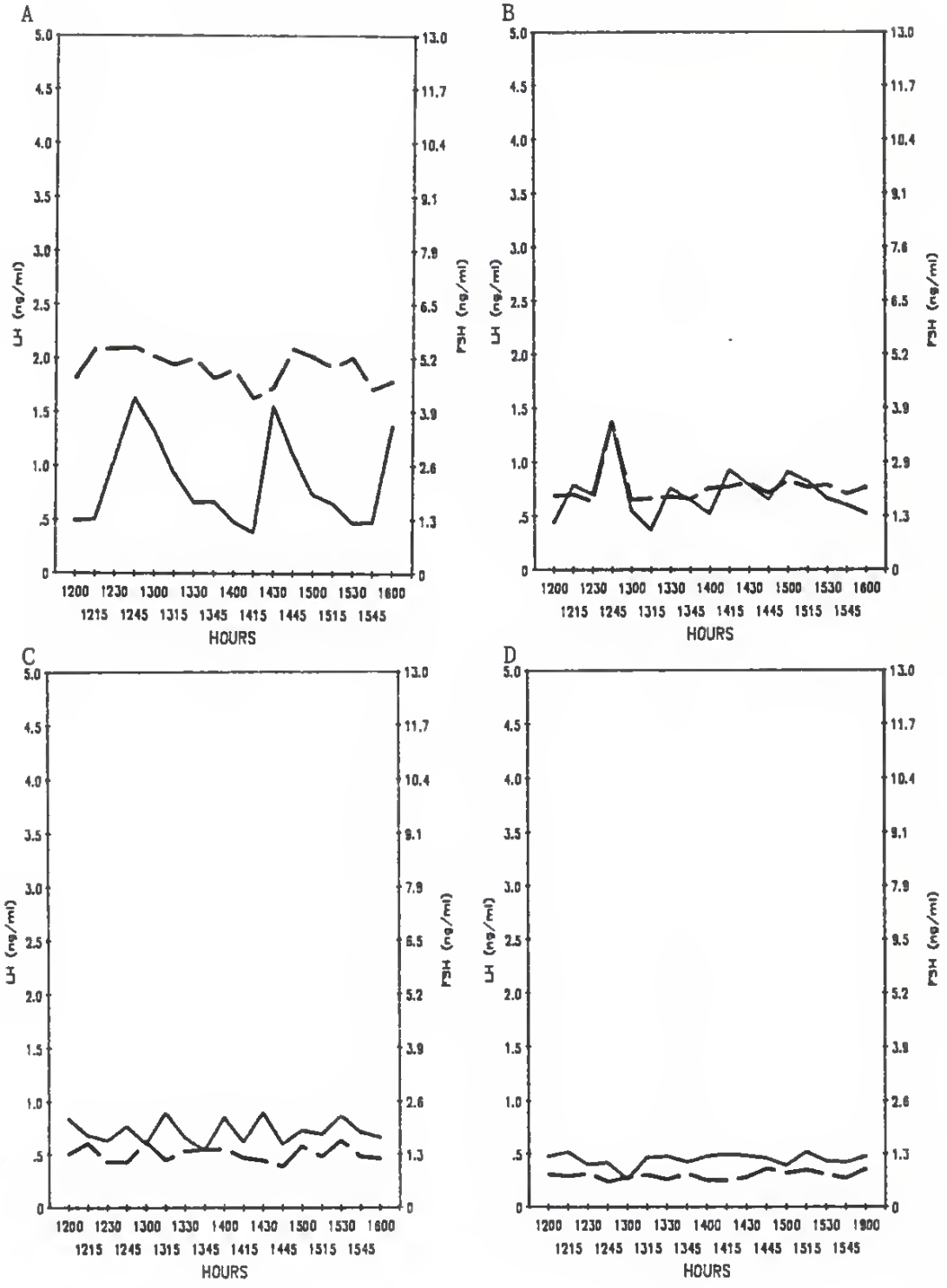
Appendix Figure 8.
Gilt G61, Treatment = A and Estrus = d 7.



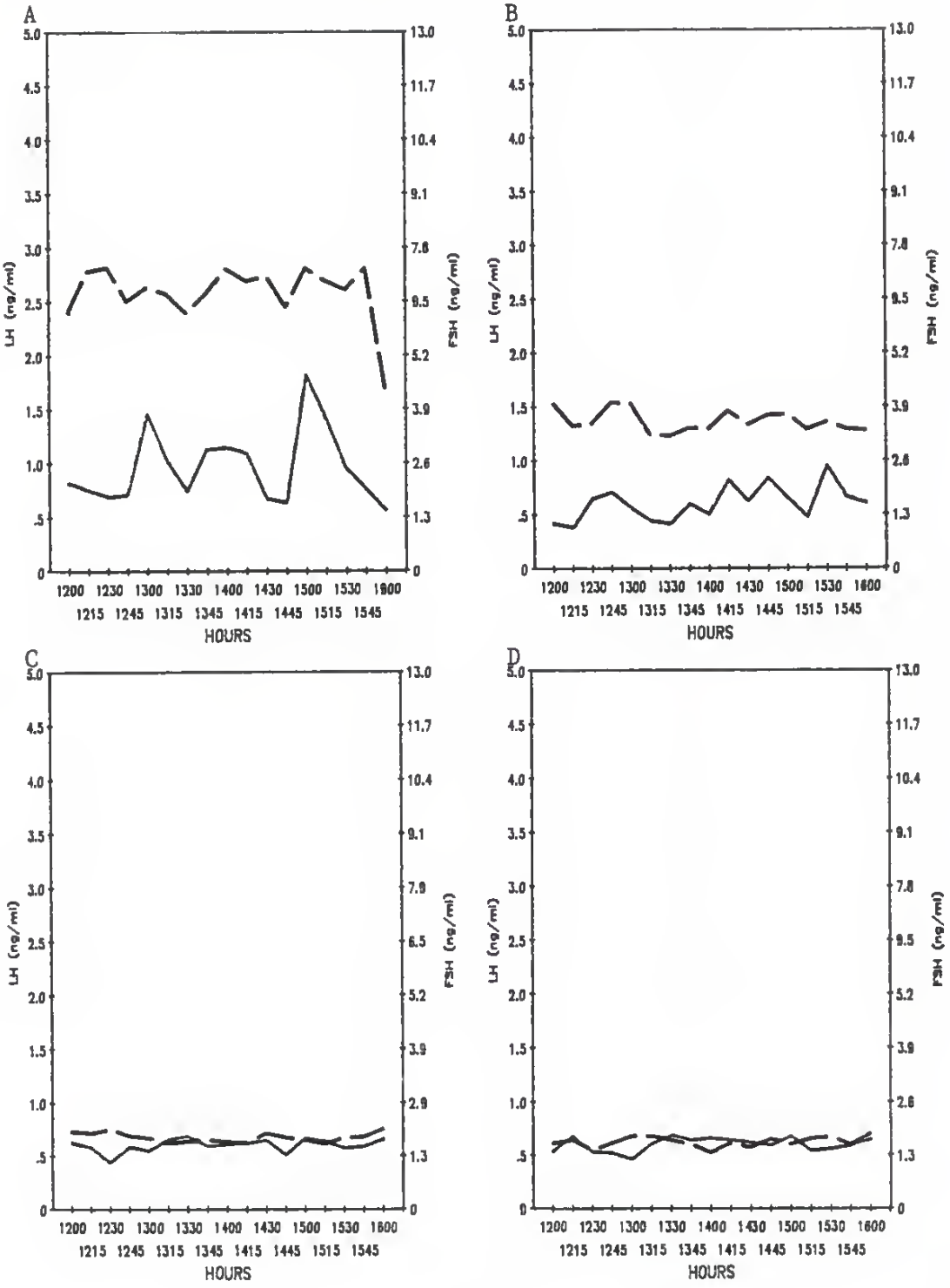
Appendix Figure 9.
Gilt G62, Treatment = A and Estrus = d 7.



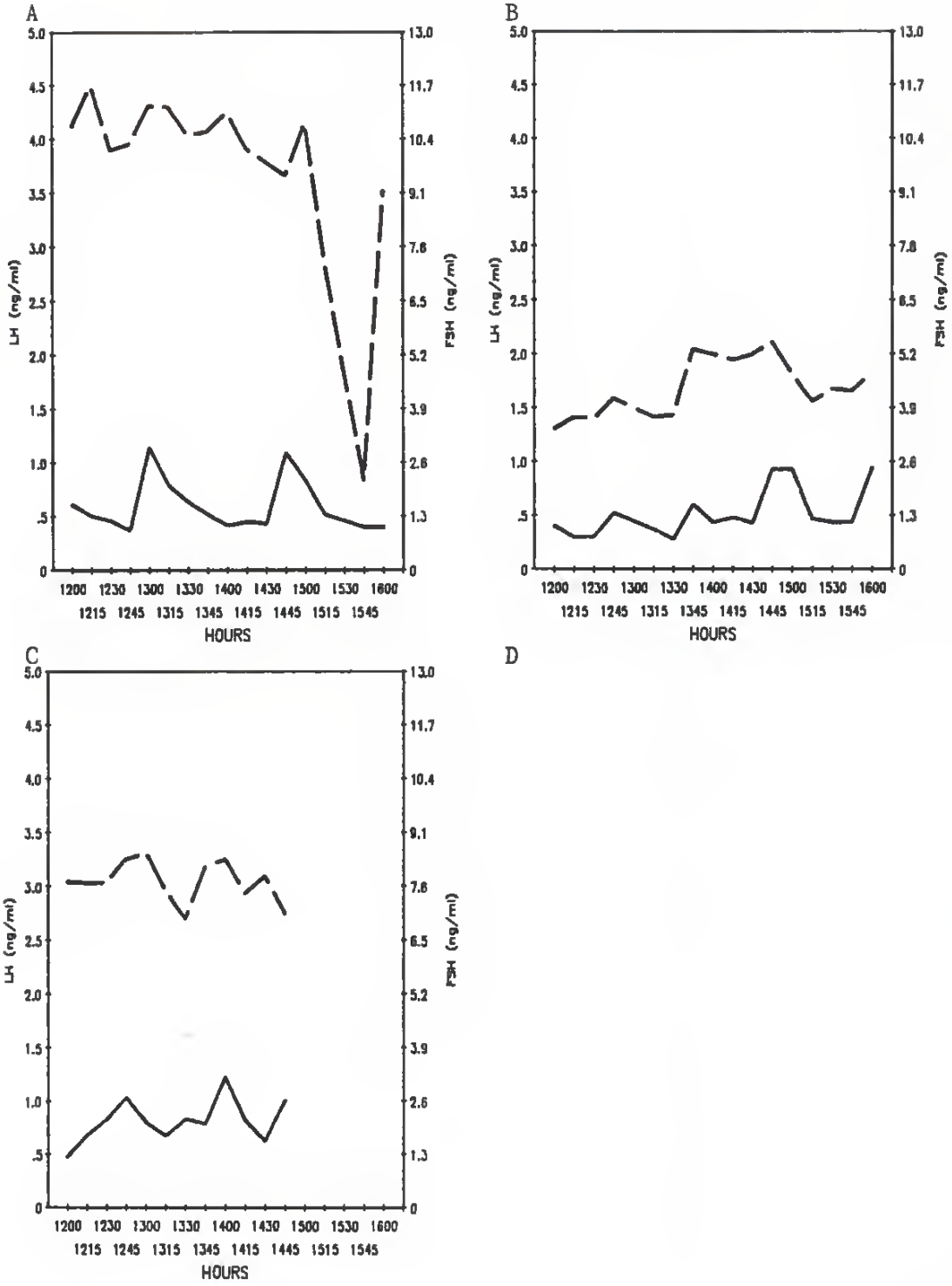
Appendix Figure 10.
Gilt G63, Treatment = A and Estrus = d 6.



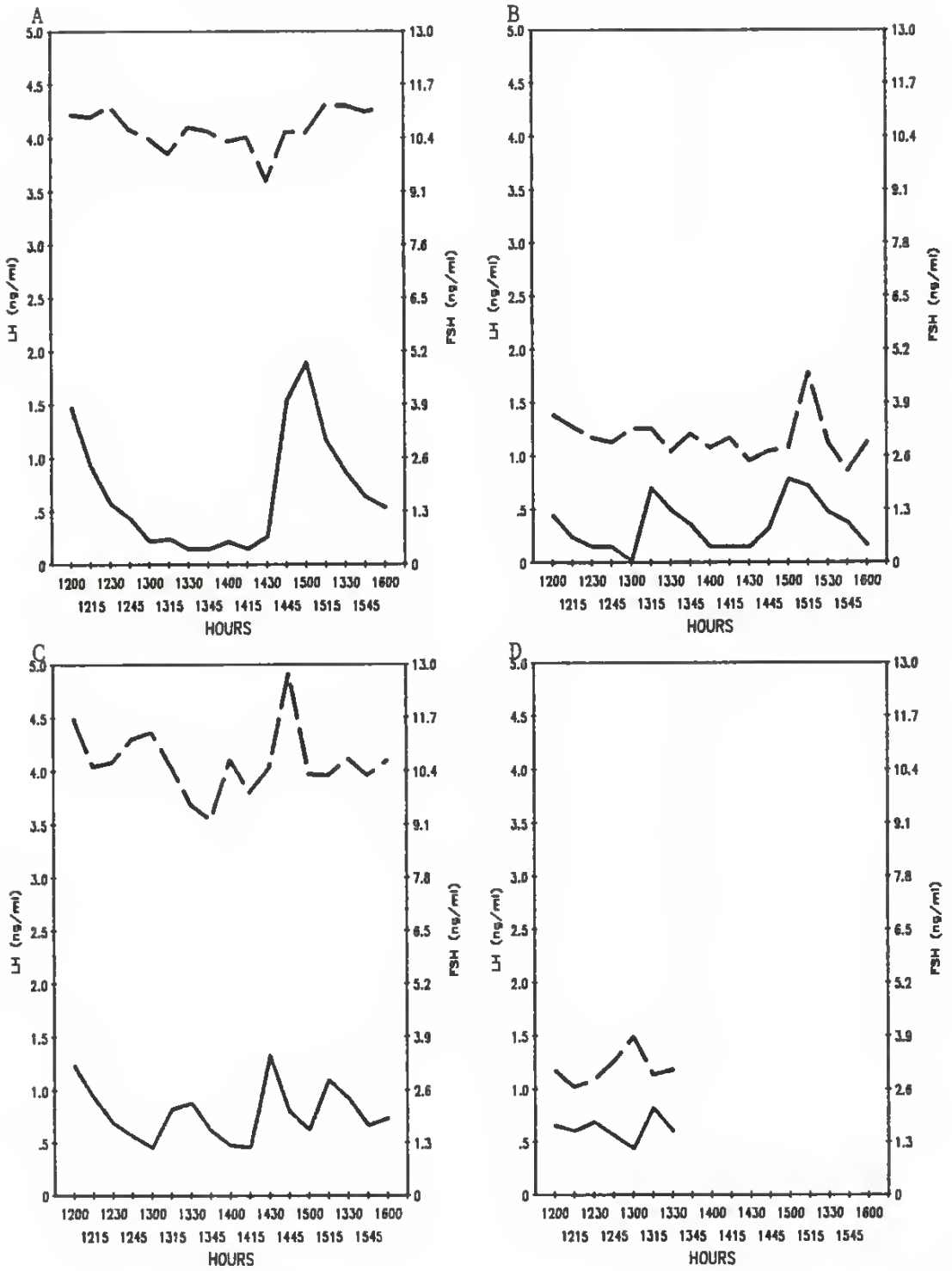
Appendix Figure 11.
Gilt G64, Treatment = A and Estrus = d 7.



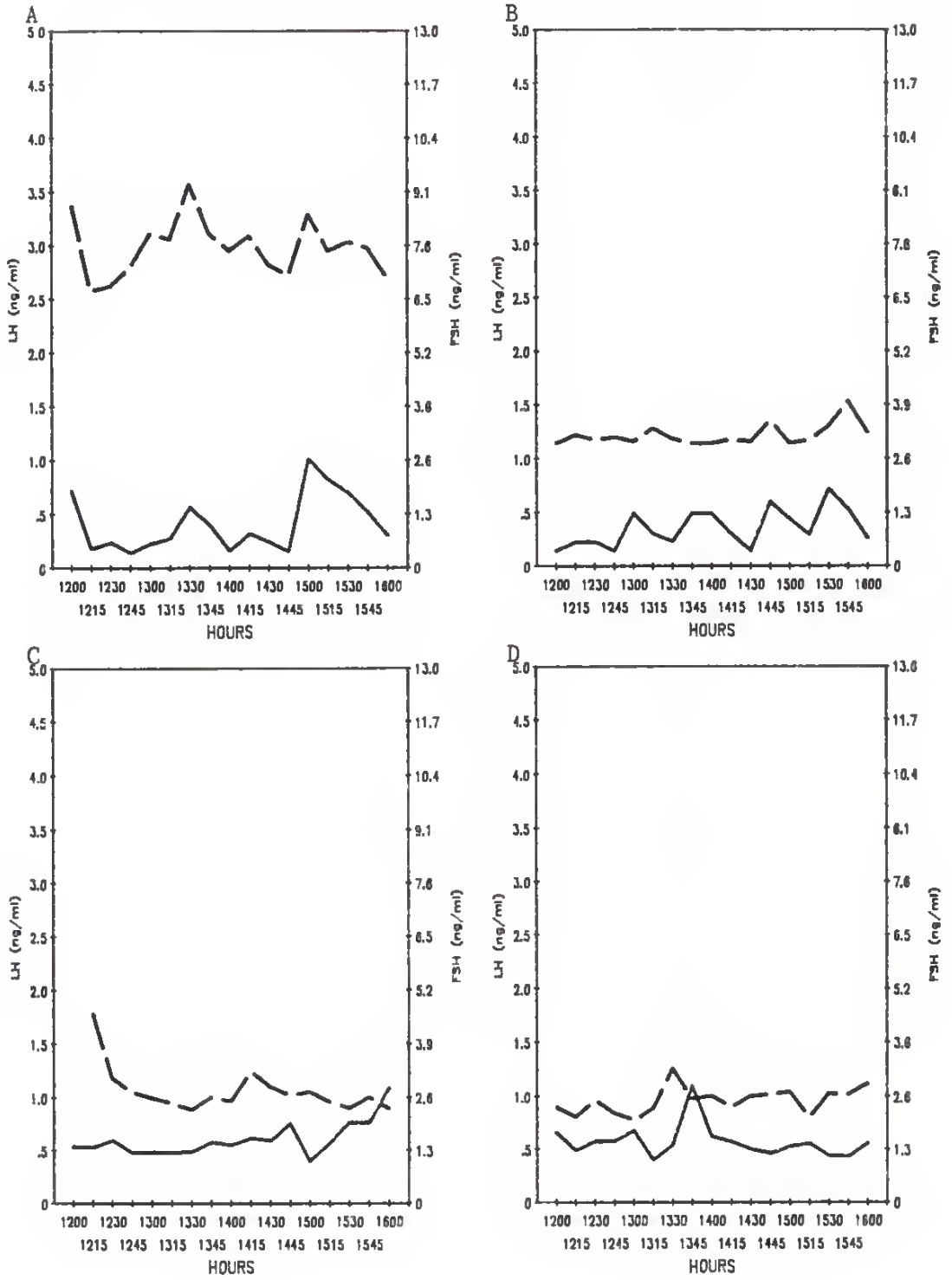
Appendix Figure 12.
Gilt G66, Treatment = A and Estrus = d 6.



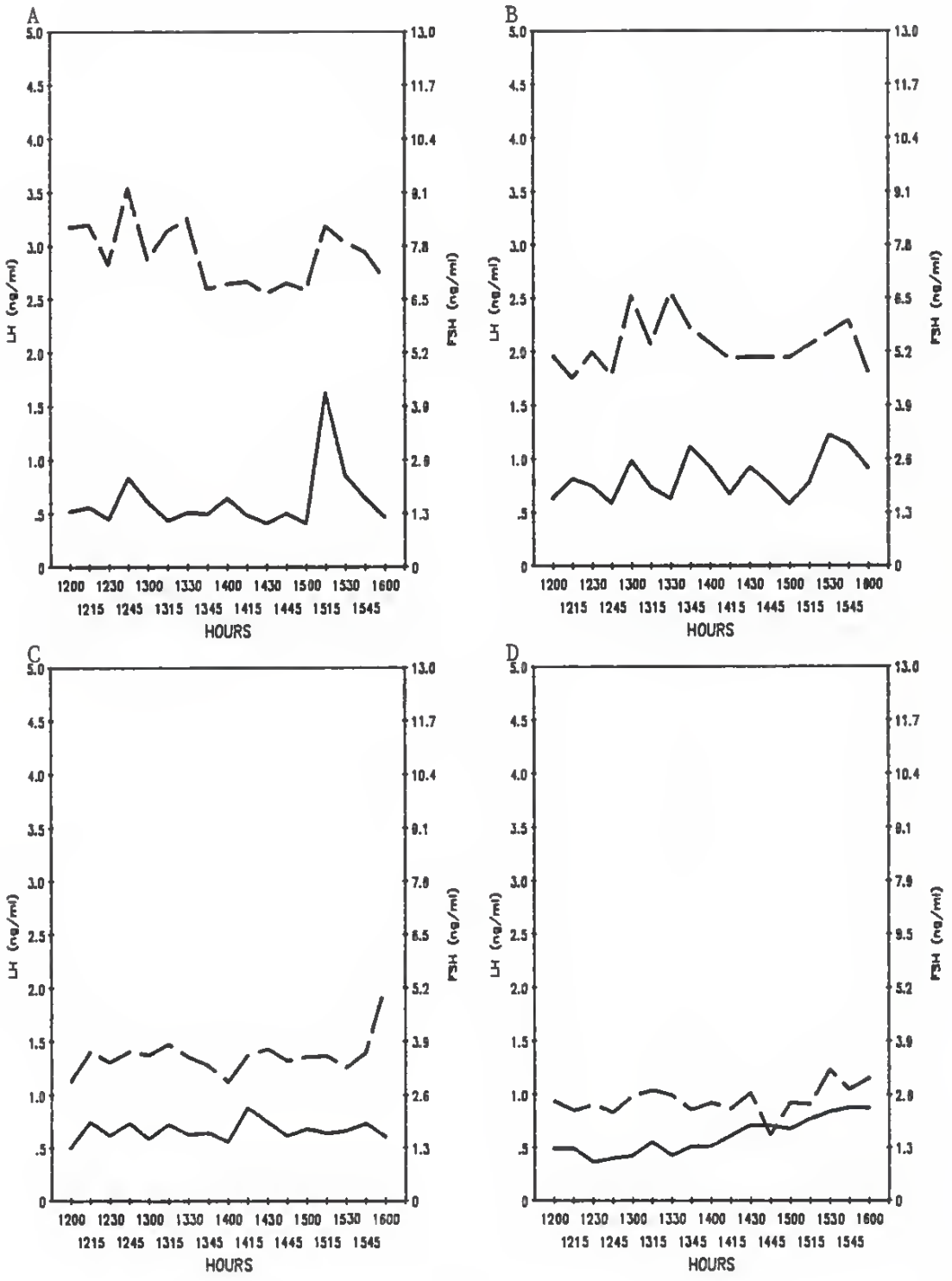
Appendix Figure 13.
Gilt Y95, Treatment = A and Estrus = d 7.5.



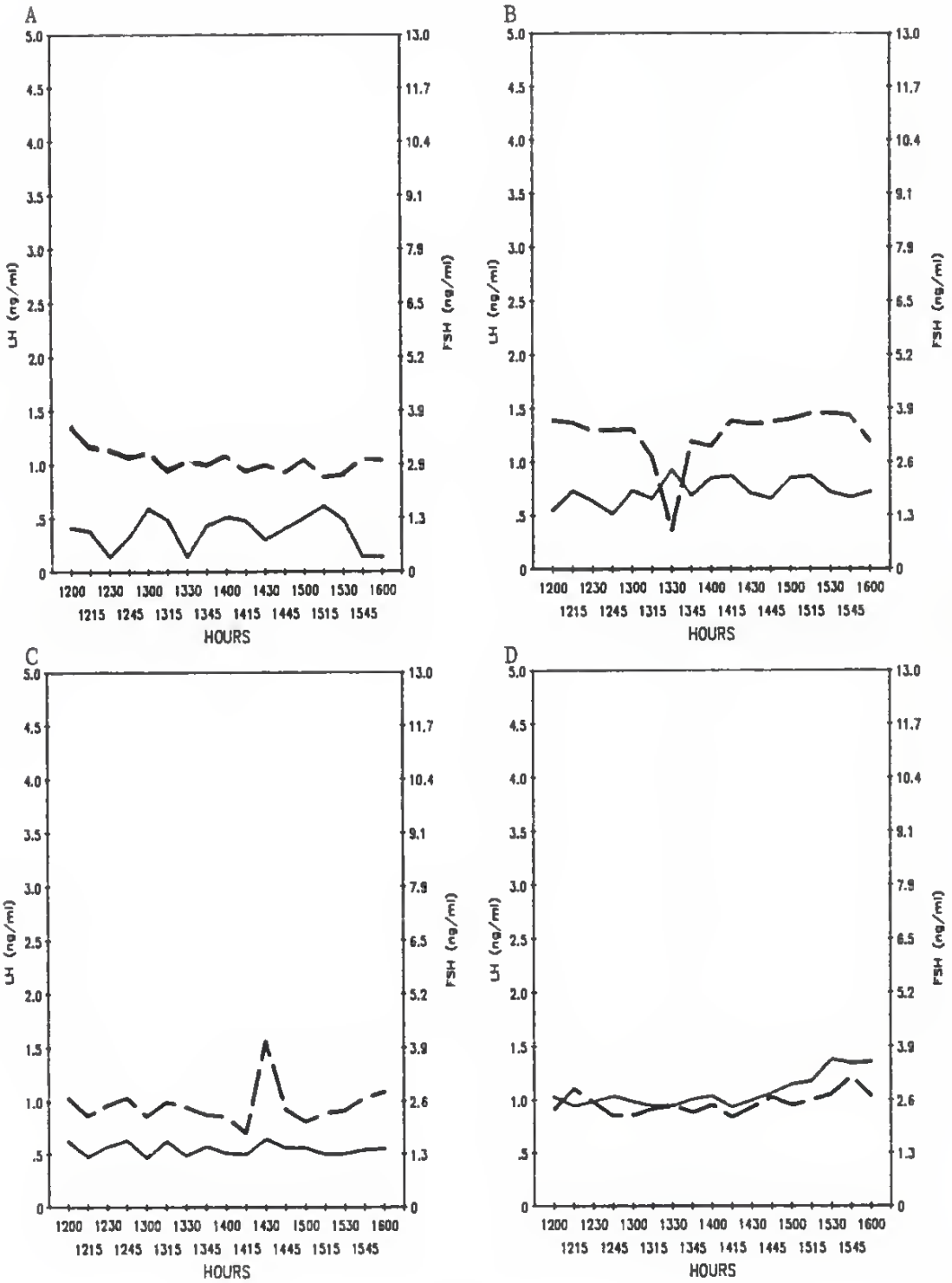
Appendix Figure 14.
Gilt Y99, Treatment = A and Estrus = d 6.



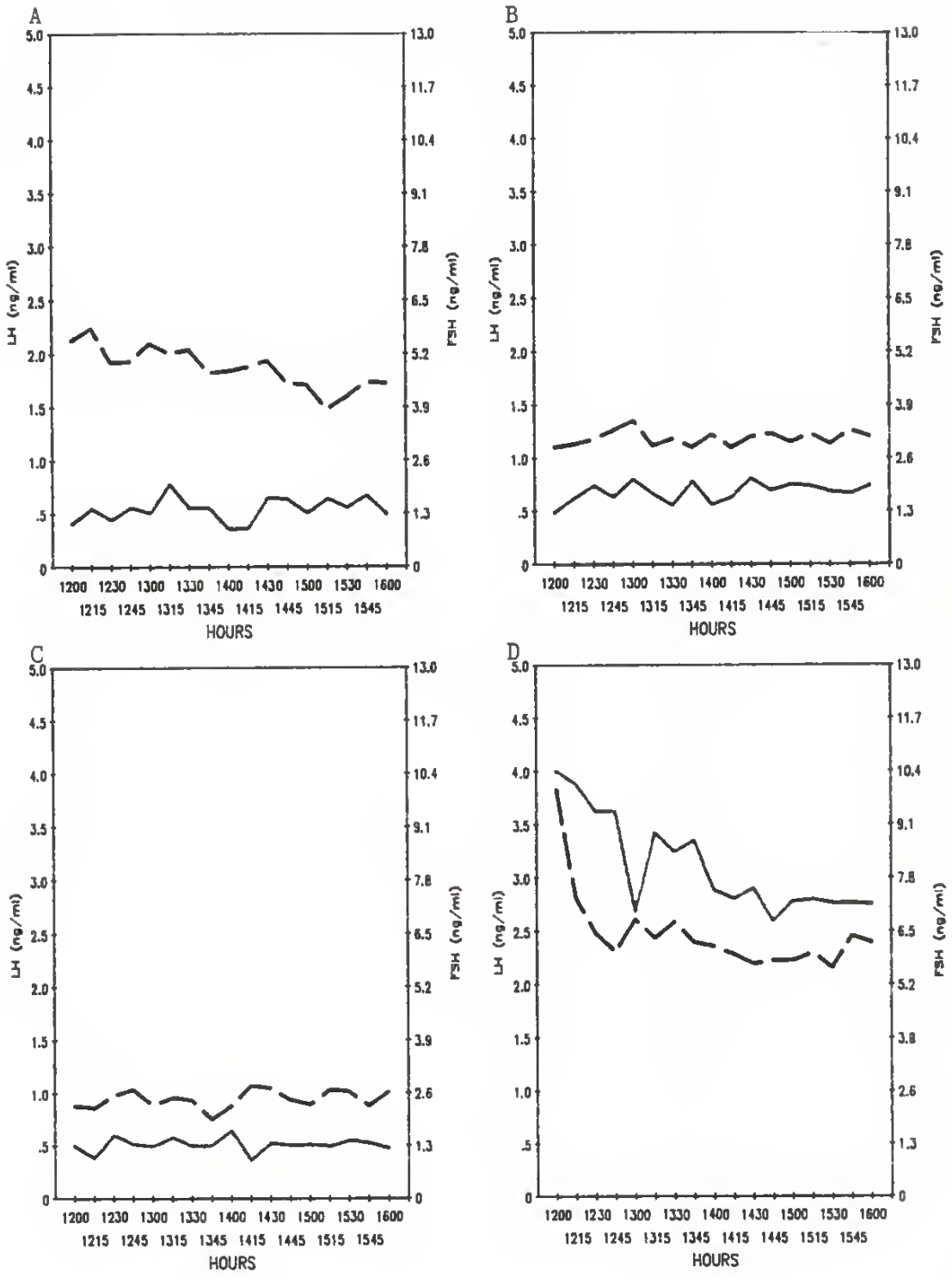
Appendix Figure 15.
Gilt G90, Treatment = F and Estrus = d 6.



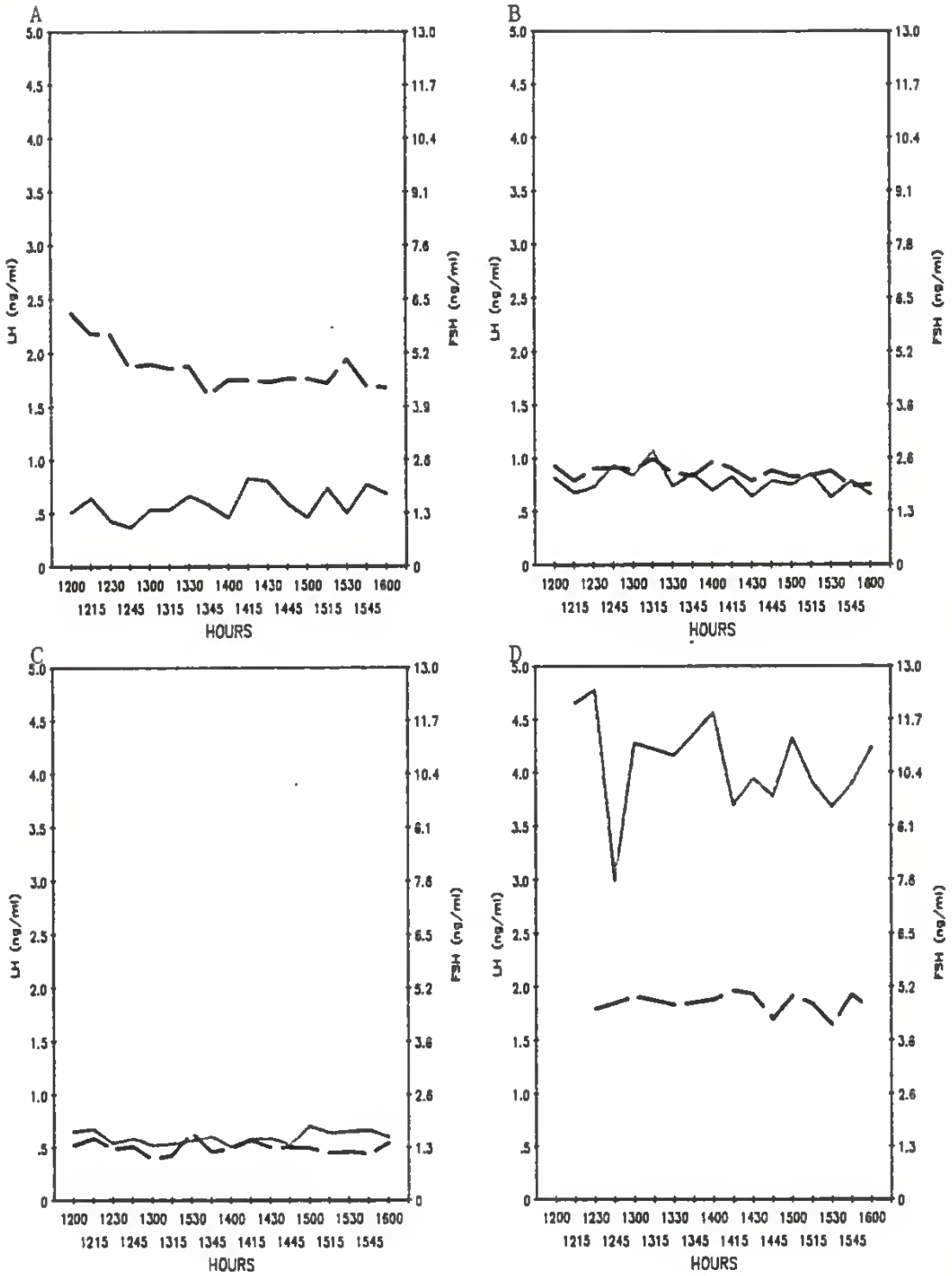
Appendix Figure 16.
Gilt G91, Treatment = F and Estrus = d 5.



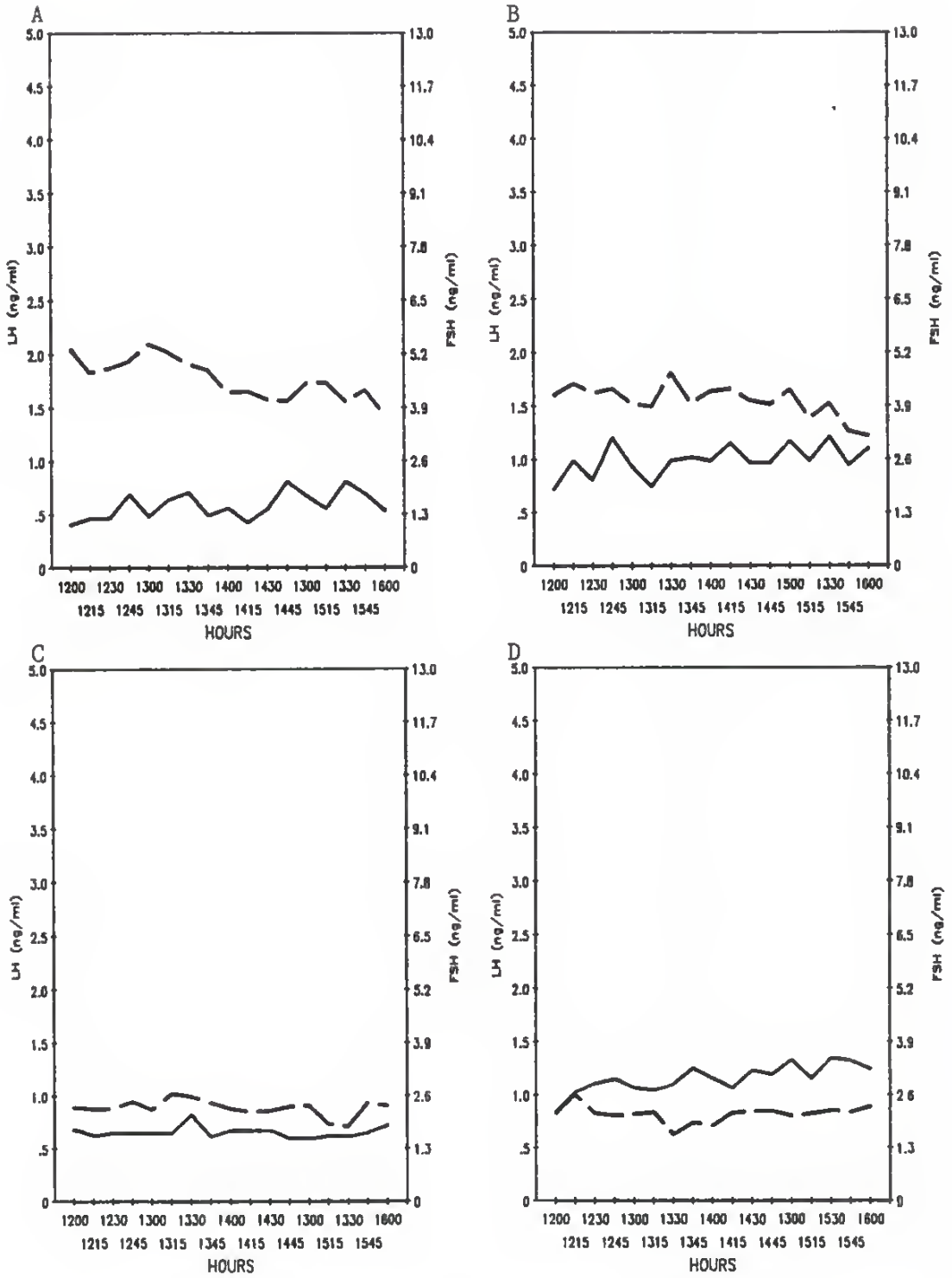
Appendix Figure 17.
Gilt G93, Treatment = F and Estrus = d 4.



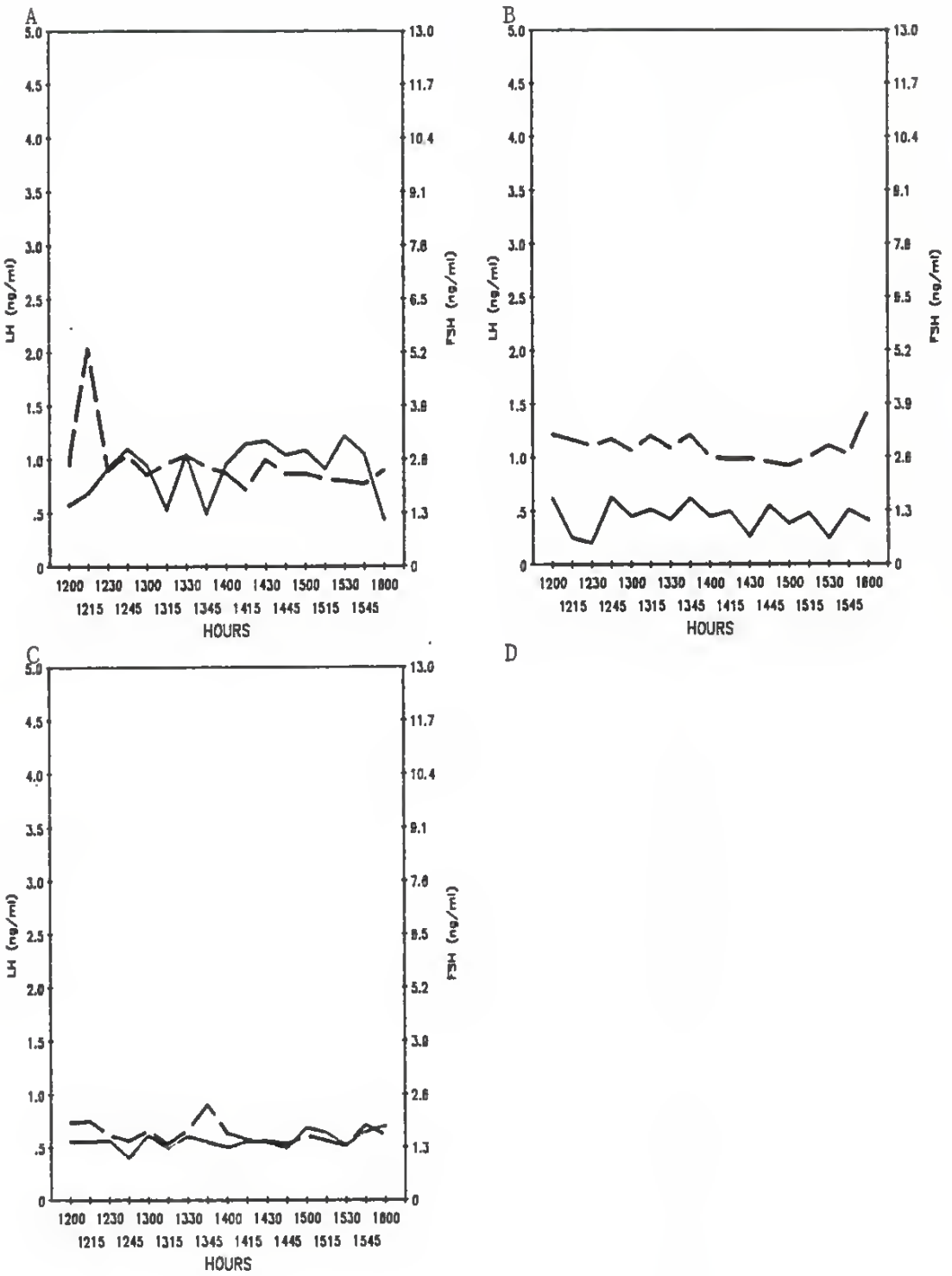
Appendix Figure 18.
Gilt G94, Treatment = F and Estrus = d 4.



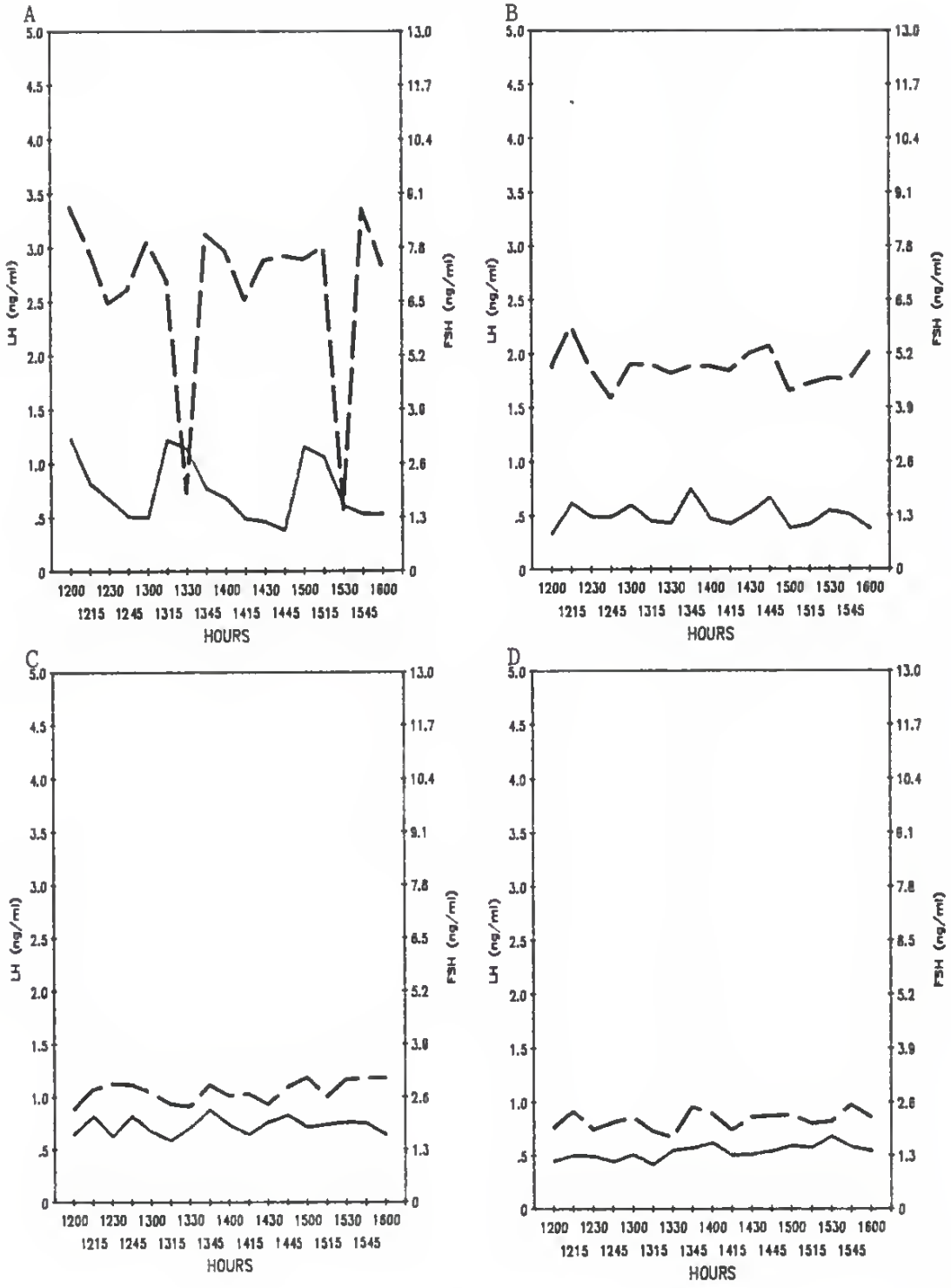
Appendix Figure 19.
Gilt G95, Treatment = F and Estrus = d 5.



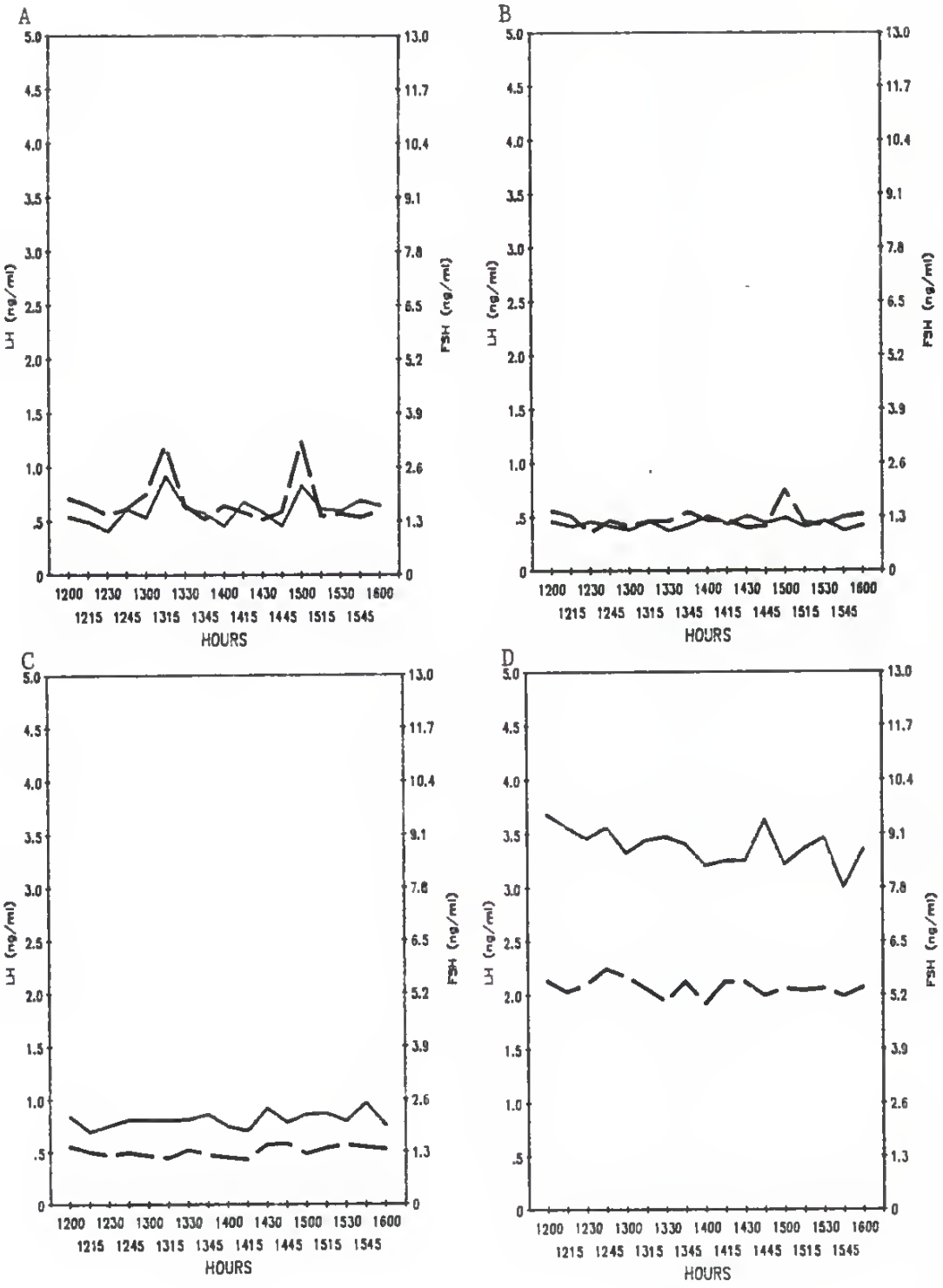
Appendix Figure 20.
Gilt Y93, Treatment = F and Estrus = d 3.5.



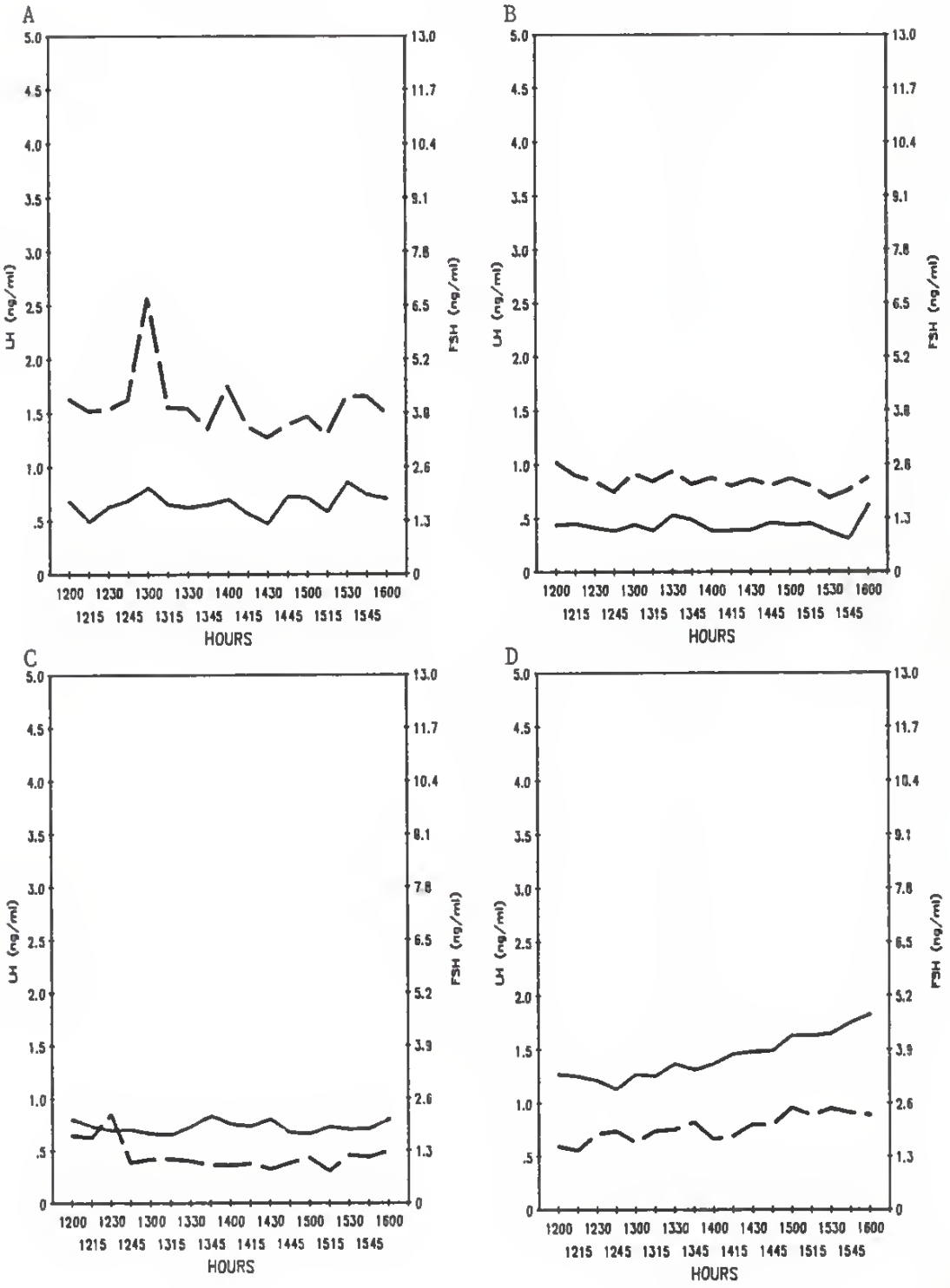
Appendix Figure 21.
Gilt G68, Treatment = A+F and Estrus = d 5.



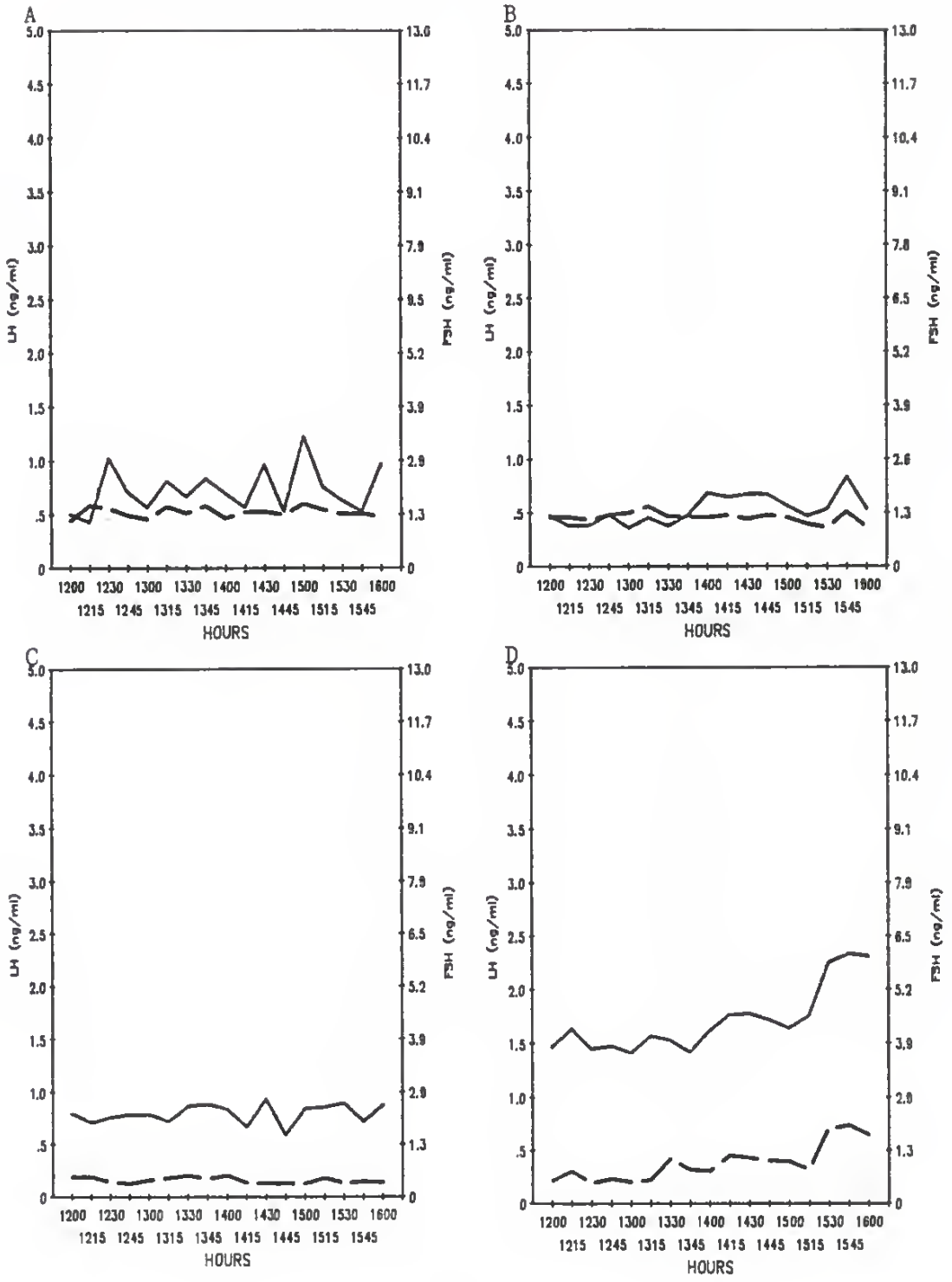
Appendix Figure 22.
Gilt G69, Treatment = A+F and Estrus = d 5.



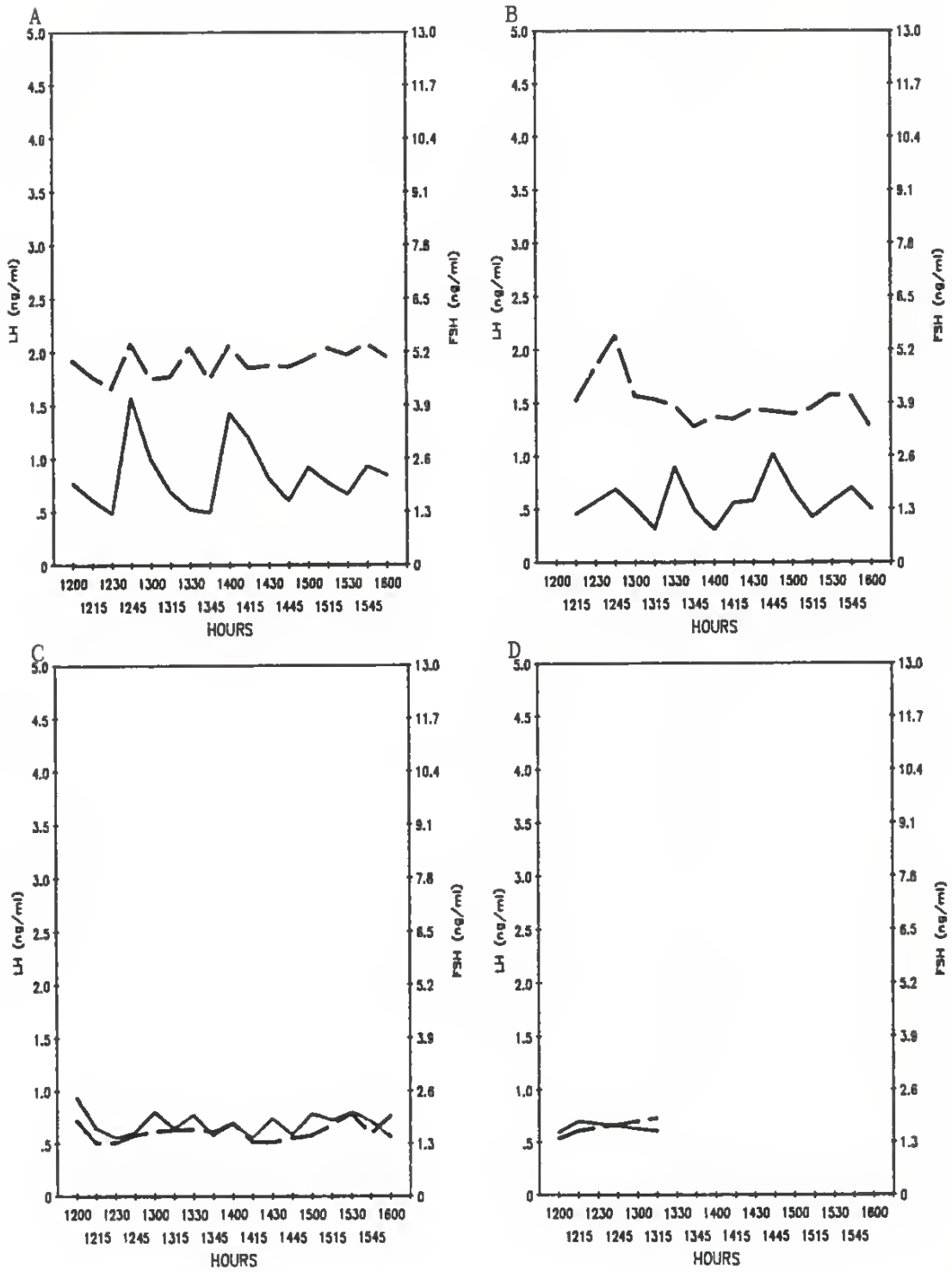
Appendix Figure 23.
Gilt G70, Treatment = A+F and Estrus = d 5.



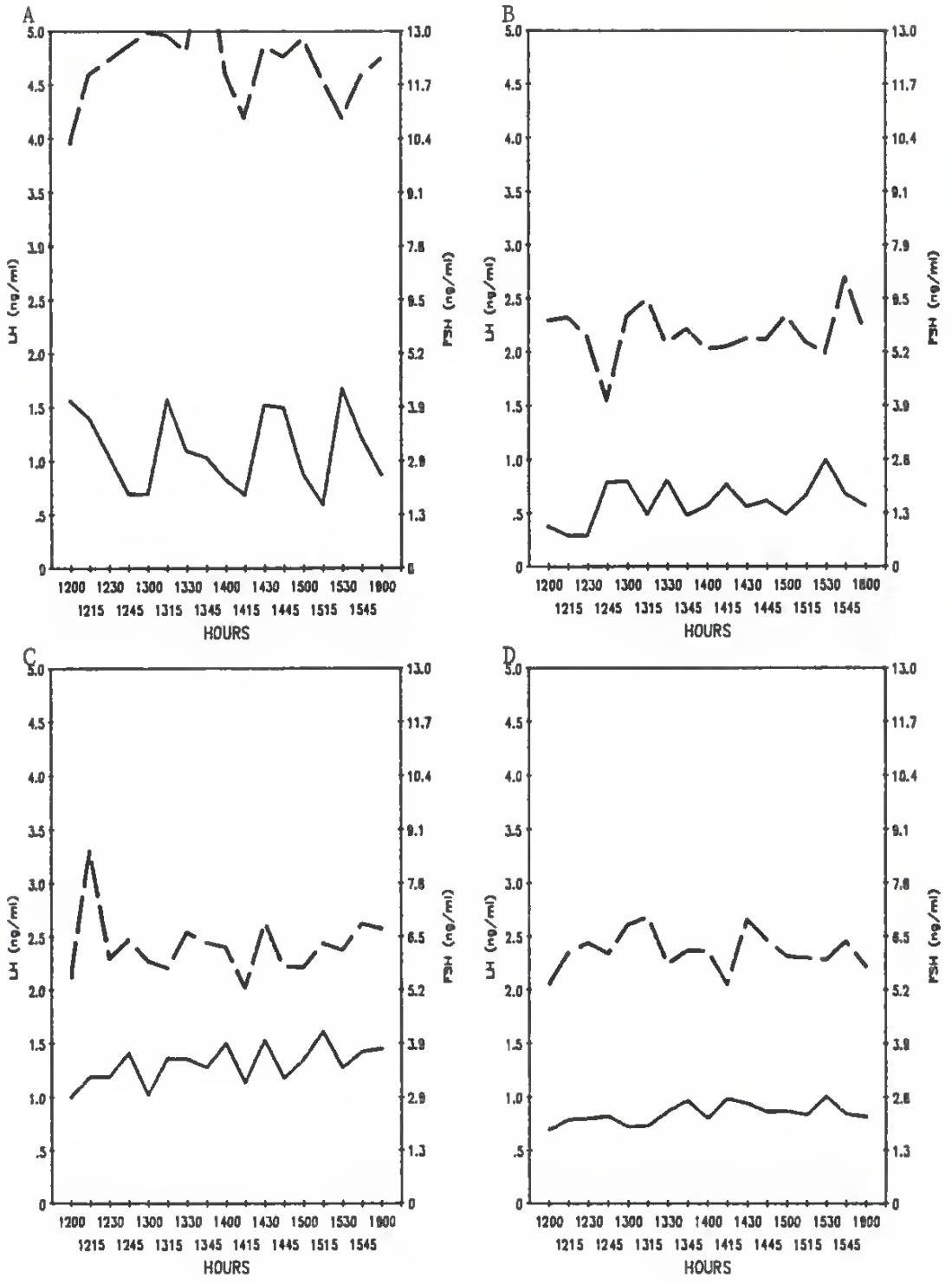
Appendix Figure 24.
Gilt G71, Treatment = A+F and Estrus = d 5.



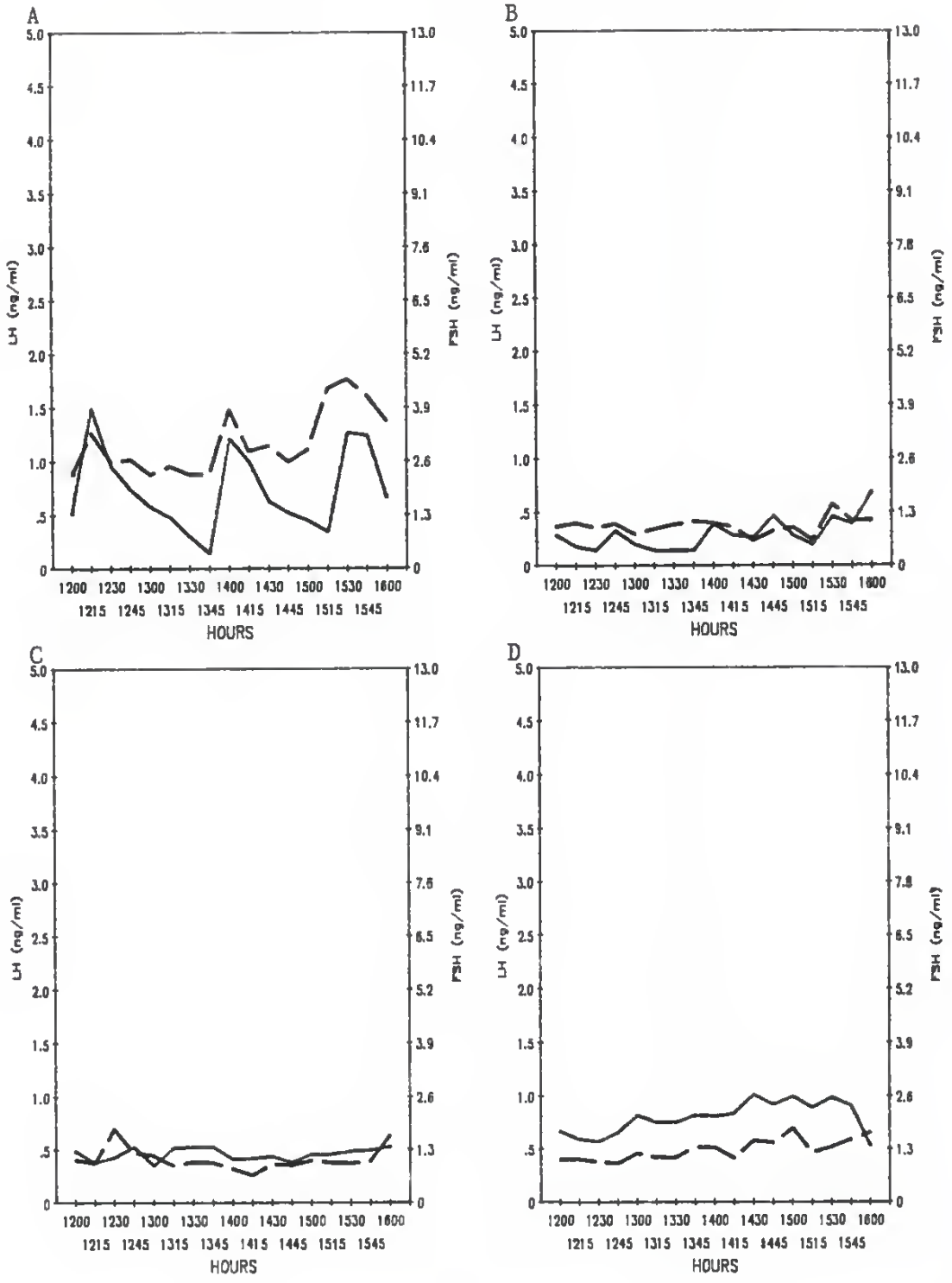
Appendix Figure 25.
Gilt G72, Treatment = A+F and Estrus = d 5.



Appendix Figure 26.
Gilt G73, Treatment = A+F and Estrus = d 6.



Appendix Figure 27.
Gilt Y96, Treatment = A+F and Estrus = d 5.



Reproductive Endocrine Function in Gilts as Affected by Level of Feeding and Treatment with Altrenogest

by

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B.S., Southeast Missouri State University, 1984

AN ABSTRACT OF A MASTER'S THESIS

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MASTER OF SCIENCE

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Nineteen nulliparous gilts were assiged to receive either 0 or 15 mg altrenogest/day for 14 consecutive days. From the ninth day of altrenogest until estrus, one-half of each altrenogest group was offered 1.54 kg of ground sorghum grain (flush) in addition to the 1.81 kg of a diet fed each day. These groupings provided the the following treatments; control, altrenogest, flush and altrenogest plus flush.

On the last day of treatment with altrenogest, those gilts receiving the 0 mg dose of altrenogest were given 25 mg of prostaglandin $F_2\alpha$ (PGF) in two injections (700 h, 15 mg and 1900 h, 10 mg) to insure luteolysis. Catheters were placed into the anterior vena cava of all gilts on the 11th or 12th day of altrenogest treatment. Blood samples were subsequently collected every 15 min from 1200 to 1600 h on day 1 through day 4 after the last treatment with altrenogest or PGF. An individual sample of serum taken at the same time each day from each gilt was analyzed for concentration of progesterone (P). Each 15 min sample of serum was analyzed for concentration of follicle stimulating hormone (FSH) and luteinizing hormone (LH). After all samples had been analyzed for P, FSH and LH, samples within each day for each gilt were pooled for analysis of concentration of estradiol-17β (E). Data were statistically analyzed for daily concentrations of E, P, average FSH, average LH and LH secretion characteristics (number of peaks, baseline concentration, peak magnum, peak amplitude and peak duration). Interval from last altrenogest treatment or from PGF injection to estrus was calculated and number of corpora lutea (CL) were determined by midventral laporotomy on day 11 to 15 after estrus.

Flushing resulted in increased ovulation rate (16.3 $\pm$ 1 vs 13 $\pm$ 1.2 CL, P=0.06) and a shortened interval to estrus (5 $\pm$ 0.2 vs 5.9 $\pm$ 0.2 days, P<0.01). Treatment with altrenogest resulted in an increased interval to estrus (5.8 $\pm$ 0.2 vs 5.1 $\pm$ 0.2 days, P<0.01).

Flushing increased the average concentration of LH (P<0.05) by 0.2 ng/ml and the LH baseline concentration (P<0.02) by 0.3 ng/ml. The data were also analyzed relative to estrus using days -5, -4, -3 and -2. Treatment with altrenogest increased E (1.6 pg/ml, P<0.05) and decreased P (0.6 ng/ml, P<0.05) while flushing increased the concentration of P (0.8 ng/ml, P<0.01) and FSH (4.6 vs 3.0 ng/ml, P=0.07). These data point to changes in FSH and (or) P as likely hormonal causes for increased ovulation rates in flushed gilts.