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# PHARMACOLOGIC CONTROL OF SWINE REPRODUCTION

Anton L. Pressing, MA, DVM, PhD

Pharmacologic intervention in swine reproduction focuses on two main events: (1) the occurrence of fertile estrus, and (2) the onset of parturition. This article is divided into two corresponding sections. The first section, control of estrus and ovulation, addresses in two parts the hormones and regimens to induce fertile estrus in prepubertal gilts or acyclic sows. A third part discusses approaches to synchronize estrus in cyclic females and to synchronize ovulation. The second section, control of parturition, primarily gives an account of compounds and regimens that are used to induce parturition or to precipitate farrowings more precisely. Two additional parts discuss induction of abortion and delay of parturition. Many compounds that are used in other countries are not approved for use in pigs or are not available in the United States. In spite of these limitations, present means to control reproduction should be carefully considered. Reproductive efficiency of swine herds is a crucial component of their economic success. There are many situations in which short-term therapeutic intervention can restore productivity of females or in which routine, prophylactic measures improve utilization of replacement gilts and the breeding herd.

Stable reproductive traits and prolificacy have been traditional attributes of domestic pigs. Modern, intensified swine production is challenging these traits. It demands an unprecedented degree of precision in reproductive performance and management of the breeding herd. Sows produce on average more than two litters per year, and breeding and farrowing of production groups must be accomplished within 1 week or less. The tight synchrony of reproductive events within groups optimizes use of labor, facilities, and breeding stock. Induced farrowings allow for better supervision and reduce the stillbirth rate. Important biologic benefits are reduced variability of piglet weaning ages, lactation lengths, and occurrence of estrus after weaning. When sows and gilts are mated over extended periods of time rather than within several days of each other, the relative synchrony of reproductive events is increasingly lost. This disrupts movement of females as a

From the Department of Veterinary Clinical Medicine and Surgery, Washington State University College of Veterinary Medicine, Pullman, Washington

group through consecutive stages of production and diminishes the biologic benefits that result from synchronous breeding and farrowing.

Pharmacologic intervention in commercial swine production presently concentrates on therapeutic measures. Exogenous gonadotropins are used to treat persistently anestrous sows or to alleviate the problem of delayed puberty onset in replacement gilts. A second area of pharmacologic intervention that has found acceptance is the induction of parturition with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) or one of its analogues. There exist other strategies that would improve reproductive efficiency of the breeding herd, but they are not widely used. Selective induction of estrus in primiparous sows, especially during the summer months, will significantly reduce the incidence of delayed returns to estrus (> 10 days). Also, routine induction of puberty has been shown to reduce the cost for gilt maintenance and to facilitate the integration of replacements into production groups. Lastly, there are regimens that cannot be adopted because certain compounds are not approved for use in swine or are not marketed in the United States. These are synchronization of estrus (progestins, aimax), induction of parturition via feed (epostane), and improved precision of induced farrowings with a combination of $PGF_{2\alpha}$ and a $\beta$-receptor–blocking agent (carazolol). A list of available compounds with their current status and use is provided in Table 1.

## CONTROL OF ESTRUS AND OVULATION

The control of estrus and ovulation is based on two different strategies. In acyclic (anovulatory) females, fertile estrus is induced through gonadotropic stimulation of follicular growth culminating in estrus and ovulation. In cyclic (ovulatory) females, estrus is synchronized by maintaining the luteal phase and delaying estrus until a predetermined date. A combination of these strategies is possible and can be used to increase the synchrony of occurrence of estrus and ovulation.

The most commonly used hormones to induce fertile estrus are pregnant mare serum gonadotropin (PMSG) and human chorionic gonadotropin (hCG). The biologic properties of PMSG include those of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). The gonadotropic actions of hCG equal primarily those of LH.[17] Because the gonadotropic effects of PMSG and hCG are complimentary, the combination of both hormones represents a very effective means to induce estrus and ovulation in acyclic pigs.[4,17,102,114] The use of the naturally occurring gonadotropins, LH and FSH, is limited because of their short half-life (30 min or less) in comparison to PMSG or hCG (≥ 40 hr).[58] Similar limitations also

**Table 1.** SUBSTANCES USED TO CONTROL REPRODUCTION IN FEMALE PIGS

| Compound | Trade Name | Dose* | Induction of |
|---|---|---|---|
| PMSG + hCG | P.G. 600† (Intervet America Inc, Millsboro, DE) | 400 + 200 IU | Fertile estrus |
| Dinoprost ($PGF_{2\alpha}$) | Lutalyse† (Upjohn, Kalamazoo, MI) | 10 mg | Parturition |
| Oxytocin | Oxytocin† (Upjohn, Kalamazoo, MI) | 5–10 IU | Labor/piglet expulsion |
| hCG | Chorionic gonadotropin | 500 IU | Ovulation |
| Estradiol | ECP | 1–2 mg | Estrous behavior |
| Cloprostenol | Estrumate (Haver, Shawnee, KS) | 175 $\mu$g | Parturition |
| Fenprostalene | Bovilene (Syntex, West Des Moines, IA) | 500 $\mu$g | Parturition |

*Dosages are guidelines provided by the manufacturer or based on references cited in this text.
†Only these substances are approved for use in pigs.

exist for gonadotropin-releasing hormone (GnRH) or one of its analogues, because only frequent (hourly) administration will induce estrus and ovulation.[82,96]

Estrus synchronization in cyclic pigs is possible with compounds that artificially extend the luteal phase of the estrous cycle. Progesterone, synthetic progestins, and other substances, such as aimax, suppress follicular development through inhibitory actions on pituitary gonadotropin and/or hypothalamic GnRH release. Of the numerous compounds that have been evaluated, only few appear to be both effective and safe. Altrenogest (Regu-Mate, Hoechst-Roussel, Somerville, NJ), a synthetic progestin, has been used successfully in pigs, but is not approved for such use.[84] Other synthetic progestins failed to synchronize estrus satisfactorily or have been found to compromise fertility of female pigs.[84,117]

## Induction of Puberty

The demand for replacement gilts in commercial pig production is predictable, occurring periodically with each farrowing group. Without reliable induction of puberty, larger numbers of gilts must be kept in store to provide the females that can be bred within 1 week or preferably less. Pubertal estrus usually occurs between 6 and 7 months of age in American and European breeds.[1,22,62,98] Because onset of puberty occurs at random, a varying number of gilts of similar age will be in estrus over a period of several weeks. Boar exposure and relocation are frequently used to induce more synchronous onset of puberty in replacement gilts, but the proportion of females in estrus during the first week is commonly 37% or less (Fig. 1).[17,114] Effective induction of synchronous pubertal estrus with exogenous hormones offers economic and biologic benefits, lowering the cost for gilt maintenance, reducing the variation in breeding and farrowing dates, and assuring more uniform lactation lengths and piglet weaning ages.

### *Prepubertal Gilt*

Prepubertal gilts are able to respond with follicular growth, estrus, and ovulation to exogenous gonadotropins and endogenous gonadotropins released by injection of GnRH as early as 100 days of age. Ovulatory and estrous responses improve as gilts approach puberty, and optimal responses have been observed in

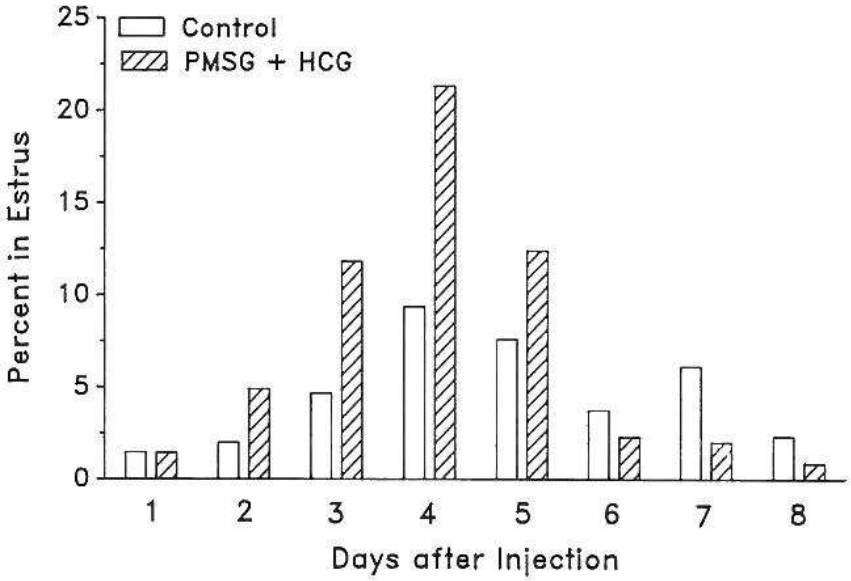


**Figure 1.** Onset of estrus in prepubertal gilts after relocation without (controls) or after treatment with 400 IU of PMSG and 200 IU of hCG (P.G. 600, Intervet America, Inc, Millsboro, DE). *From* Britt JH, Day BN, Webel SK, et al: Induction of fertile estrus in prepubertal gilts by treatment with a combination pregnant mare's serum gonadotropin and human chorionic gonadotropin. J Anim Sci 67:1148, 1989; with permission.

gilts between 150 and 160 days of age or older.[45,89] Common regimens used to induce fertile, pubertal estrus are the combined use of PMSG (400 to 500 IU) and hCG (200 to 250 IU), treatment with PMSG alone (500 to 1000 IU), and a combination of hCG (500 IU) and estradiol-17$\beta$ (1 mg).

**Combined Administration of PMSG and hCG.** The combination of PMSG (400 IU) and hCG (200 IU) is an effective means of inducing fertile estrus in prepubertal gilts of 5 months of age or older, and initiates estrus in 75 to 90% of treated gilts and ovulation in 90 to 100%.[89] The occurrence of estrus is synchronized (Fig. 1). Few gilts are in estrus within the first 3 days after treatment.[4,17,102,114] Onset of estrus generally peaks on day 4, and most gilts will be in heat between day 4 and 6 posttreatment.[8,17,114] Most females (range: 85 to 100%) initiate or complete the ovulatory process within 96 to 144 hours after treatment.[106]

Hormone treatment does not alter the reproductive performance of gilts. Farrowing rate (range: 78 to 91%) and litter size (range: 7.5 to 10.1) were similar for gilts serviced at either induced or spontaneous pubertal estrus.[17,91,102,114] Although estrus and ovulation occur with various doses of PMSG and hCG, the most effective and economical combination is 400 to 500 of PMSG and 200 to 250 IU of hCG.[4,105] Combinations of FSH (100 to 200 IU) and hCG (200 to 300 IU) appear to be less effective in inducing estrus and ovulation than the combination of PMSG and hCG.[115] A commercial product containing 400 IU of PMSG and 200 IU of hCG (P.G. 600, Intervet America, Inc, Millsboro, DE) is approved for use in acyclic gilts in the United States.

**Alternative Regimens.** The administration of PMSG, hCG alone, and hCG with estradiol are common alternatives to the combined use of PMSG and hCG. Although these regimens are used in other countries, none is approved for use in pigs in the United States.

*PMSG.* Treatment with 500 to 1500 IU of PMSG induces follicular growth and ovulation in a high percentage of acyclic gilts (range: 80 to 100%).[89] Ovulation rates and the number of gilts in estrus, however, are reduced in comparison to treatments using both PMSG and hCG.[4,5,49,105] When high doses of PMSG (600 IU or more) are used to induce a superovulatory response, reproductive performance of gilts is not consistently improved. A higher number of immature ova and increased embryonic loss limit the usefulness of higher doses of PMSG to increase litter size.[3,51]

*hCG Alone or in Combination with Estrogens.* Administration of 500 to 750 IU of hCG induces ovulation in a large proportion of gilts (range: 50 to 100%), but the rate of estrus is low.[39,41,42] Gilts begin to ovulate uniformly at about 40 hours after hCG administration, and the ovulatory process is well-synchronized within a group.[39,41,42,64,65,94] When hCG is combined with estradiol or estrogenic compounds, expression of heat and conception rates are improved, but litter size is usually reduced.[42,91,99]

*GnRH.* Hourly pulsatile infusion of 10 to 50 ng of GnRH/kg body weight consistently initiates estrus and ovulation in immature and peripubertal gilts.[82,96] Estrus occurs within 3 to 4 days after initiation of treatment. Duration of estrus (40 $\pm$ 2 hr), ovulation rate (13 $\pm$ 1), and the pattern of endocrine changes in LH, estradiol, and progesterone are similar to those observed during spontaneous pubertal estrus.[96] Less frequent administration of GnRH resulted in less consistent estrous and ovulatory responses of prepubertal gilts.[21,100] Presently, there is no reliable and economical delivery system for the frequent infusion of GnRH, and the releasing hormone has remained an experimental tool.

### *Delayed Puberty Gilt*

Delayed puberty is a persistent problem in commercial pig production; between 10 to 30% of selected gilts are removed for not being observed in

heat.[26,34,112] When gilts exceed the average age of puberty onset relative to penmates by two or more estrous periods, therapeutic measures should be initiated unless the gilts will be culled. Delayed puberty gilts that are truly acyclic will respond to exogenous gonadotropins with estrus and ovulation rates similar to those of gilts in which puberty is induced at a much younger age. After treatment with PMSG (500 to 750 IU) or PMSG and hCG (400 to 500 IU and 200 to 250 IU), about 60 to 75% of gilts will be in estrus, and 80% will ovulate.[15,40,72]

When gilts fail to show signs of heat after gonadotropin treatment, behavioral anestrus is frequently the underlying cause. Many delayed puberty gilts (30 to 60%) have cyclic ovarian activity but do not exhibit distinct signs of heat.[26,31,33] Because sensitivity to estrogen is decreased in these females, gonadotropin treatment is ineffective in correcting the problem.[33] If behaviorally anestrous gilts are treated during the luteal phase, diestrus will be prolonged. Gonadotropin treatment induces accessory corpora lutea, and estrogen by itself has luteotrophic effects during diestrus in pigs.[13,52,88]

## Induction of Fertile Estrus in Sows

In batch farrowing systems, it is important that sows are weaned and bred in tight synchrony. Collective weaning serves as the event that initiates follicular growth and synchronous estrus. Commonly, 80% of sows are in heat and bred within 7 days after weaning.[85] However, various factors, such as season, parity, lactational weight loss, and litter size, affect the reproductive performance of farrowing groups as well as individual sows. Hormonal induction of postweaning estrus has been practiced with the goals of shortening the weaning-to-estrus interval, of preventing delayed returns to estrus (>10 days), and of treating persistently anestrous sows. Attempts to shorten lactational anestrus and to breed sows before weaning may be useful in extensive rearing systems with lactation lengths of 5 weeks or more.

### *Postweaning Sow*

Exogenous gonadotropins alone or in combination with estradiol shorten the weaning-to-estrus interval and improve the synchrony of postweaning estrus. The rebreeding interval decreased by 1 day (.9 ± .26 day; range: .5 to 2.5 day) after treatment of multiparous sows with PMSG (500 to 1000 IU), PMSG and hCG (400 IU and 200 IU), or PMSG (1000 IU) followed by hCG (500 IU). Females given gonadotropins returned to estrus within 4.0 ± .2 days, and those not treated returned within 4.9 ± .4 days.[28,47,79,80] Incidence of delayed returns to estrus (>10 days) and conception rates did not differ between treatment groups.

Improvements in litter size are small or inconsistent after treatment with PMSG, although ovulation rates increase considerably. Ovulation rates increased 82.4%. Ovulation rates increased 82.4% (25.9 vs. 14.2 corpus lutea), and the number of viable embryos was 51% higher (14.5 vs. 9.6) until day 40 of gestation in multiparous sows given 1000 or 1200 IU of PMSG.[28,80] However, corresponding increases in litter size do not occur at farrowing because of high embryonic loss and early fetal death. The number of pigs per litter was only slightly higher (.5 to 1.2 pigs/litter) or were similar to those of untreated sows following various gonadotropin treatments, such as PMSG (1200 IU), PMSG and hCG (400 IU and 200 IU), or FSH and hCG (400 IU and 200 IU).[6,79,80,120] The economic benefits of estrus induction in herds without depressed fertility appear to be small.

### *Delayed Returns to Estrus*

The prevalence of delayed returns to estrus (>10 days) is greater among primiparous than multiparous sows, and occurs across all parities at a higher rate during summer and early fall.[2,7,19,68,70,111,113] A common characteristic of herds with anestrous problems is lengthened weaning-to-estrus intervals of 10 days or more.[18,99,118] Exogenous gonadotropins alone or in combination with estradiol alleviate this problem.[18,38,67,99,118] Treatment with PMSG (500 IU to 1200 IU) the day after weaning induced estrus within 7 days in 93 to 95% of primiparous sows during summer and early fall. In contrast, a considerable number of sows (38 to 42%) not given PMSG failed to be in heat within 7 days of weaning.[18,67] The anestrous condition lasted for extended periods (>30 days). About 90% of these sows failed to cycle within the first month after weaning.[67,99]

Collectively, these and other studies have shown that various doses and regimens, such as PMSG (500 to 1500 IU), PMSG and hCG (400 IU and 200 IU), or hCG plus estradiol (500 IU plus 1 mg) are equally effective in preventing delayed returns to estrus in primiparous and multiparous sows. Estrus occurs in a high proportion of females relative to untreated sows within 7 days of treatment (92 ± 3% vs. 60 ± 2%), and the average length of the weaning-to-estrus interval decreases by approximately 8 days (5.3 ± .9 vs. 13 ± 1.6 days), although extremes of 18 days have been reported.[18,38,67,99,118] Reproductive efficiency of sows is only marginally improved when disturbing influences occurring during the summer and fall season are absent. The number of females showing estrus within 7 days of weaning during other periods of the year (November to June) was similar for PMSG-treated sows and sows not treated with PMSG.[67] Gonadotropin treatment in herds with delayed returns to estrus did not compromise farrowing rates or improve litter size.[18,67,99,118] In contrast, treatment regimens that include estradiol are consistently associated with smaller litter size.[38,99]

### *Persistent Anestrus*

When sows have entered a period of delayed returns to estrus, it is not uncommon for them to remain anestrous for 4 weeks or more, especially if they are primiparous.[67,99] Persistent anestrus after weaning (>30 days) disrupts breeding management, increases the demand for replacement gilts, and causes substantial economic loss when sows are culled after having remained unproductive for an extended period. Approximately one third of sows are culled owing to reproductive problems, and a considerable proportion of these females are removed for not being observed in heat.[32,34,90,108,112] To avoid accumulation of nonproductive sow days, treatment should be initiated within 7 to 10 days of weaning. Hormonal regimens that have proven effective in inducing pubertal or postweaning estrus without adverse effects on farrowing rate and litter size are equally effective in alleviating persistent anestrus in sows.[36,74,75,102]

After treatment with 1000 IU of PMSG (14 to 42 days postweaning), estrus was observed in 78 to 100% of sows within 5 days or less, and conception rate was 67 to 95%.[36,75] The combined use of PMSG (400 IU) and hCG (200 IU) showed similar results in chronically anestrous sows 10 to 100 days postweaning.[74,102] Estrus occurred in 70 to 94% within 8 days of treatment and between 70 and 80% of the sows showing estrus farrowed. To stimulate expression of heat, estrogen (1 mg of estradiol benzoate or cypionate) has been used in combination with hCG (200 to 500 IU) or PMSG and hCG (400 IU and 200 IU). But the inclusion of estradiol decreased conception rates and litter size.[79,86,99] Treatment with PMSG (800 to 1200 IU) or PMSG (400 IU) and hCG (200 IU) appears to be preferable when the rate of estrous induction, subsequent farrowing rate, and litter size are considered.

Anestrous sows belong to any of three categories. Some sows are truly acyclic, some have ongoing ovarian cycles without distinct outward signs of heat, and some are subestrous, with only weak signs of heat frequently escaping heat detection. Inadvertent use of gonadotropins or estrogens during the luteal phase will induce secondary corpora lutea and prolong the diestrus period by approximately 14 days.[52,88] Consequently, such sows will not respond to treatment within the expected time frame of 1 week or less. Treatments should be initiated early, within 7 to 10 days of weaning, to prevent accumulation of nonproductive sow days. Sows not returning to estrus within 7 days of treatment should be culled.

### *Lactating Sow*

Induction of fertile estrus during lactation would allow initiation of pregnancy prior to weaning. However, increases in litters per sow per year appear feasible only in extensive production systems that have lactation periods of 1 month or more. Occurrence of estrus and conception rates after gonadotropin treatment or pulsatile GnRH infusion remain unsatisfactory until the fourth or fifth week of lactation.[16] Administration of PMSG (700 IU) induced estrus in a small percentage of sows during the first week of lactation (14%).[29] Treatment with PMSG (1500 IU) between day 7 and 15 of lactation followed 4 days later by hCG (750 to 1500 IU) was associated with highly variable, but generally low, conception rates (range: 13 to 80%). In these studies, sows were artificially inseminated two to three times 24 to 40 hours after hCG, independent of signs of heat.[53,57] Gonadotropins become increasingly effective after the third week of lactation, especially when pigs are periodically removed from the sow before treatment.[30,57]

Stage of lactation also affects estrous responses to hourly pulsatile infusion of GnRH. The proportion of sows in estrus increased from 50 to 100% between the second and fourth week of lactation.[16] The present findings suggest that hormonal induction of fertile estrus during lactation would be useful in extensive rearing systems. Pigs could be weaned after 6 weeks or longer, while farrowing intervals would be comparable to those of intensified systems with short lactations.

## Synchronization of Estrus and Ovulation

### *Estrus Synchronization*

Estrus synchronization allows the efficient use of randomly cycling females. Mature, cyclic gilts that have been synchronized can be added to sow groups for breeding at predetermined times. In farm animals, specifically bovines, control of estrous cycles is achieved in two ways. First, the luteal phase is terminated prematurely with prostaglandins, and estrus occurs spontaneously in a proportion of females. Second, the onset of spontaneous estrus is delayed with progestins until its occurrence is desired. Initiating premature luteolysis to control estrous cycles is not effective in the pig. The porcine corpus luteum remains refractory to $PGF_{2\alpha}$ or its analogues until days 12 to 14 after ovulation.[37] The remaining period until spontaneous corpus luteum regression is too short to be useful for estrus synchronization. In contrast, suppression of ovarian cycles has been practiced successfully with various compounds. Progesterone, synthetic progestins, or aimax (a bithio-urea derivative) prevent cyclic ovarian activity by inhibiting endogenous gonadotropin or GnRH release.[45,76]

The use of aimax was discontinued in many countries because the compound showed teratogenic effects.[72] Treatment with progesterone or many of the early synthetic progestins (e.g., chlormadinone acetate [CAP], medroxyprogesterone acetate [MAP]) gave unsatisfactory results or had adverse effects. Use of these

compounds was associated with poor estrous synchronization, reduced fertility, decreased litter size, and development of follicular cysts.[12,107,117] Of the many progestational compounds that have been evaluated, only two, SA-45.249 (a norprogestogen) and altrenogest (a progestogen, [Regu-Mate]), effectively synchronize estrus without compromising reproductive performance.[84,117] When these compounds are given to a group of cycling females for at least 2 weeks, cyclic ovarian activity will cease. The reasons for the ensuing synchronicity of estrus after the withdrawal of compounds are twofold. Corpora lutea are at least 14 days old and have already undergone luteolysis or begin to regress.[84,88] Secondly, endogenous gonadotropin levels that were suppressed for the duration of treatment rebound after drug withdrawal and stimulate renewed, preovulatory follicular growth. After administration of altrenogest (15 to 20 mg/day), estrus occurs between 4 to 8 days after drug withdrawal in at least 90% of females.[84,117] None of the progestins is approved for use in food animals in the United States.

Comparable endocrine mechanisms regulate follicular growth and hence cyclicity of sows during lactation and following weaning. Gonadotropin secretion remains low during most of lactation, resulting in little initial, and later only modest, follicular development. The low gonadotropin levels rebound at weaning, initiating a sequence of preovulatory follicular growth, estrus, and ovulation.[16] The synchronous occurrence of estrus is further enhanced when exogenous gonadotropins are given 1 day after weaning or following withdrawal of compounds that suppress gonadotropin secretion until weaning.[27,28,47,79,92,93] Similarly, treatment of acyclic females with exogenous gonadotropins also synchronizes occurrence of estrus, because the period of preovulatory follicular growth until estrus is highly uniform in sows and gilts (commonly less than 1 week).[48,96] Most gilts and sows experience estrus within 4 to 6 days after treatment.

### *Synchronization of Ovulation*

The synchronization of "timing" of ovulation is a modified approach to estrous induction and has been used in production systems with preset dates for artificial insemination. Initial treatment with PMSG alone or in combination with hCG, followed approximately 3 days later by hCG, initiates follicular growth and substitutes exogenous hCG in place of the preovulatory endogenous LH discharge. The onset of ovulation after administration of hCG is rather precise. The ovulatory process begins between 40 to 46 hours after hCG injection (250 to 1000 IU) and rarely starts before 40 hours.[3,39,64,65,94,95,123] This timing allows the insemination of females at set times independent of signs of estrus.[28,93] Optimal fertility is observed in sows inseminated between 12 to 16 hours before onset of ovulations.[66]

Induction of estrus in combination with synchronized ovulation has been extensively used in large Eastern European herds. Weaned sows or postpubertal gilts in which estrus has been synchronized receive PMSG (1000 to 1250 IU) followed 55 to 72 hours later by hCG (500 IU). Females are inseminated twice, 22 to 26 hours and 36 to 42 hours after injection of hCG. Farrowing rates are commonly 71% (±2) for gilts, and 79% (±1) for sows, and pigs born alive number 8.6 (±.5) and 10.0 (±.3), respectively.[11] Various doses of hCG (125 to 750 IU) have been evaluated. With increasing doses of hCG, ovulations occur earlier and are more synchronized. However, the number of corpora lutea and both ovarian and uterine weight decrease following higher doses of hCG (≥500 IU).[103,104] A combination of hCG (300 IU) and GnRH (300 μg) also has been used. Although ovulations tend to occur earlier (approximately 36 hours after injection) the synchrony of ovulations is not consistently improved relative to treatment with hCG alone.[9,10,20]

## CONTROL OF PARTURITION

Control of parturition is part of a concerted effort to optimize reproductive performance of the breeding herd. The administration of $PGF_{2\alpha}$ or one of its analogues provides an effective, safe technique to induce parturition after day 110 of gestation. Routine use of this regimen will save pigs if records about gestation length are accurate and management makes an active commitment to supervise farrowings. Assisting sows with difficult deliveries, using oxytocin to promote expulsion of delayed piglets (interpiglet interval > 20 min), or resuscitation of hypoxic pigs will reduce stillbirth rates by 50%, saving about half a pig per litter.[54,116] Additional benefits are more efficient use of farrowing rooms, decreased variation in lactation lengths, and more uniform age of piglets, which facilitates cross-fostering and improves performance of weaned pigs.

The corpus luteum of pigs must be maintained and secrete progesterone if pregnancy is to be established and maintained to term. Natural onset of parturition is initiated by the fetus. Fetal cortisol concentrations increase within 2 days of delivery and initiate endocrine changes that result in a steep decline of progesterone, an increase of estrogens, and a rapid rise of $PGF_{2\alpha}$. Secretion of relaxin and oxytocin result from the rise in $PGF_{2\alpha}$ concentrations, which peak around the time of parturition. Because corpora lutea of pregnancy as well as corpora lutea of the estrous cycle become sensitive to $PGF_{2\alpha}$ by day 12, treatment after this date will terminate gestation.[46] If treatments before 110 days of gestation are avoided, induced farrowings take a physiologic course. Duration of parturition, piglet viability, and sow performance during lactation are similar to those following natural delivery of pigs.[35,43,44,46,54,59,69,101] Although many products are available, $PGF_{2\alpha}$ (Lutalyse; Upjohn, Kalamazoo, MI) is the only prostaglandin approved for use in pigs.

### Induction of Farrowing

#### *Use of Prostaglandins*

Presently, the only effective and practical method to induce parturition in the pig is the use of prostaglandins several days in advance of the spontaneous occurrence of parturition. Gestation length in swine is reasonably precise; approximately 114 to 116 days (day 0 = first day of estrus), and most sows on commercial units farrow within 2 days of a mean gestation length of 115 days.[46,101] When $PGF_{2\alpha}$or one of its analogues is used after day 110 of gestation, the average length of the interval between injection and onset of parturition is commonly less than 30 hours (27.4 ± .7 hr; range: 31.2 to 23.2 hr).[35,43,44,54,59,60,69,73] Approximately two of three sows will commence parturition between 20 to 36 hours after administration of $PGF_{2\alpha}$ (65 ± 6.5%) or a prostaglandin analogue cloprostenol (63 ± 3.2%).[43,44,54,60,73,101] If treatment is initiated during the morning, farrowings are concentrated during working hours of the next day.

Onset of parturition following treatment with synthetic prostaglandins tends to occur earlier than after use of the parent compound $PGF_{2\alpha}$. Also, the rate of failure to induce parturition within 36 hours is less for a commonly used analogue, cloprostenol (5.0 ± 1.7%), than for $PGF_{2\alpha}$ (15.9 ± 1.4%).[43,44,54,60,69,73,101] Following the use of $PGF_{2\alpha}$, the interval from injection to onset of farrowings was 29.5 ± .6 hours (range: 24.3 to 31.4 hr); that for prostaglandin analogues was 25.2 ± .7 hours (range: 23.2 to 28 hr).[43,44,54,59,69,110] Although parturition induction is generally used in all females beyond 110 days of gestation, it is particularly useful for females not farrowing by day 114 or 115 of gestation. Selective induction of parturition represents an attractive option for larger operations, reducing treat-

ment cost, decreasing the interval from prostaglandin treatment to onset of parturition (18.4 ± 3.5 hr), and minimizing potential risks of early parturition on piglet viability.[101]

When considering the use of prostaglandins in a farrowing program, various aspects of this management technique need to be kept in mind. Side effects of the naturally occurring $PGF_{2\alpha}$ in swine occur within minutes of injection but are transient. Animals primarily show hyperpnea and sometimes have increased salivation, urination, and defecation. Nestbuilding behavior is common in penned sows. Sows in crates may engage in intense rooting, pawing, and biting of bars. Side effects and hyperactivity are of short duration and commonly cease within 60 to 90 minutes of $PGF_{2\alpha}$ treatment.[35,121,122] The prostaglandin analogues are essentially free of behavioral and systemic side effects.[43,44,110,122]

Induction of parturition should not be attempted before day 110 of gestation, because piglet viability will be severely compromised.[46,69,110,124] Few adverse effects on stillbirth rate, piglet weight, and postnatal survival have been observed when $PGF_{2\alpha}$ or an analogue is given on day 111 of gestation or later.[35,43,44,46,54,59,69,101] Similarly, there were no adverse effects on sow performance during lactation, rate of return to estrus, or subsequent fertility.[23,61,73,109]

The primary value of prostaglandins is their efficacy in inducing and synchronizing the occurrence of farrowings. This facilitates labor management and farrowing attendance, effectively reducing perinatal losses.[25,54,116] Other potential benefits, such as a decrease in the occurrence of puerperal disease or a shorter duration of farrowings, may depend on factors specific to a herd and are not clearly proven. The duration of farrowings after prostaglandin treatment is mostly unaltered.[24,59,60,63,101] However, decreases as well increases in the duration of piglet delivery have been reported.[25,73,109] In herds with a history of puerperal disease (metritis-mastitis-agalactia), the use of prostaglandins generally has decreased incidence of the problem.[23,25,63,101] In some cases, however, prostaglandins were not effective in reducing the occurrence of puerperal disease.[56,109]

### *Other Compounds*

Exogenous glucocorticoids do not have any practical value for the induction of parturition in sows when compared with prostaglandins. Although dexamethasone induces parturition, injections must be given for several days, and precision of parturition induction is poor. When dexamethasone was given once daily for 3 to 4 days (75 to 100 mg/day/sow) 1 to 2 weeks prior to anticipated spontaneous delivery (day 115 of gestation), farrowings occurred on average 72 hours or longer after the last injection.[46,60]

Epostane also has been evaluated for its efficacy in parturition induction. The compound rapidly inhibits progesterone synthesis and induces farrowings within approximately 32 hours when given orally for 2 consecutive days (5 or 10 mg/kg body weight) or once parenterally (5 mg/kg body weight, subcutaneously). Treatment had no adverse effects on the number of pigs born alive or pigs weaned or the resumption of cyclicity of weaned sows.[83] Epostane is presently not marketed in the United States.

## Synchronization of Farrowing

Repeated efforts have been made to increase the synchrony of parturition onset after prostaglandin treatment and reduce the proportion of sows farrowing late (>30 hr). Progesterone, progestational compounds, and relaxin have been used successfully in advance of prostaglandin treatment but are not approved or

are not readily available.[50] Oxytocin alone, carazolol alone (a β-adrenergic antagonist), and oxytocin and carazolol have been combined with prostaglandin treatment. Farrowings occur earlier and are better synchronized and duration of farrowing decreases after use of carazolol.[14,35,59,119]

### *Prostaglandins and Oxytocin*

The interval to onset of farrowings is shortened and the synchrony of farrowings increases when oxytocin is given within 20 to 24 hours after administration of $PGF_{2\alpha}$ or one of its analogues.[35,50,59,119] Treatment with 5 to 30 IU of oxytocin 20 hours after prostaglandin injection on day 112 of gestation induced from 78 (5 IU), 82 (10 IU), to 100% of sows (20 or 30 IU) to farrow during the next working day. Working hours were defined as an 8-hour period following treatment with oxytocin.[119] Depending on dose, approximately 40 to 50% of females begin to farrow within 6 hours of oxytocin treatment, which allows supervision of these farrowings during the day. In comparison, fewer sows farrowed within 26 hours (30%) or 28 hours (40%) after prostaglandin treatment without oxytocin.[35,119]

Although doses of 20 to 30 IU of oxytocin precipitate earlier parturition in a larger proportion of sows, the higher doses are frequently associated with interruptions of piglet delivery. Use of more than 10 IU of oxytocin has been shown to induce uterine tetany for up to 15 minutes.[50] Correction of dystocia is time-consuming, and frequently piglets are hypoxic or dead when extracted. Continuation of piglet delivery may require further treatment with low doses of oxytocin.[35] The likelihood of such complications decreases substantially when low doses of oxytocin are used ($\leq$10 IU).[35,59,119]

### *Prostaglandins and Carazolol*

Carazolol, a $\beta_{1,2}$-adrenergic blocking agent, has been found to reduce the duration of parturition, stillbirth rate, and the incidence of dystocia when given alone at the onset of labor (1 mg/100 kg body weight, intramuscularly). The compound prevents premature uterine relaxation by reducing the effect of epinephrine on uterine smooth muscle contractility.[14,50] Carazolol also has been used after prostaglandin treatment, either in combination with oxytocin or alone.[59,119] The combined use of carazolol (3 mg/sow) and oxytocin (2.5 IU) reduced the average length of the interval between treatment and onset of parturition relative to treatment with carazolol alone (1.7 vs. 2.6 hr) in one experiment but not in a second experiment.[59] It appears that use of carazolol alone (3 mg/sow) 20 hours after prostaglandin administration is a reliable method to initiate precise onset of parturition.[59] The treatment precipitates early onset of labor (range: 1.2 to 2.6 hr), shortens the duration of parturition, and is free of the adverse side effects that may occur after oxytocin use.

## Induction of Abortion

Although prostaglandins are not commonly used for induction of abortion or synchronization of estrus in commercial swine production, some situations require the termination of pregnancy. Among these are accidental or undesirable matings, pseudopregnancy (sows failing to farrow on schedule or remaining anestrous without detectable signs of pregnancy), expulsion of mummies, and the expectancy of small litter sizes during episodes of infectious reproductive disease. In several studies, treatment with $PGF_{2\alpha}$ or the prostaglandin analogue cloprostenol resulted in the majority of sows aborting within 1 to 2 days after treatment and

their return to estrus within 4 to 14 days. No adverse effects on subsequent reproductive performance of aborted females have been observed.[71,77,97] Some reports indicate that a single injection of $PGF_{2\alpha}$ (dinoprost tromethamine) is effective in inducing abortion. The percentage of gilts aborting varied between 60 to 100%.[37,71,77] However, two injections of $PGF_{2\alpha}$ (twice 10 mg 12 hr apart) were more effective than a single treatment of $PGF_{2\alpha}$ (100 vs. 42%) and equaled the results observed after a single injection of a prostaglandin analogue, cloprostenol (500 $\mu$g/gilt).[97]

### Delay of Parturition

Parturition can be delayed by the use of $\beta_2$-adrenergic agonists that exert tocolytic effects.[87,125] Clenbuterol, one such compound, delays onset of parturition or interrupts parturition in sows. When clenbuterol (150 $\mu$g/sow) was given during onset of labor before delivery of the first pig, parturition was delayed 15 hours. Treatment with the agent after delivery of one to three piglets interrupted parturition for approximately 3 hours. Short delays as well as interruption of parturition did not have detrimental effects on perinatal survival rate or maternal behavior.[125] Prolonged delays of parturition with repeated, higher doses (300 $\mu$g every 6 hr) for several days increased stillbirth rate to 40%.[87]

## SUMMARY

### Acyclic Females

PMSG and hCG have been used alone or in combination to induce fertile estrus in prepubertal gilts and anestrous sows. The combined use of PMSG (400 to 500 IU) and hCG (200 to 250) consistently induces estrus (75 to 90%) and ovulation (90 to 100%). Most females will be in heat between 4 and 7 days after treatment. Farrowing rate (80 to 90%) and litter size (7.5 to 10) are generally similar to those of untreated females. Use of PMSG (500 to 1500 IU) alone or hCG alone (500 to 750 IU) is less effective, compromising either rate of ovulation (PMSG) or expression of heat (hCG). Inclusion of estradiol (1 to 2 mg/female) improves the occurrence of estrus, but litter size is usually decreased.

### Cyclic Females

Because porcine corpus lutea are refractory to the luteolytic effects of prostaglandins until days 12 to 14 of the estrous cycle, suppression of ovarian cycles is the only effective means to synchronize estrus in the pig. Only few compounds that regulate ovarian activity were found to be effective and safe. Altrenogest, a synthetic progestin, is used in some countries to synchronize estrus in replacement gilts. When the compound is fed for at least 14 days (15 to 20 mg/day), estrus occurs within 4 to 8 days in 90% of females after drug withdrawal. Exogenous gonadotropins given 1 day after withdrawal of the compound enhance synchronous occurrence of estrus.

### Gestating Females

Treatment with $PGF_{2\alpha}$ or one of its analogues is an effective, safe technique to induce farrowing after day 110 of gestation. Farrowings commence in 60% or

more of females within 18 to 32 to hours after prostaglandin injection. Additional use of oxytocin 20 hours after prostaglandin treatment concentrates farrowings during the second day. Farrowings commence in approximately 50% of females within 6 hours after oxytocin administration. Low doses of oxytocin (5 to 10 IU) should be used, because higher doses are associated with an increase in dystocia. Prostaglandins induce abortion throughout gestation in the pig.

## References


1. Allrich RD, Christenson RK, Ford JJ: Age at puberty and estrous activity of straightbred and reciprocal crossbred gilts. Anim Reprod 8:281, 1985
2. Aumaitre A, Dagorn J, Legault C, et al: Influence of farm management and breed type on sow's conception-weaning interval and productivity in France. Livestock Prod Sci 3:75, 1976
3. Baker RD, Coggins EG: Control of ovulation rate and fertilization in prepuberal gilts. J Anim Sci 27:1607, 1968
4. Baker RD, Downey BR: Induction of estrus, ovulation and fertility in prepuberal gilts. Ann Biol Anim Biochem Biophys 15:375, 1975
5. Baker RD, Rajamahendran R: Induction of estrus, ovulation and fertilization in prepuberal gilts by a single injection of PMSG, hCG, and PMSG:hCG combination. Can J Anim Sci 53:693, 1973
6. Bates RO, Day BN, Britt JH, et al: Reproductive performance of sows treated with P.G. 600$^{R}$ [abstract]. In Proceedings Am Assoc Swine Pract, Indianapolis, 1987, p 79
7. Benjaminsen E, Karlberg K: Postweaning oestrus and luteal function in primiparous and pluriparous sows. Res Vet Sci 30:318, 1981
8. Bergfeld J: Versuche zur biotechnischen pubertätsinduktion bei weiblichen jungschweinen. Arch Exp Vet Med 31:375, 1977
9. Bergfeld J, Brüssow KP, George G: Untersuchungen zur ovulationsdynamik und -potenz in jungsauengruppen verschiedener betriebe nach anwendung unterschiedlicher behandlungen zur ovulationsstimulation. Arch Exp Vet Med 38:735, 1984
10. Bergfeld J, George G, Brüssow KP: Untersuchungen zur ovulationsdynamik und -potenz in altsauengruppen mehrerer betriebe nach anwendung unterschiedlicher behandlungen zur ovulationsstimulation. Arch Exp Vet Med 38:849, 1984
11. Bergfeld J, Hühn U: Stand und perspektive der biotechnik der fortpflanzung bei der sau. Mh Vet Med 38:688, 1983
12. Bertschinger H: Die zyklussynchronisation beim schwein. Schweiz Arch Tierheilk 109:588, 1967
13. Bosc MJ, Martinat-Botté F, Terqui M: Practical uses of prostaglandins in pigs. Acta Vet Scand 77(suppl):209, 1981
14. Bostedt H, Rudloff PR: Prophylactic administration of the beta-blocker carazolol to influence the duration of parturition in sows. Theriogenology 20:191, 1983
15. Braune S, Schlegel W: Untersuchungen über möglichkeiten einer pubertätsvorverlagerung mit hilfe der brunst- bzw. ovulationssynchronisation. Mh Vet Med 30:727, 1975
16. Britt JH, Armstrong JD, Cox NM, et al: Control of follicular development during and after lactation in sows. J Reprod Fertil Suppl 33:37, 1985
17. Britt JH, Day BN, Webel SK, et al: Induction of fertile estrus in prepubertal gilts by treatment with a combination pregnant mare's serum gonadotropin and human chorionic gonadotropin. J Anim Sci 67:1148, 1989
18. Britt JH, Esbenshade KL, Heller K: Responses of seasonally anestrous gilts and weaned primiparous sows to treatment with pregnant mare's serum gonadotropin and altrenogest. Theriogenology 26:697, 1986
19. Britt JH, Szarek VE, Levis DG: Characterization of summer infertility of sows in large confinement units. Theriogenology 20:133, 1983
20. Brüssow KP, Bergfeld J: Untersuchungen zur verlagerung der ovulationen bei jungsauen durch veränderung der injektionstermine im rahmen des verfahrens der ovulationssynchronisation. Arch Exp Vet Med 38:840, 1984
21. Carpenter LS, Anderson LL: Pulsatile infusion of luteinizing hormone-releasing hormone: Effects on luteinizing hormone secretion and ovarian function in prepubertal gilts. Anim Reprod Sci 9:261, 1985
22. Caton JS, Jesse GW, Day BN, et al: The effect of confinement on days to puberty in gilts. J Anim Sci 62:1203, 1986

23. Cerne F: Induction of farrowing with cloprostenol on a commercial pig breeding farm in Yugoslavia. Vet Rec 103:469, 1978
24. Cerne F: Die einleitung der geburt beim schwein mit prostaglandinanalogen. Zuchthygiene 15:132, 1980
25. Cerne F, Jöchle W: Clinical evaluations of a new prostaglandin analog in pigs: 1. Control of parturition and of the MMA-Syndrome. Theriogenology 16:459, 1981
26. Christenson RK, Ford JJ: Puberty and estrus in confinement-reared gilts. J Anim Sci 49:743, 1979
27. Christenson RK, Pope CE, Zimmerman-Pope VA, et al: Synchronization of estrus and ovulation in superovulated gilts. J Anim Sci 36:914, 1973
28. Christenson RK, Teague HS: Synchronization of ovulation and artificial insemination of sows after lactation. J Anim Sci 41:560, 1975
29. Cole HH, Hughes EH: Induction of estrus in lactating sows with equine gonadotrophin. J Anim Sci 5:25, 1946
30. Crighton DB: Induction of pregnancy during lactation in the sow. J Reprod Fertil 22:223, 1970
31. Cronin GM, Hemsworth PH, Winfield CG, et al: The incidence of, and factors associated with, failure to mate by 245 days of age in the gilt. Anim Reprod Sci 5:199, 1982/1983
32. Dagorn J, Aumaitre A: Sow culling: Reasons for and effect on productivity. Livestock Prod Sci 6:167, 1979
33. Dalin AM, Einarsson S: Sexual maturity and anoestrus in gilts. Pig News and Information 3:299, 1986
34. D'Allaire S: Culling patterns in swine breeding herds [abstract]. *In* Swine Herd Health Programming Conference, St. Paul, MN, 1986, p 145
35. Dial GD, Almond GW, Hilley HD, et al: Oxytocin precipitation of prostaglandin-induced farrowing in swine: Determination of the optimal dose of oxytocin and optimal interval between prostaglandin $F_{2\alpha}$ and oxytocin. Am J Vet Res 48:966, 1987
36. Dial GD, BeVier GW, Hixon JE, et al: Endocrine pathogenesis of postweaning anestrus in swine: Response of the persistently anestrous sow to hormonal stimuli. Am J Vet Res 45:1737, 1984
37. Diehl JR, Day BN: Effect of prostaglandin $F_{2\alpha}$ on luteal function in swine. J Anim Sci 39:392, 1974
38. Dyck GW: Estrus and pregnancy in primiparous sows treated with pregnant mare's serum gonadotropin or estradiol-17$\beta$ and progesterone. Can J Anim Sci 56:693, 1976
39. Dziuk PJ, Baker RD: Induction and control of ovulation in swine. J Anim Sci 21:697, 1962
40. Dziuk PJ, Dhindsa DS: Induction of heat, ovulation and fertility in gilts with delayed puberty. J Anim Sci 29:39, 1969
41. Dziuk PJ, Polge C: Fertility in swine after induced ovulation. J Reprod Fertil 14:207, 1962
42. Dziuk PJ, Polge C: Fertility in gilts following induced ovulation. Vet Rec 77:236, 1965
43. Einarsson S: Comparative trial with natural prostaglandin and an analogue (cloprostenol) in inducing parturition in sows. Acta Vet Scand 77(suppl):321, 1981
44. Einarsson S, Fischier M, Karlberg K: Induction of parturition in sows using prostaglandin $F_{2\alpha}$ or the analogue cloprostenol. Nord Vet Med 33:354, 1981
45. Esbenshade KL, Ziecik AJ, Britt JH: Regulation and action of gonadotrophins in pigs. J Reprod Fertil Suppl 40:19, 1990
46. First NL, Bosc MJ: Proposed mechanisms controlling parturition and the induction of parturition in swine. J Anim Sci 48:1407, 1979
47. Fisher BA, Jensen AH, Diehl JR: Effect of PMS and PMS/HCG in the postweaning sow. J Anim Sci 43:283 [abstract 284], 1976
48. Foxcroft GR, Hunter MG: Basic physiology of follicular maturation in the pig. J Reprod Fertil Suppl 33:1, 1985
49. Guthrie HD: Induction of ovulation and fertility in prepuberal gilts. J Anim Sci 45:1360, 1977
50. Guthrie HD: Control of time of parturition in pigs. J Reprod Fertil Suppl 33:229, 1985
51. Guthrie HD, Hendricks DM, Handlin DL: Plasma hormone levels and fertility in pigs induced to superovulate with PMSG. J Reprod Fertil 41:361, 1974

52. Guthrie HD, Polge C: Control of oestrus and fertility in gilts with accessory corpora lutea by prostaglandin analogues, ICI 79,939 and ICI 80,996. J Reprod Fertil 48:427, 1976
53. Guthrie HD, Pursel VG, Frobish LT: Attempts to induce conception in lactating sows. J Anim Sci 47:1145, 1978
54. Hammond D, Matty G: A farrowing management system using cloprostenol to control the time of parturition. Vet Rec 106:72, 1980
55. Hansel W, Convey EM: Physiology of the estrous cycle. J Anim Sci 57(suppl 2):404, 1983
56. Hansen LH, Jacobsen MJ: Puerperalerkrankungen in einem MMA-Bestand nach prostaglandininduzierter geburt beim schwein. Tierärztl Praxis 5:325, 1977
57. Hausler CL, Hodson HH Jr, Kuo DC, et al: Induced ovulation and conception in lactating sows. J Anim Sci 50:773, 1980
58. Heap RB, Flint APF: Pregnancy. *In* Austin CR, Short RV (eds): Reproduction in Mammals: Hormonal Control of Reproduction, ed 2. Cambridge, Cambridge University Press, 1984, p 184
59. Holtz W, Schmidt-Baulain R, Meyer H, et al: Control of prostaglandin-induced parturition in sows by injection of the beta-adrenergic blocking agent carazolol, or carazolol and oxytocin. J Anim Sci 68:3967, 1990
60. Hühn R, König I, Hühn U, et al: Ergebnisse experimenteller untersuchungen zur beeinflussung der geburt beim schwein. Arch Exp Vet Med 31:921, 1977
61. Hühn R, Lutter K, Hühn U: Untersuchungen zum einfluß der biotechnischen geburtsauslösung auf ausgewählte leistungen von partussauen und ferkeln. Arch Exp Vet Med 34:175, 1980
62. Hughes PE: Factors affecting the natural attainment of puberty in the gilt. *In* Cole DJA, Foxcroft GR (eds): Control of Pig Reproduction. London, Butterworths, 1982, p 117
63. Humke VR, Seidel L, Scherp H: Untersuchungen zur geburtsinduktion beim schwein mit dem luteolytisch wirksamen prostaglandin $F_{2\alpha}$ analogen HR 837. Dtsch Tierärztl Wschr 86:221, 1979
64. Hunter RHF: Porcine ovulation after injection of human chorionic gonadotrophin. Vet Rec 81:21, 1967
65. Hunter RHF: Ovulation in the pig: Timing of the response to injection of human chorionic gonadotrophin. Res Vet Sci 13:356, 1972
66. Hunter RHF: Physiological factors influencing ovulation, fertilization, early embryonic development and establishment of pregnancy in pigs. Br Vet J 133:461, 1977
67. Hurtgen JP, Leman AD: Use of PMSG in the prevention of seasonal post-weaning anestrus in sows. Theriogenology 12:207, 1979
68. Hurtgen JP, Leman AD, Crabo B: Seasonal influence on estrous activity in sows and gilts. J Am Vet Med Assoc 176:119, 1980
69. Jainudeen MR, Brandenburg AC: Induction of parturition in crossbred sows with cloprostenol, an analogue of prostaglandin $F_{2\alpha}$. Anim Reprod Sci 3:161, 1980
70. Karlberg K: Factors affecting postweaning oestrus in the sow. Nord Vet Med 21:105, 1980
71. Kilian DB, Davis DL, Long TP, et al: Effects of $PGF_2$ alpha and ovariectomy in pregnant gilts [abstract 459]. J Anim Sci 41:361, 1975
72. King GJ: Deformities in piglets following administration of methallibure during specific stages of gestation. J Reprod Fertil 20:551, 1969
73. King GJ, Robertson HA, Elliot JI: Induced parturition in swine herds. Can Vet J 20:157, 1979
74. King GJ, Walton JS, Bosu WTK: Potential treatments for anestrus in gilts and sows. Can Vet J 23:288, 1982
75. King RH, Williams IH, Barker I: Induction of oestrus in anoestrus, first litter sows with pregnant mares' serum gonadotrophin. Anim Reprod Sci 5:41, 1982
76. Kraeling RR, Barb CR: Hypothalamic control of gonadotrophin and prolactin secretion in pigs. J Reprod Fertil Suppl 40:3, 1990
77. Kraeling RR, Rampacek GB: Susceptibility of the pig corpus luteum to $PGF_{2\ alpha}$ at various stages of pregnancy [abstract 452]. J Anim Sci 45(suppl 1):180, 1977
78. Kraeling RR, Rampacek GB: Synchronization of estrus and ovulation in gilts with estradiol and prostaglandin $F_{2\alpha}$. Theriogenology 8:103, 1977
79. Lancaster RT, Foxcroft GR, Boland MP, et al: Fertility of sows injected with exogenous

estradiol and/or gonadotrophins to control postweaning estrus. Anim Reprod Sci 8:365, 1985
80. Longenecker DE, Day BN: Fertility level of sows superovulated at post-weaning estrus. J Anim Sci 27:709, 1968
81. Love RJ: Definition of a seasonal infertility problem in pigs. Vet Rec 103:443, 1978
82. Lutz JB, Rampacek GB, Kraeling RR: Induction of ovulation in the prepubertal gilt by pulsatile administration of gonadotropin releasing hormone. Domest Anim Endocrinol 2:61, 1985
83. Martin PA, Hammitt DG, Strohbehn RS, et al: Induction of parturition in swine with epostane, a competitive inhibitor of 3$\beta$-hydroxysteroid dehydrogenase. J Anim Sci 64:497, 1987
84. Martinat-Botté F, Bariteau F, Badouard B, et al: Control of pig reproduction in a breeding programme. J Reprod Fertil Suppl 33:211, 1985
85. Maurer RR, Ford JJ, Christenson RK: Interval to first postweaning estrus and causes for leaving the breeding herd in Large White, Landrace, Yorkshire and Chester White females after three parities. J Anim Sci 61:1327, 1985
86. Meredith MJ: The treatment of anoestrus in the pig. A review. Vet Rec 104:25, 1979
87. Nagy A: Retard of the farrow before hysterectomie for safety of the operation on the 114th day of pregnancy. *In* Proceedings Sixth International Pig Veterinary Congress, Mexico City, 1982, p 247
88. Neill JD, Day BN: Relationship of development stage to regression of the corpus luteum in swine. Endocrinology 74:335, 1964
89. Paterson AM: The controlled induction of puberty. *In* Cole DJA, Foxcroft GR (eds): Control of Pig Reproduction. London, Butterworths, 1982, p 139
90. Peet B: British standards of longevity. *In* Swine Herd Health Programming Conference, St Paul, 1986, p 161
91. Pejsak Z, Hogg A: The effect of hormonal preparations on ovulation and estrus induction in gilts and sows [abstract]. *In* The George A. Young Swine Conference & Annual Nebraska SPF Swine Conference, Lincoln, NE, 1990, p 106
92. Polge C: Effective synchronisation of oestrus in pigs after treatment with ICI compound 33828. Vet Rec 77:232, 1965
93. Polge C, Day BN, Groves TW: Synchronisation of ovulation and artificial insemination in pigs. Vet Rec 83:136, 1968
94. Pope WF, Wilde MH, Xie S: Effect of electrocautery of nonovulated day 1 follicles on subsequent morphological variation among day 11 porcine embryos. Biol Reprod 39:882, 1988
95. Pope WF, Xie S, Broermann DM, et al: Causes and consequences of early embryonic diversity in pigs. J Reprod Fertil Suppl 40:251, 1990
96. Pressing A, Dial GD, Esbenshade KL, et al: Hourly administration of GnRH to prepubertal gilts: Endocrine and ovulatory responses from 70 to 190 days of age. J Anim Sci 70:232, 1992
97. Pressing A, Dial GD, Stroud CM, et al: Prostaglandin-induced abortion in swine: Endocrine changes and influence on subsequent reproductive activity. Am J Vet Res 48:45, 1987
98. Rampacek GB, Kraeling RR, Kiser TE: Delayed puberty in gilts in total confinement. Theriogenology 15:491, 1981
99. Richter L, Westendorf P: Untersuchungen zur verbesserung der reproduktionsleistung bei sauen nach dem ersten wurf durch hormonale brunststimulation. Dtsch Tierärztl Wschr 89:81, 1982
100. Rojanasthien S, Kunavongkrit A, Einarsson S: Luteinizing hormone (LH) response to different doses of synthetic gonadotropin releasing hormone (GnRH) in prepubertal gilts. Acta Vet Scand 27:257, 1986
101. Roost H, Weichelt U, Weichelt K, et al: Erfahrungen und ergebnisse bei der durchführung der partiellen geburtsinduktion bei sauen der F 150 in einer 1000er sauenanlage. Mh Vet Med 41:118, 1986
102. Schilling E, Cerne F: Induction and synchronization of estrus in prepuberal gilts and anestrous sows by a PMSG/HCG-compound. Vet Rec 91:471, 1972
103. Schlegel W, Ahrens M, Braune S: Weitere untersuchungen zur unterschiedlichen dosierung von HCG bei der ovulationssynchronisation der jungsauen. Mh Vet Med 31:574, 1976

104. Schlegal W, Braune S, Ahrens M: Vergleichende untersuchungen zum einsatz von 500 bzw. 250 IE HCG bei der ovulationssynchronisation der jungsauen. Mh Vet Med 31:571, 1976
105. Schlegel W, Heinze A, Fleischer R, et al: Untersuchungen zum einfluß von PMSG/HCG-gemischen auf die ovarien und uteri von jungsauen bei einem einsatz zur zyklusstimulation im rahmen der pubertätsinduktion zur vorverlegung des erstbesamungsalters. Arch Exp Vet Med 37:899, 1983
106. Schlegel W, Krebs R, Braune S, et al: Untersuchungen zum ovulationsverlauf nach biotechnischer pubertätsinduktion von jungsauen. Arch Exp Vet Med 31:439, 1977
107. Seerly RW, Ray DE, Fritschen RD: Estrus synchronization, an experiment which could lead to better timed swine breeding and farrowing. South Dakota Farm Home Res 14:7, 1967
108. Seyfarth D, Keil W, Schlenker G: Analyse der nutzungsdauer von sauen einschliesslich abgangsursachen in der DDR. Mh Vet Med 24:921, 1981
109. Smith WC, Alley MR, Holmes RJ, et al: The induction of parturition in sows using prostaglandin $F_{2\alpha}$. N Z Vet J 30:34, 1982
110. Silver M, Comline RS, Fowden AL: Fetal and maternal endocrine changes during the induction of parturition with the PGF analogue, cloprostenol, in chronically catheterized sows and fetuses. J Dev Physiol 5:307, 1983
111. Stevenson JS, Pollman DS, Davis DL, et al: Influence of supplemental light on sow performance during and after lactation. J Anim Sci 56:1282, 1983
112. Stone MW: Sow culling survey in Alberta. Can Vet J 22:363, 1981
113. Stork MG: Seasonal reproductive inefficiency in large pig breeding units in Britain. Vet Rec 104:49, 1979
114. Varley MA, English PR, Davidson FM, et al: Control of estrus and ovulation in peripubertal gilts with allytrenbolone or a combination of natural gonadotrophins. Vet Rec 124:186, 1989
115. Wähner M, Schlegel W, Wierzbowski A, et al: Untersuchungen zum einsatz von FSH/HCG-gemischen zur pubertätsinduktion von jungsauen und deren einfluß auf follikelreifung und -bildung sowie Uterusentwicklung im 2. östrus. Mh Vet Med 37:529, 1982
116. Wendler A: Utilizing a farrowing attendant to achieve 95% survival. Compend Contin Educ Pract Vet 10:21, 1988
117. Webel SK, Day BN: The control of ovulation. *In* Cole DJA, Foxcroft GR (eds): Control of Pig Reproduction. London, Butterworths, 1982, p 197
118. Webster WR: Evaluation of a pregnant mares' serum and human chorionic gonadotrophin mixture for alleviating summer infertility in sows. Aust Vet J 54:26, 1978
119. Welp C, Jöchle W, Holtz W: Induction of parturition in swine with a prostaglandin analog and oxytocin: A trial involving dose of oxytocin and parity. Theriogenology 22:509, 1984
120. Whyte PBD: The induction of oestrus in recently weaned sows with low doses of gonadotrophins. J South Afr Vet Assoc 48:129, 1977
121. Widowski TM, Curtis SE: Behavioral responses of periparturient sows and juvenile pigs to prostaglandin $F_{2\alpha}$. J Anim Sci 67:3266, 1989
122. Widowski TM, Curtis SE, Dziuk PJ, et al: Behavioral and endocrine responses of sows to prostaglandin $PGF_{2\alpha}$ and cloprostenol. Biol Reprod 43:290, 1990
123. Xie S, Broermann DM, Nephew KP, et al: Ovulation and early embryogenesis in swine. Biol Reprod 43:236, 1990
124. Young IM, Harvey MJA: Routine induction of farrowing with dinoprost in a commercial sow breeding unit over a year. Vet Rec 115:539, 1984
125. Zerobin K, Kundig H: The control of myometrial functions during parturition with a $\beta_2$-mimic compound, planipart. Theriogenology 14:21, 1980