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Manipulation of the Estrous Cycle in Swine

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Introduction

As production schedules become more intense, greater demands are placed on the reproductive system of the gilt and sow. Compared with their predecessors, today's female swine are expected to attain puberty at an earlier age, breed and become pregnant the first time they are mated by the boar, farrow larger litters, wean a larger number of heavier pigs, return to estrus in a shorter time period after weaning, breed and settle on the first service after weaning, and remain a productive part of the sow herd for a longer period of time. Unfortunately, it is quite difficult for the gilt and sow to live up to these lofty goals.

While there are no magic elixirs that can replace the need for sound management and husbandry, producers can use various hormonal treatments to help maintain reproductive efficiency. These hormonal treatments can be used to induce puberty and synchronize estrus in gilts, minimize the wean-to-estrus interval in sows, and treat the anestrous condition in gilts and sows. To effectively use these hormonal treatment strategies, a clear understanding of the interrelationships among reproductive hormones is necessary.

This publication gives a brief overview of the reproductive anatomy of the female and addresses how the hormones involved in female reproduction change and influence one another during an estrous cycle. Also, several hormonal treatments that can be used to manipulate the estrous cycle of swine are discussed.

Female Reproductive Anatomy of Swine

Hypothalamus

The hypothalamus, which is located at the base of the brain, produces and secretes gonadotropin-releasing hormone (GnRH). This hormone stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland. GnRH production and release from the hypothalamus are controlled by hormonal feedback from the ovaries.

Pituitary Gland

The pituitary gland, located beneath the hypothalamus, is divided into an anterior and posterior portion. The anterior pituitary synthesizes and secretes FSH and LH. FSH stimulates follicle growth of the ovaries and estrogen release from the ovaries. LH is responsible for the release of eggs from the follicles (ovulation) and the development, maintenance, and function of the *corpus luteum*, or yellow body. Because the pig is a multiparous species (gives birth to multiple offspring), there will be several *corpora lutea* present on each ovary.

The posterior portion of the pituitary gland is responsible for the release of oxytocin, which is involved in farrowing (parturition) and milk ejection.

Ovaries

The ovaries are a part of the female reproductive tract that is located in the abdominal and pelvic cavities. The ovaries produce the eggs and the two classes of female sex hormones, estrogens (the most important being estradiol) and progestins (the most important being progesterone). Each egg develops within a fluid-filled follicle located on the ovary. These follicles produce estradiol. At the time of ovulation, the wall of each mature follicle ruptures, and an egg with the surrounding fluid is released into the tubular part of the reproductive tract. The cells remaining in each ruptured follicle grow and fill the empty space left by the ovulated egg and fluid, forming a *corpus luteum*. Each *corpus luteum* produces progesterone.

Estradiol is involved in mating behavior, secondary sex characteristics, maintenance of the female duct system, and mammary growth. Progesterone is responsible for the maintenance of pregnancy and is also involved in mammary growth.

Oviduct

The oviduct is the portion of the reproductive tract that receives the eggs after ovulation. It has a funnel-shaped portion located close to the ovary called the *infundibulum*, which aids in the entry of the eggs into the oviduct. The oviduct is the site where fertilization of the eggs occurs. Fertilized eggs remain in the oviduct approximately 2 days before they enter the uterus.

Uterus

The uterus in swine consists of a short uterine body and two long uterine horns. Before implantation, the uterus secretes proteins, carbohydrates, and lipids that provide nourishment for the preimplantation embryo. Following implantation, nourishment for the developing embryo is provided by the blood supply of the dam to the embryonic membranes (placenta) that are attached to the uterine wall. The nutrients are then transported to the embryo by the umbilical vein.

The uterus is the major source of prostaglandin F-2 alpha (PGF) in the pig. This hormone is involved in regulating the life span of the *corpora lutea* in cycling and pregnant gilts and sows. At the time of farrowing, PGF (and oxytocin) stimulates uterine contractions, which are involved in expulsion of the newborn pigs.

Cervix

The cervix is located between the uterus and vagina and consists of muscular and dense connective tissue. Typically, the cervical opening into the body of the uterus is small and plugged with cervical mucus. At farrowing the walls of the cervix relax, allowing the pigs to pass from the uterine horns into the vagina. The cervix also serves as the site of semen deposition. During mating the cervix constricts around the boar's penis, and this pressure is the stimulus that causes the boar to ejaculate.

Vagina

The tubular portion of the tract leading posterior from the cervix to the urethral opening is the vagina. The visible, external portion of the tract is referred to as the vulva. When the female approaches or is in standing heat (the period when she is receptive to the boar), the vulva will often become red and swollen.

Endocrinology

The reproductive organs control the reproductive process by communicating with each other through the production of hormones. Hormones are chemical compounds that are produced in one part of the body and carried by the bloodstream to another part of the body where they influence such functions as puberty, estrous cycles, pregnancy, and parturition. A summary of the female reproductive hormones is given in Table 1.

Puberty

Puberty in females is defined as the time of the first expressed estrus with ovulation. Puberty should not be considered to represent sexual maturity, even though the female is capable of being bred and conceiving. A high percentage of animals bred at puberty will often have difficulty with farrowing. Also, gilts bred at the age of puberty will typically have smaller litters because fewer eggs are ovulated during the first heat period than will be ovulated in subsequent heat periods. Because of this, it is generally recommended that gilts not be bred until the second or third heat period following puberty.

The hormonal changes associated with puberty are poorly understood. Research shows that many of the hormonal events associated with estrus can occur before the age when gilts normally exhibit estrus. For example, the hypothalamus can secrete GnRH, the anterior pituitary can secrete FSH and LH, and ovulation can be stimulated to occur well before gilts are old enough to begin exhibiting estrus. Puberty is attained only when these individual events begin to occur at regular intervals and when the gonadotropins (FSH and LH) are produced at high enough levels to initiate follicle growth, oocyte (egg) maturation, and ovulation.

Estrous Cycle

The changes that occur in the reproductive hormones during an estrous cycle are illustrated in Figure 1. Following ovulation, which usually occurs 24 to 36 hours after the start of standing heat for gilts and 36 to 48 hours after the start of standing heat for sows, each ruptured follicular tissue forms a *corpus luteum*. The *corpora lutea* produce and secrete progesterone, which has a negative influence on follicular growth by preventing the secretion of FSH and LH (Figure 2). Progesterone inhibits the secretion of FSH and LH by suppressing the release of GnRH from the hypothalamus and by directly influencing the secretion of FSH and LH by desensitizing the anterior pituitary to GnRH. This period of the estrous cycle when progesterone dominates is referred to as the luteal phase. The high level of progesterone causes the female to be uninterested in the boar.

Around days 12 to 14 of the estrous cycle, progesterone concentrations begin to decline. If the female is not pregnant at this time, PGF is released from the uterus and causes the rapid regression or destruction of the *corpora lutea* (a process called luteolysis). With the destruction of the *corpora lutea*, progesterone levels rapidly decline, and their inhibitory control on the growth of follicles is removed. Following luteolysis, a slight increase in FSH secretion and an increase in the number of LH pulses occur that stimulate

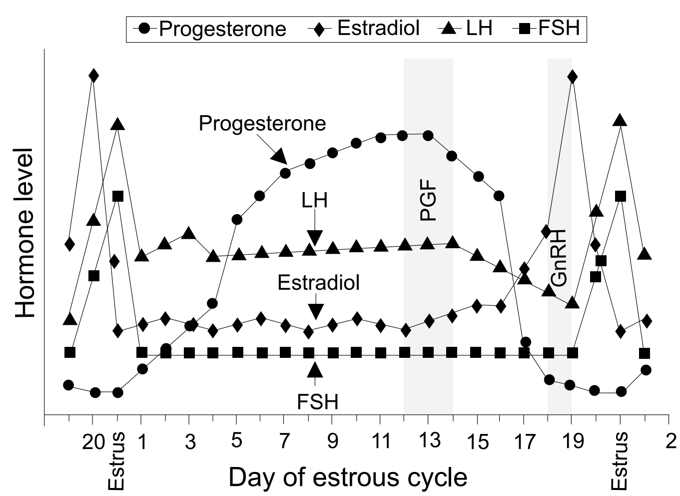

Figure 1. Changes in reproductive hormones throughout the estrous cycle. (LH = luteinizing hormone; FSH = follicle-stimulating hormone; PGF = prostaglandin F-2 alpha; GnRH = gonadotropin-releasing hormone.)

Table 1. Hormones involved in female reproduction.

Gland	Hormone	Major Functions
Hypothalamus	Gonadotropin-releasing hormone (GnRH)	(1) FSH and LH release from anterior pituitary
Anterior pituitary	Follicle-stimulating hormone (FSH)	(1) Follicle growth on ovaries (2) Estrogen release from ovaries
	Luteinizing hormone (LH)	(1) Ovulation (2) Corpus luteum formation, maintenance, and function
Posterior pituitary	Oxytocin	(1) Parturition (2) Milk ejection
Ovaries	Estrogens (estradiol)	(1) Mating behavior (2) Secondary sex characteristics (3) Maintenance of female duct system (4) Mammary growth
	Progestins (progesterone)	(1) Maintenance of pregnancy (2) Mammary growth
	Relaxin	(1) Expansion of pelvis (2) Dilation of cervix
	Inhibin	(1) Prevents release of FSH
Uterus	Prostaglandin F-2 alpha (PGF)	(1) Regression of corpus luteum (2) Parturition
Placenta	Human chorionic gonadotropin (HCG)	(1) LH-like
	Pregnant mare serum gonadotropin	(1) FSH-like
	Estrogens	see ovary above
	Progestins	see ovary above
	Relaxin	see ovary above

follicular growth. This part of the estrous cycle is called the follicular phase. As the follicles develop, they produce estradiol, which increases steadily during the latter stages of the estrous cycle. Once estradiol concentrations reach a high enough level, the preovulatory surge of FSH and LH occurs, and ovulation follows. Estradiol is also responsible for the characteristic responses of a gilt or sow in estrus or standing heat (swollen and red vulva, immobile stance, and erect ears).

Pregnancy

If the female is mated and becomes pregnant, the pattern of hormonal changes is altered. The critical point occurs 12 to 14 days after breeding. If viable embryos are present at this time, luteolysis is prevented by the inhibition of PGF release from the uterus. This allows progesterone levels to remain high and maintain the pregnancy. During pregnancy, progesterone has the same inhibitory effect on follicular growth as it does during the luteal phase of the estrous cycle. Therefore, follicular growth and estrus do not occur when the female is pregnant.

Parturition

The average length of the gestation is 114 days, but it can range from 111 to 116 days. Because progesterone is the hormone responsible for maintaining pregnancy, the concentration of progesterone must decline before farrowing can occur. This process involves the regression of the *corpus luteum* because this luteal tissue is the primary source of progesterone during pregnancy. The mechanisms involved

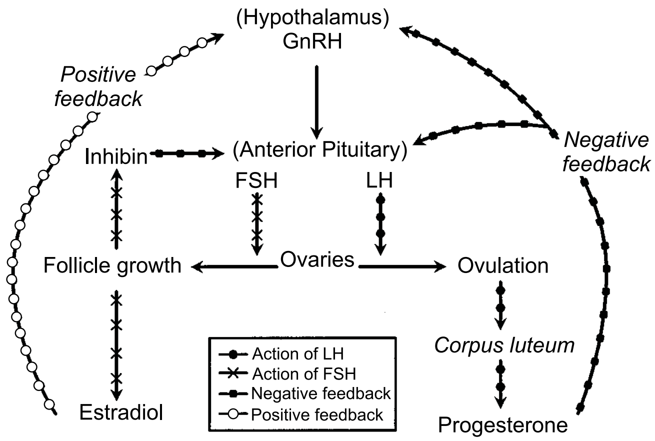

Figure 2. Interactions among the female reproductive hormones.

with the regression of the *corpora lutea* at the time of farrowing are not well understood. The fetuses are thought to stimulate the initiation of the farrowing process, with one of the resulting actions being the release of PGF from the uterus. This results in luteolysis and a decrease in the concentration of progesterone.

Post-weaning

During lactation, follicular growth and ovulation do not occur even though there are no *corpora lutea* present and progesterone concentrations are low. Apparently the nursing action of the pigs inhibits the release of GnRH from the hypothalamus, which prevents the secretion of LH and FSH from the anterior pituitary. Weaning removes the inhibitory effect of nursing on GnRH secretion. The increased GnRH stimulates the production and secretion of LH and FSH. This leads to follicular growth and ovulation, usually within 3 to 8 days after weaning.

Hormonal Treatments To Control Estrus

Inducing Puberty in Gilts

To effectively stimulate puberty in gilts, it is critical to know the pubertal status in a group of gilts and the typical age of the onset of puberty under the conditions of the specific farm. Puberty usually occurs in gilts at 6 to 7 months of age, but it can vary considerably based on the genetics and management of the gilts. Gilts should not be treated with hormones to induce puberty unless they are within 1 month of the natural onset of estrus. If gilts are too young, estrus might be induced, but they will often return to an anestrous state. If gilts are within 30 days of the natural onset of puberty, most will respond to treatment with gonadotropins by expressing estrus and continuing to cycle.

Puberty in gilts can be induced by treatment with a single 5-ml injection of P.G.600® (Intervet Inc.). This compound is a combination of pregnant mare serum gonadotropin (PMSG; 400 IU) and human chorionic gonadotropin (hCG; 200 IU). PMSG mimics the reproductive hormone FSH and results in follicular growth, increased levels of estradiol, and estrus. The hCG component of P.G.600 mimics the hormone LH that leads to ovulation. Numerous studies have shown that a high percentage (50 percent to 70 percent) of prepubertal gilts injected with P.G.600 will exhibit estrus within 7 days following treatment (Figure 3).

The lack of response to treatment with P.G.600 is most often associated with treating gilts that have already reached puberty. Cycling gilts will not respond to P.G.600 during the luteal phase of the estrous cycle because of the negative feedback of progesterone. The benefits of P.G.600 treatment if gilts are injected during the follicular phase of the estrous cycle are questionable because estradiol concentrations have already begun to increase, leading to higher levels of FSH and LH.

Synchronizing the Second Estrus in Gilts

Because producers typically do not breed gilts at the time of puberty, an effective means of synchronizing the second estrus period would be beneficial. While P.G.600 can be used to effectively induce puberty in a group of gilts, all of the gilts may not return to heat at the same time in subsequent periods due to variations in length of estrous cycles.

A strategy that one could theoretically use to resynchronize the second estrus in P.G.600-treated gilts is to give a luteolytic dose of lutalyse (PGF; 2-ml) approximately 18 days after inducing puberty with a single 5-ml injection of P.G.600 (Figure 4). The *corpora lutea* in pigs will not undergo luteolysis in response to a luteolytic dose of lutalyse during the first 12 days of the estrous cycle. However, beyond day 12 of the estrous cycle, lutalyse will cause the *corpora lutea* to regress, leading to a decrease in the concentration of progesterone, followed by follicular growth, estrus, and ovulation. Therefore, one can speculate that giving a single injection of lutalyse to a group of gilts 18 days after P.G.600 treatment should result in a more synchronous second estrus.

It should be noted that research has not been conducted to document the effectiveness of this hormonal treatment strategy.

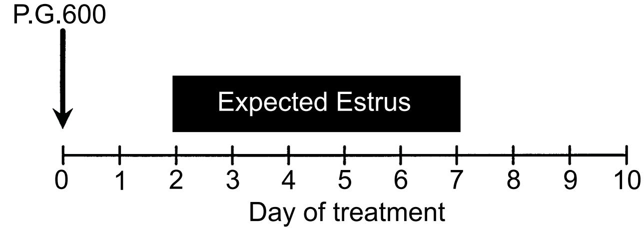

Figure 3. Inducing puberty in gilts with P.G.600. Prepubertal (noncycling) gilts are given P.G.600 at 5 to 6 months of age (within 1 month of the natural onset of puberty).

Synchronizing Estrus in Cycling Gilts

Once gilts have begun cycling, the combination of P.G.600 and PGF is not an effective treatment for synchronizing estrus. In circumstances where the cyclic status of gilts is not known, or if it is known that most gilts are cyclic, one can synchronize estrus by pen-mating for 3 weeks and giving a 2-ml injection of lutalyse 2 weeks later (Figure 5). Research has shown that lutalyse is effective for inducing luteolysis, abortion, and a prompt return to estrus (typically within 3 to 7 days) in pregnant gilts beyond the second week of gestation and that subsequent fertility is acceptable if gilts are aborted during the first trimester. Although this method of estrus synchronization can be used successfully, it can increase the age at first farrowing and nonproductive days because gilts are bred at an age that is approximately equal to the age at third estrus rather than second estrus. Furthermore, many producers are hesitant to abort gilts after they have become pregnant.

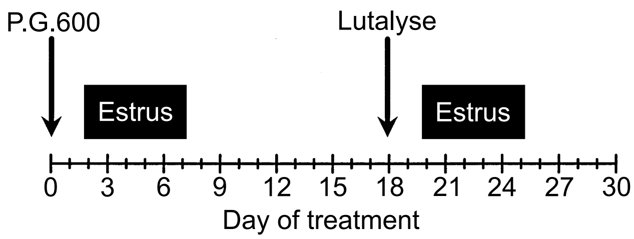

Figure 4. Synchronizing the second estrus in gilts with P.G.600 and lutalyse (PGF). Prepubertal (noncycling) gilts are given P.G.600 to induce puberty and then given a luteolytic dose of PGF 18 days later.

Another approach for synchronizing estrus in gilts that have attained puberty is to feed a progestin for 14 to 18 days. The progestin inhibits maturation of follicles and estrus while permitting the *corpora lutea* to regress naturally. After the progestin is withdrawn, the follicles mature, and estrus occurs within approximately 3 to 7 days. Studies demonstrate that feeding the progestin altrenogest (Regumate™) at a rate of 15 to 20 mg per day for 14 to 18 days is effective for synchronizing estrus in cyclic gilts (Figure 6) and that subsequent litter size is not adversely affected. Unfortunately, this compound does not have Food and Drug Administration (FDA) approval for use in swine.

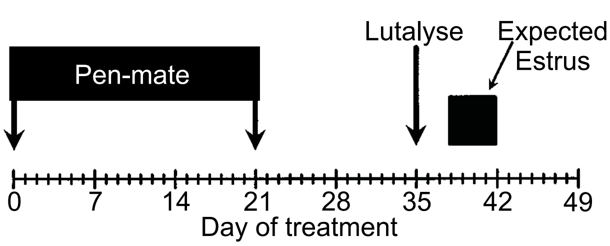

Figure 5. Synchronizing estrus in cycling gilts with pen-mating and lutalyse (PGF). Cycling gilts are pen-mated for 3 weeks and then given a luteolytic dose of PGF 2 weeks later.

Inducing a Prompt Return to Estrus in Weaned Sows

As the time of weaning has been reduced from 35 to 42 days of age to 18 to 24 days of age, a higher percentage of sows have become anestrus or have experienced a delayed return to estrus after weaning. This appears especially true for the more prolific, modern, high-lean-growth genotypes. Also, these conditions are more likely to occur during the summer and fall months and are most common in first-litter sows.

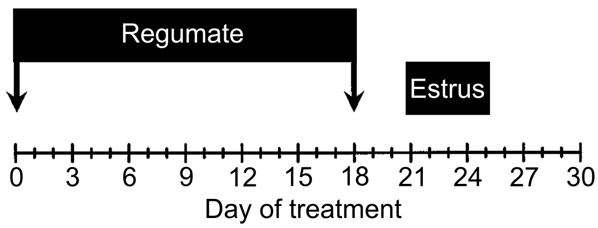

Figure 6. Synchronizing estrus in cycling gilts with altrenogest (Regumate™). Cycling gilts are fed Regumate for 18 days.

A strategy for improving the weaning-to-estrus interval and reducing the anestrus condition in weaned sows is to administer a 2-ml injection of lutalyse within 24 hours after farrowing and to inject a 5-ml dose of P.G.600 to sows at the time of weaning (Figure 7). Additional benefits of the lutalyse treatment after farrowing for the current litter include reduced mortality in newborn pigs and heavier pigs at weaning.

The mechanisms by which these compounds improve sow reproductive performance are not completely understood. It is thought that lutalyse has a "cleaning out" effect on the sow's reproductive system by aiding in the expulsion of the tissues associated with pregnancy (placenta). Lutalyse treatment may improve litter weight gains in the current litter by a more rapid removal of the *corpora lutea* of pregnancy. This would be accomplished by earlier luteolysis and a more rapid removal of the negative effect that progesterone has on milk production. The administration of P.G.600 at the time of weaning most likely reduces the incidence of anestrus by stimulating follicular growth, thus increasing the concentration of estradiol.

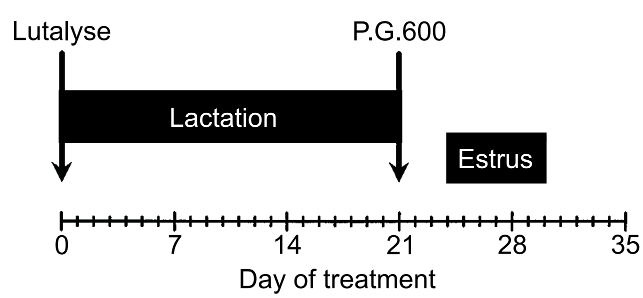

Figure 7. Inducing a prompt return to estrus in weaned sows. Sows are given an injection of lutalyse shortly after farrowing and an injection of P.G.600 at the time of weaning.

Summary

In today's competitive pork industry, it is imperative that producers achieve a high level of reproductive efficiency. Poor performance in the breeding barn can quickly lead to problems in the production schedule and pig flow through the facilities. Producers must be willing to adopt technologies and management strategies that reduce the nonproductive days in the life of the sow. The hormonal treatment strategies previously discussed are tools that producers can use to help in that regard.

None of the strategies discussed in this publication should be expected to achieve a 100 percent success rate. Also, these treatments will not likely be effective if used in an attempt to cover poor management and husbandry. However, when used correctly, the outcome from these hormonal treatments should be satisfactory.

Where trade names are used, no endorsement is intended, nor criticism implied of similar products not named.