PHYSIOLOGY AND ENDOCRINOLOGY SYMPOSIUM: Factors influencing follicle development in gilts and sows and management strategies used to regulate growth for control of estrus and ovulation¹

Robert V. Knox²

Department of Animal Sciences, University of Illinois, Urbana-Champaign, IL 61801

ABSTRACT: Factors that affect follicle health and growth can influence estrus, ovulation, conception, and litter size. Since the majority of the breeding herd is composed of sows, production schedules are established based on synchronized follicle growth following weaning. Insemination of sows over a 3- to 4-d period after weaning facilitates farrowing over fewer days and helps improve the uniformity of pigs at weaning. Synchronized inseminations of the group are reduced when disturbance to the follicular phase results in delayed estrus. The failure of >15 follicles to uniformly progress beyond the 6.0 mm size within 4 d during the follicular phase is associated with delayed estrus and ovulation, reduced ovulation rate, and reduced farrowing rate. In sows, the follicular phase is initiated at weaning by removal of the suckling inhibition, whereas in cycling gilts, luteolysis and clearance of progesterone begins the process. The timing and patterns of follicle-stimulating hormone and luteinizing hormone stimulation to the ovary determine follicle

health and selection for ovulation. Interestingly, abnormal wean-to-estrus intervals in sows and deviations from a 19- to 22-d estrous cycle in gilts are associated with reduced fertility. However, in both cases, it is not entirely clear whether the abnormal intervals are a direct result of problems occurring prior to or only during the follicular phase. In prepubertal gilts, the signal for initiating the follicular phase remains elusive, but could reside in differential sensitivity and response to hormone signals at the level of the ovary and brain. Although the mechanisms are not clear, factors such as boar exposure, stress, feed intake, growth rate, and birthweight have been shown to stimulate an early follicular phase. In contrast, inhibitors to follicle growth have been associated with season, heat stress, photoperiod, negative energy balance, poor body condition, slow growth, fewer parities, and short lactation length. Hormonal aids for inducing and delaying the follicular phase, as well as for inducing ovulation are available to aid in synchronized breeding schedules.

Key words: estrus, follicular phase, gilt, infertility, puberty, sow

© The Author(s) 2019. Published by Oxford University Press on behalf of the American Society of Animal Science. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

J. Anim. Sci. 2019.97:1433–1445
doi: 10.1093/jas/skz036

¹Based on presentation given at the Physiology and Endocrinology Symposium: Regulation of the Growing Follicle Pool-Basic and Applied Aspects titled “Factors influencing follicle development in gilts and sows and management strategies used to regulate growth for control of estrus and ovulation” at the 2018 Annual Meeting of the American Society of Animal Science held in Vancouver, BC, Canada, July 8–12, with publication sponsored by the *Journal of Animal Science* and the American Society of Animal Science.

²Corresponding author: rknox@illinois.edu

Received October 1, 2018.

Accepted January 21, 2019.

INTRODUCTION

The initiation of the follicular phase is a critical starting point for fertility in pigs and results in the overt symptoms of puberty, regular cyclic activity, and expression of estrus after weaning in sows. The modern swine production industry relies on the consistent and predictable flow of pigs into the food chain. For the purposes of efficiency and disease control, pigs are often produced and managed from birth to market in batches with little spread in age. A small spread in age requires that

weaned sows and replacement gilts are detected in estrus and inseminated within only few days of each other. This is important since schedules for batch production of pigs are established by weaning a group of sows on the same day. The larger the spread in breeding days, the greater the spread in farrowing days, and the more variation there will be in sow fertility and piglet age at weaning. The significance of this means that pig production schedules are established by the onset of the follicular phase and expression of estrus. Although there appears to be many similarities for how follicles are selected for ovulation, there may also be differences due to physiological stage of animal maturity. For example, immature gilts must grow quickly to reach pubertal body weight at an early age, whereas mature cycling gilts need to reach and remain in the optimum breeding weight range, and lactating sows must minimize loss of body weight and condition prior to breeding (Soede et al., 2011). It is not clear if the endocrine status before or at the start of the follicular phase affects follicle size, numbers, and their health, but if involved, this could implicate progesterone in cyclic gilts and prolactin in weaned sows. Other factors can also enhance or inhibit the follicular phase in pigs with either outcome most readily apparent by expression of or failure to display estrus within a defined number of days or weeks from starting boar exposure, the previous estrus, weaning, or gonadotropin treatment.

The follicular phase in the pig has been an important focus for research as it determines both expression of estrus and ovulation (Foxcroft and Hunter, 1985). The entire phase also regulates the number of follicles that survive and grow to ovulate and the quality of their ova. The number of follicles that ovulate (ovulation rate) is the first limit to litter size in the pig, one of the most economically important reproductive traits (Clutter 2009). Over the years, advanced selection methods using extensive records from animals and their relatives have helped to gradually increase litter size, despite being a lowly heritable trait (Kemp and Soede, 2012). However, with increased litter size, the frequency of lightweight pigs has also increased (Baxter and Edwards, 2013). These lightweight pigs have lower survival and poorer growth throughout life. The problem could originate from increased ovulation rate and the resulting uterine crowding (Town et al., 2005). Because ovulation rate is moderately heritable and positively correlated with litter size, females with high ovulation rate tend to show embryo crowding, with negative effects on placental

development and piglet birthweight (Town et al., 2005; Da Silva et al., 2017a).

THE PHYSIOLOGY OF THE FOLLICULAR PHASE

The physiology of the estrous cycle and follicular phase in pigs has been extensively reviewed (Foxcroft and Hunter, 1985; Guthrie, 2005; Knox, 2005; Soede et al., 2011) and so only a brief summary will be presented. The follicular phase typically lasts 4 to 6 d in pigs, and among weaned sows and gilts, the sizes of the follicles and the hormones involved show similar patterns in progression toward ovulation. The patterns of reproductive hormones before and after ovulation, and pictures of the ovaries, and associated ultrasound image are shown in Fig. 1. Although there may be various populations of small- and medium-sized follicles on the ovaries during lactation, the luteal phase, and in the months and weeks before puberty, large ovulatory-sized follicles only appear on the days just before expression of estrus.

In describing follicle populations, differences in follicle counts can change based on the method of measurement and the classification of their size (Table 1). For example, surface measures of follicles tend to be slightly larger than real-time ultrasound measures. This could result because ultrasound is used to measure the diameter of the nonechoic follicular fluid space, whereas surface measures also include the tunica and germinal epithelium layers. There is general consensus that antral surface follicles can be classified as small, medium, large, and cystic (Knox 2005). There are numerous small-sized follicles present at the start of the follicular phase; however, these rapidly decline in number as a result of atresia (Fig. 2). By mid-follicular phase, only 40% of the medium follicles present are still healthy (Guthrie et al., 1995). Small follicles have predominantly follicle-stimulating hormone (FSH) receptors (Liu et al., 2000) and their decline in numbers is associated with a reduction in FSH early in the follicular phase. Medium-sized follicles have both FSH and luteinizing hormone (LH) receptors and can produce estrogen and inhibin. It is possible that competition for binding FSH and LH determines the growth and health of follicles selected to ovulate. The large-sized follicles have predominantly LH receptors and show no evidence of atresia during the peri-estrous period. At estrus, the follicles present can be heterogeneous in size, granulosa cell numbers, and estrogen (Hunter and Wiesak, 1990). Most ultrasound data identify

Figure 1. Patterns (a) for the major reproductive hormones during the follicular phase of the estrous cycle in pigs and (b) associated ultrasound images showing small, medium, and large follicles, and corpora hemorrhagica (L-R). E2 = estradiol; GnRH = gonadotropin-releasing hormone; LH = luteinizing hormone; FSH = follicle-stimulating hormone, and P4 = progesterone.

Table 1. In weaned sows ($n = 21$), ovarian follicles assessed ($n = 597/d$) by size class * for numbers on days 1 and 2 of estrus

Follicle Class	Size, mm	d 1	d 2
Small	<3.5	2.5	0.5
Medium 1 (M1)	3.5–4.99	6.5	4.5
Medium 2 (M2)	5.0–6.49	14.9	14.2
Large 1 (L1)	6.5–7.99	6.8	9.1
Large 2 (L2)	8.0–9.99	2.1	2.0
Large 3 (L3)	10.0–11.99	1.2	2.2

*Data obtained from digital recordings of ovarian ultrasound at 24-h intervals.

large follicles averaging 7 to 8 mm at estrus (Nissen et al., 1997; Lucy et al., 2001; Knox et al., 2002), but these measures can also vary by parity (Ulguim et al., 2018) and among sows before ovulation (Soede et al., 1998). Soede et al. (1992) counted all follicles >4 mm at estrus and observed counts were closely related to number of corpora lutea (CL). Knox and Rodriguez-Zas (2001) reported a 0.3- to 0.8-mm increase in average size of the largest follicles from the first to the second day of estrus. The numbers and sizes of the follicles that are present and the proportion of sows with those classes are

shown in Fig. 3a and b. Nearly all sows have M1- to L1-sized follicles, but very few have small or L3 follicles. These data indicate between sow variation for the largest and smallest follicles. It is also notable that few M1 follicles are present at estrus, but numerous M2 follicles are present on both days of estrus. In weaned sows, the number of large follicles (≥ 6.5 mm) at estrus (Table 1) does not account for the number of CL (18 to 23) counted on day 30 of gestation (Knox et al., 2018). This suggests that the M2- and larger-sized follicles present at estrus ovulate in response to the LH surge and form CL. It is not clear if the observed variation in follicle size at estrus results in variation in CL size. However, a recent study indicated that within sow, there appears to be little variation in CL size (Da Silva et al., 2017b). In sows, ovulation is reported to occur over 1 to 3 h (Flowers and Esbenschade, 1993), but in some females, there is evidence that a few follicles ovulate late and contribute to increased embryonic loss (Pope et al., 1988; Pope et al., 1990). When follicles are synchronized to ovulate, the duration of ovulation is not related to variation in early embryo cell numbers (Soede and Kemp, 1993). However, it is possible that under less favorable

Figure 2. In sows ($n = 16$), numbers of follicles ($n = 2,203$) assessed for size classification* on days 1 through 5 after weaning. Data obtained from digital recordings of ovarian ultrasound scans. *See Table 1.

Figure 3. In weaned sows ($n = 21$), follicles assessed ($n = 597/d$) by size class* for numbers (a) and proportion of sows with that class (b) on days 1 and 2 of estrus. Data obtained from digital recordings of ovarian ultrasound at 24-h intervals. *See Table 1.

scenarios where the quality of selectable follicles is limiting, asynchronous follicle development may occur. In this situation, the medium-sized follicles present at estrus may not respond to the LH surge at the same rate and manner as the larger follicles

and could therefore be delayed in their progression toward ovulation. Because it has been reported that the ova from smaller follicles are less competent to develop into embryos (Bagg et al., 2007), it could also be likely that these follicles if ovulated would

form smaller-sized or less functional CL. Although gonadotropin-releasing hormone (GnRH) agonist induction of ovulation advances and synchronizes a group of sows with large follicles to ovulate within 24 h of each other (Knox et al., 2017), it is not clear what size follicles ovulate, whether the interval to ovulation is similar for different-sized follicles, and what impact follicle size will have on formation and function of the CL.

THE PHYSIOLOGY OF THE FOLLICULAR PHASE IN PREPUBERTAL GILTS

The endocrine signal that initiates puberty remains elusive. Well ahead of the time when gilts display pubertal estrus, the ovaries can respond to exogenous hormones such as equine chorionic gonadotropin (eCG; i.e., pregnant mare's serum gonadotropin) and human chorionic gonadotropin (hCG) to grow and ovulate follicles. In addition, exogenous GnRH can induce LH release and the hypothalamic pituitary axis (HPX) can respond to estrogen feedback (Elsaesser, 1982; Paterson, 1982; Christenson et al., 1985). However, these responses to exogenous hormones may not indicate full maturity and normal function in response to endogenous hormone concentrations. Perhaps the best evidence to support this concept is that there is considerable variation in the gilt response to the exogenous hormones in large follicle development, ovulation rate, expression of estrus, and estrous cycle length. For example, when prepubertal gilts are treated with PG600, 20% may not develop large follicles, and another 10% to 20% may ovulate but fail to express estrus (Knox et al., 2000). This response does improve significantly with age, boar exposure (Breen et al., 2005) or dose of gonadotropin (Breen et al., 2006). In the weeks before puberty, the ovaries of gilts are characterized as honeycomb (1- to 3-mm follicles), grape (≥ 6 mm), or intermediate (Grasso et al., 1988) type. The classification, however, is unrelated to days to puberty and the ovary switches in type classification between 140 to 180 d of age (Dufour et al., 1985). It also appears that in the prepubertal gilt, follicles are recruited in waves, but only grow to ~ 6 mm in size before undergoing atresia. Our ultrasound observations (unpublished) support this and indicate that for gilts not receiving boar exposure, by 180 d of age, the majority of females (75%) had follicles that were < 5 mm in size. Perhaps of more importance, Christenson et al. (1985) noted that at 130 d of age, the majority of follicles present on the gilt ovary are not healthy. It is not clear if the rate of atresia changes as the gilts near maturity.

Although data are limited, observations suggest that maturation of the HPX may be incomplete and a limiting factor to puberty. Barb et al. (2010) observed that LH pulse frequency increased in response to exogenous estrogen between days 90 to 150 and 150 to 200 of age. Additional data reviewed by Christenson et al. (1985) noted that although FSH and LH concentrations were doubled in ovariectomized (OVX) gilts, there were no remarkable changes in the patterns of their release when compared with intact gilts up to ~ 180 d of age. Furthermore, there were no differences in the concentration of estrogen in blood during these periods in OVX and intact gilts. Collectively the data suggest that without stimulation, the majority of gilts have an immature HPX and ovary at 26 wk of age. The gonadostat theory indicates that the pubertal follicular phase is initiated by an increase in LH pulse frequency resulting from a change in sensitivity of the HPX to negative feedback from low concentrations of circulating estrogen (Hughes, 1982). However, the inability of the follicles to respond and release an estrogen surge may also be involved (Elsaesser, 1982). Blood samples obtained before the follicular phase at puberty show no remarkable patterns above baseline for LH, estrogen, or progesterone (Karlsson et al., 1982).

The permissive conditions that allow release of gonadotropins and maturation of ovarian follicles may depend upon signals that are received in relation to body weight and fat (Foxcroft et al., 2001), growth rate and age (Tummaruk et al., 2001; Amaral Filha et al., 2009), or environment (Hughes et al., 1990). It is difficult to separate out these effects, but gilts that exhibit slow growth are lighter and have less backfat at selection, tend to show delayed puberty, and are more likely to be culled (Magnabosco et al., 2016).

Delayed puberty and anestrus are leading problems for commercial breeding farms that raise replacement gilts (Knox et al., 2013). Among herds, 10% to 30% of gilts fail to display estrus within 60 to 80 d of boar exposure. At slaughter, half of these gilts will show inactive ovaries with only small- to medium-sized follicles, whereas the other half will have CL (Heinonen et al., 1998). The reasons that half of the gilts displayed silent heat are uncertain, but stronger symptoms of standing, longer estrus, and swollen vulvas are each associated with earlier puberty (Eliasson, 1991; Rydhmer et al., 1994; Romoser et al., 2017). There are perceptions that silent heat results from less effective estrous detection. And although this may be true in some cases, silent heat is also reported in many research studies

with controlled estrous detection procedures, high rates of estrous expression, and with estradiol concentrations elevated in circulation (Hughes, 1982). These observations appear to point to an underdeveloped HPX that is unable to mount a positive feedback response to low concentrations of circulating estrogen.

Several factors have been identified as inhibitors to early puberty in gilts (Cronin et al., 1983). In recent years, focus on gilt development and sow longevity has identified litter of origin, birthweight, growth rate, and body composition as key factors. Almeida et al. (2017b) reported that low birthweight gilts had different populations of follicles on the ovary when approaching expected age at puberty (Almeida et al., 2017a). In addition, low birthweight gilts have slower growth and often cannot achieve the target growth rate of 600 g/d at the time of selection (Kummer et al., 2009). Smaller birthweight pigs may be less competitive during lactation and development in nutrient intake and feed conversion, and as a consequence grow slower and reach puberty later. Miller et al. (2011) reported that moderate feed restriction during gilt development reduced weight gain, delayed puberty, and reduced expression of estrus. Similarly, limiting feed during development to produce light weight gilts at 160 d, reduced the numbers of follicles >3 mm, and appears to implicate ovarian follicle populations in effects on the timing of puberty (van Wetters et al., 2011). Stress effects on follicle development are not clear, but Young et al. (2008) reported that space restriction during development delayed puberty, while having no effect on growth rate (850 g/d). This effect is interesting, but could also result from lower boar contact quality under crowded conditions. Reviews of the effects of stress on follicle growth and expression of estrus often show inconsistent responses and may result from individual animal risk factors, the type and severity of the stress, and when the stress is applied (Einarsson et al., 2008). Seasonal infertility often associates with heat stress and photoperiod and continues to be a significant problem for commercial swine production (Hurtgen and Leman, 1980; Peltoniemi and Virolainen, 2006). In commercial barns using advanced temperature and lighting control systems, 10% to 20% of age-matched gilts still show delayed puberty or anestrus. This failure rate, while seemingly low, causes significant challenges to production systems due to limited housing space and the continual need for replacement females. The inability to predict the extent, timing, and the type of fertility failure for the gilts suggests

more complex interactions are involved. If multiple factors are involved, then for an individual gilt, any single factor in the complex could wind up becoming the deciding factor for the fertility response. This scenario would make diagnosis difficult as the problem might link to a single or even multiple reproductive pathways. The best example of a multifactor complex on fertility would include season. Seasonal delays in puberty attributed to photoperiod can be advanced by melatonin administration to prepubertal gilts during development (Diekmann et al., 1991; Paterson et al., 1992). In addition, prepubertal gilts exposed to heat stress show reduced pituitary FSH and LH, lower follicle numbers, delayed puberty, and lower ovarian response to exogenous gonadotropins (Flowers et al., 1989; Flowers and Day, 1990). Taken together, a multifactorial approach to discovering the source of failure may be required in order to link the symptoms and pathways in the different gilts.

Enhancers to induce a follicular phase in days or weeks following a stimulus have been reported. The best studied of these involves the boar exposure effect. Prepubertal gilts that have reached a minimum stage of maturity can respond to boar exposure, with the response noted in the number of days to puberty. The proportion of gilts responding synchronously also increases with age (van Wetters et al., 2006). Age at exposure or introduction appears important because Eastham et al. (1984) observed that rearing gilts with boars during development have no effect on advancing age at puberty. Pearce and Hughes (1987) investigated the components of the boar to stimulate puberty and concluded that olfactory stimuli had the greatest impact, but that tactile, auditory, and visual cues were also important. Boar pheromones identified in saliva influence gilts through nasal receptors and the olfactory bulb (Kirkwood et al., 1981). Melrose et al. (1971) reported that 5 α -androst-16-en-3-one is one of the key boar pheromones and spraying it into the nose of gilts induced approximately half to stand in respond to the backpressure test, whereas the saline spray induced none to stand. The mechanism of the boar effect for inducing follicle development in gilts is still unclear, but it is thought to be mediated by a change in LH pulse frequency, although the data are limited and not conclusive (Hughes et al., 1990; Langendijk et al., 2006). Despite an unknown pathway, the effect of the boar on puberty can be altered by changing the duration and intensity of exposure (Caton et al., 1986; Paterson et al., 1989) and the boar used (Signoret et al., 1990). The intensity effect is evident in commercial settings as Kaneko

and Koketsu (2012) used record analysis to show that farms using direct boar contact reported earlier age (–13 d) at first service than those using indirect boar contact. Controlled studies have also shown that physical boar contact is superior to fenceline exposure for advancing puberty, likely due to the efficiency of close contact pheromone transfer (Pearce and Paterson, 1992; Zimmerman et al., 1998). In addition to boar exposure, the added effects of transport, relocation, and mixing have been shown in research and commercial settings to induce a synchronized estrus in a proportion of gilts within 5 to 7 d of the events (Eastham et al., 1986; Signoret et al., 1990).

It would appear that the ultimate limiting factor in the attainment of puberty in gilts is gonadotropin stimulation to the ovary, because a high proportion of prepubertal gilts express a fertile estrus soon after treatment with eCG and hCG (Schilling and Cerne, 1972; Britt et al., 1989; Sporke et al., 2005). These gonadotropins have potent FSH- and LH-like activity and select medium-sized follicles to grow to ovulatory size and increase their production of estrogen, with behavioral estrous expression occurring 4 to 5 d after treatment. The combination of eCG and hCG in effective doses induces a synchronized ovulation of a normal number of large follicles. However, with dosing changes, and abnormal ovary responsiveness, follicles may develop out of synchrony and fail to ovulate. As a result, follicles could grow faster and ovulate early or grow slower and fail to ovulate. This could affect expression of estrus and formation of cysts (Breen et al., 2006). Although not reported at high rates, mono and polycystic follicle development can have detectable effects on fertility and have been associated with the reproductive tracts of culled females (Heinonen et al., 1998; Almond, 2007).

THE FOLLICULAR PHASE IN MATURE CYCLING GILTS

The first detected estrus in gilts prior to 30 wk of age is often classified in the commercial swine industry as a heat-no-serve (HNS). This is the first indicator of puberty in the selected gilt and this designation implies the female should cycle once more to reach maturity before insemination at second estrus. In commercial breeding farms, gilts are housed in small to large groups for puberty induction and estrous detection. Following identification of a HNS, these gilts are often marked and relocated to a stall for breeding. Once gilts begin to cycle, the expected estrous cycle length is

based on a 21-d average, but includes a 19- to 22-d range. There are, however, concerns of gilts failing to cycle a second time or showing irregular estrous intervals (Knox et al., 2013). In one study examining hormone concentrations in gilts exhibiting extended estrous cycles, progesterone remained elevated for an additional 5 to 6 d, whereas the follicular phase was of normal duration (Knox et al., 2003). A recent report indicated that the timing of relocation of pubertal gilts from pens to stalls prior to breeding affected cycle length in a small proportion of the gilts (Knox et al., 2016). Gilts moved to stalls in the first week during formation of CL had shorter estrous cycles, whereas those moved in the last week before insemination exhibited longer intervals. In each case, fertility was reduced when compared with gilts with normal cycle lengths.

During the luteal phase, FSH is elevated and LH is low, and numerous small and medium follicles are present on the ovaries of gilts. Although many of the follicles are atretic, their proportions are unrelated to size of the follicle or day of the luteal phase (Guthrie and Cooper, 1996). In the mature gilt, luteolysis associated with the decline in progesterone (Guthrie and Polge, 1976) initiates the follicular phase with hormones and follicle populations changing abruptly in just a few days (Foxcroft and van de Wiel, 1982; Guthrie, 2005). The length of the follicular phase does not differ (6.5 d) in high- and low-ovulating gilts (Knox et al., 2003), in duration (5.8 d) following induced luteolysis (Knox and Zimmerman, 1993), or withdrawal of progestagen (Kraeling et al., 1981; Stevenson and Davis, 1982). Exogenous manipulation of FSH and LH during the follicular phase can affect follicle health, selection, and ovulation rate. In genetic lines of pigs selected for increased ovulation rate, differences in FSH in the late luteal and early follicular phases influence follicle populations before ovulation. Higher ovulation rate appears to result from a greater proportion of medium-sized follicles (>5 mm) that can remain healthy later into the follicular phase (Yen et al., 2005). It would appear that limiting concentrations of FSH at the start of the follicular phase may be determined by the production of inhibin by the medium-sized follicles. Noguchi et al. (2010) reported FSH concentrations in the follicular phase were inversely related to inhibin A, with greater production of this hormone by the large follicles approaching estrus.

There are few studies that have indicated a stimulatory effect of boar exposure during the estrous cycle on expression of a second estrus, but the data that are available suggest a positive effect (Paterson

and Lindsay, 1981; Bartlett et al., 2009). Feeding level can also influence ovulation rate and interval to estrus. Increased energy during the second half of the estrous cycle (flushing) increased ovulation rate (Rhodes et al., 1991), whereas low feeding levels reduced size of follicles, ovulation rate, and embryos (Chen et al., 2012). Under controlled conditions, no effect of moderate heat stress or differing light intensity could be shown on follicle development, interval to estrus, estrus expression, or on ovulation rate (Canaday et al., 2013). However, under commercial conditions, the incidence of long- and short-estrous cycles was increased within season.

THE FOLLICULAR PHASE IN WEANED SOWS

As 75% of most breeding groups are composed of sows, labor, estrous detection, semen delivery, and insemination are scheduled based on day of weaning. A predictable timing for estrus relies on the initiation of the follicular phase soon after weaning. Although sows are the most fertile females on the farm in terms of pig production (Koketsu and Dial, 1997), they are also highly susceptible to reproductive failure due to their metabolic and physiological state after lactation. The follicles and hormone patterns during later lactation and during the follicular phase following weaning are similar to those of gilts. There are numerous follicles <5 mm present on the ovary during lactation, with populations changing in size, numbers, and atresia (Britt et al., 1985). It would appear that elevated prolactin and the negative inhibition of the nursing stimulus suppresses follicle health and the follicular phase. At weaning, both effects are removed and the typical endocrine and follicle changes progress toward ovulation (Foxcroft et al., 1987; Soede et al., 2011). Although the majority of sows return to estrus within 4 to 6 d after weaning, variation in the wean-to-estrus interval (Weitze et al., 1994) and its effects on fertility (Kemp and Soede 1996) are important. Factors associated with variation in the wean-to-estrus interval include season, parity, lactation length, and farm (Britt et al., 1983; Knox and Rodriguez-Zas, 2001; Belstra et al., 2004; De Rensis et al., 2017). The risks for delayed return to estrus increase when combined with summer and fall, young parity sows, and short lactation lengths. Interestingly, in several controlled research studies, the effects of heat stress on wean-to-estrus interval in primiparous sows are not apparent (Williams et al., 2013). This may lend further support to the notion that multiple factors must be involved in the

origin of the problem. However, under commercial conditions, seasonal infertility effects are common, with one study reporting smaller and fewer numbers of follicles at weaning and prior to ovulation (Lopes et al., 2014). This matches the observations of Lucy et al. (2001) that associated a pattern of delayed follicle development with an extended wean-to-estrus interval. In anestrus sows following weaning, reduced concentrations of LH have been detected (van de Wiel and Booman, 1993). Treating sows with gonadotropins at weaning improves estrus expression, most notably in young parity sows during summer and fall (Bates et al., 1991; De Rensis et al., 2017). Similar to gilts, boar exposure improves expression of estrus and ovulation in primiparous (Langendijk et al., 2000) and multiparous sows (Pearce and Pearce 1992). However, increasing frequency of boar exposure does not improve expression of estrus (Knox et al., 2002), but might be confounded with the occurrence of refractory behavior that can last more than 8 h in some sows (Knox et al., 2004).

Delayed return to estrus soon after weaning can affect sows of all parities, but is most often observed in parity 1 and 2 sows that have lost excessive weight, body fat, and protein as a result of mobilization of body stores to support lactation. This occurs in younger females due to the stress of first farrowing and lactation, their smaller body size, and lower capacity for feed intake. However, any sows showing significant decline in feed intake on 2 or more days in lactation (Koketsu et al., 1996), especially when nursing a large litter, can result in a negative energy balance, weight loss, and extended wean-to-estrus interval (Eissen et al., 2003). Kemp and Soede (2012) suggested that the metabolic state of the modern hyperprolific sow after weaning may not be able to support development of the correct number of high-quality follicles for ovulation in such a short period of time after weaning. The authors indicated that follicle development and expression of estrus can be improved in these sows if given more time by skipping the first postweaning estrus (Werlang et al., 2011) or delaying estrus through use of exogenous progestagen. Another approach to improve follicle development was to employ split-weaning in late lactation in order to minimize metabolic stress. Interestingly, manipulation of the follicular phase is also being used to try and improve piglet weaning weights. Intermittent suckling can be used to induce lactating sows to ovulate (Terry et al., 2013), and these females can be inseminated with the similar fertility to conventionally weaned sows (Kemp and

Soede, 2012). However, although the procedure allows many sows to express estrus during lactation, some only express estrus after weaning. These types of procedures could be valuable, but will need to be carefully monitored for effect, as intermittent suckling (Gerritsen et al., 2014) and split weaning (Knox and Probst-Miller, 2004) can each associate with ovarian cysts.

SUMMARY AND CONCLUSIONS

The concentrations and patterns of the reproductive hormones and the associated changes in the ovarian surface follicle populations during the follicular phase are quite similar between gilts and sows. Difference between these females may reside in the signal that initiates the follicular phase. In prepubertal gilts, this may involve changing sensitivity to estrogen feedback, in mature cyclic gilts, clearance of progesterone, and in lactating sows, removal of nursing piglets. Despite the large differences in maturational age, the stimulatory effects of the boar on induction of a follicular phase appear to be quite consistent and can work to advance puberty, estrus after weaning, and prevent extended estrous cycles. In all stages of maturity, it also appears that feed intake and metabolic state influence follicle health and selection. In prepubertal gilts, high-feed intake increases growth rate and facilitates early puberty, whereas in cyclic gilts, it can increase ovulation rate. For weaned sows, methods that prevent or limit incidence of days off feed or low-feed intake during lactation help advance estrus following weaning.

It will be necessary to elucidate additional factors and the different pathways involved in order to stimulate the start and prevent delays in the follicular phase for gilts and sows. In addition, identifying the factors that allow for selection of a uniform cohort of follicles at the start of the follicular phase will be vital for improving the synchrony of estrus and ovulation.

LITERATURE CITED

- Almeida, F., A. Alvarenga Dias, L. Moreira, A. Fiúza, and H. Chiarini-Garcia. 2017a. Ovarian follicle development and genital tract characteristics in different birthweight gilts at 150 days of age. *Reprod. Dom. Anim.* 52:756–762. doi:10.1111/rda.12976
- Almeida, F. R. C. L., B. Laurensen, L. X. Pereira, K. J. Teerds, and N. M. Soede. 2017b. Effects of birthweight on reproductive system development and onset of puberty in gilts. *Reprod. Fertil. Dev.* 29:254–261. doi:10.1071/RD15036
- Almond, G. W. 2007. Infertility associated with abnormalities of the estrous cycle and the ovaries. In: R. S. Youngquist and W. R. Threlfall, editors, *Current therapy in large animal theriogenology*. Saunders Elsevier Inc., St. Louis, MO. p. 773–777.
- Amaral Filha, W. S., M. L. Bernardi, I. Wentz, and F. P. Bortolozzo. 2009. Growth rate and age at boar exposure as factors influencing gilt puberty. *Livest. Sci.* 120:51–57. doi:10.1016/j.livsci.2008.04.009
- Bagg, M. A., M. B. Nottle, D. T. Armstrong, and C. G. Grupen. 2007. Relationship between follicle size and oocyte developmental competence in prepubertal and adult pigs. *Reprod. Fertil. Dev.* 19:797–803. doi:10.1071/RD07018
- Barb, C. R., G. J. Hausman, and R. R. Kraeling. 2010. Luteinizing hormone secretion as influenced by age and estradiol in the prepubertal gilt. *Anim. Reprod. Sci.* 122:324–327. doi:10.1016/j.anireprosci.2010.10.006
- Bartlett, A., S. J. Pain, P. E. Hughes, P. Stott, and W. H. E. J. van Wettere. 2009. The effects of PG600 and boar exposure on oestrus detection and potential litter size following mating at either the induced (pubertal) or second oestrus. *Anim. Reprod. Sci.* 114:219–227. doi:10.1016/j.anireprosci.2008.08.020
- Bates, R. O., B. N. Day, J. H. Britt, L. K. Clark, and M. A. Brauer. 1991. Reproductive performance of sows treated with a combination of pregnant mare's serum gonadotropin and human chorionic gonadotropin at weaning in the summer. *J. Anim. Sci.* 69:894–898. doi:10.2527/1991.693894x
- Baxter, E. M., and S. A. Edwards. 2013. Determining piglet survival. In: H. Rodriguez-Martinez, N. M. Soede and W. L. Flowers, editors, *Control of pig reproduction IX*. Context Products Ltd, Leicestershire, UK. p. 129–143.
- Belstra, B. A., W. L. Flowers, and M. T. See. 2004. Factors affecting temporal relationships between estrus and ovulation in commercial sow farms. *Anim. Reprod. Sci.* 84:377. doi:10.1016/j.anireprosci.2004.02.005
- Breen, S. M., K. L. Farris, S. L. Rodriguez-Zas, and R. V. Knox. 2005. Effect of age and physical or fence-line boar exposure on estrus and ovulation response in prepubertal gilts administered PG600. *J. Anim. Sci.* 83:460–465. doi:10.1016/j.anireprosci.2004.02.005
- Breen, S. M., S. L. Rodriguez-Zas, and R. V. Knox. 2006. Effect of altering dose of PG600 on reproductive performance responses in prepubertal gilts and weaned sows. *Anim. Reprod. Sci.* 95:316–323. doi:10.1016/j.anireprosci.2005.12.007
- Britt, J. H., J. D. Armstrong, N. M. Cox, and K. L. Esbenshade. 1985. Control of follicular development during and after lactation in sows. In: G. R. Foxcroft, D. J. A. Cole and B. J. Weir, editors, *Control of pig reproduction II*. 33. *Journals of Reproduction and Fertility Ltd*, Cambridge, UK. p. 37–54.
- Britt, J. H., B. N. Day, S. K. Webel, and M. A. Brauer. 1989. Induction of a fertile estrus in prepubertal gilts by treatment with a combination of pregnant mare's serum gonadotropin and human chorionic gonadotropin. *J. Anim. Sci.* 67:1148–1153. doi:10.2527/jas1989.6751148x
- Britt, J. H., V. E. Szarek, and D. G. Levis. 1983. Characterization of summer infertility of sows in large confinement units. *Theriogenology* 20:133–140. doi:10.1016/0093-691X(83)90032-8
- Canaday, D. C., J. L. Salak-Johnson, A. M. Visconti, X. Wang, K. Bhalerao, and R. V. Knox. 2013. Effect of variability in lighting and temperature environments for mature gilts housed in gestation crates on measures of reproduction and animal well-being. *J. Anim. Sci.* 91:1225–1236. doi:10.2527/jas.2012-5733
- Caton, J. S., G. W. Jesse, B. N. Day, and M. R. Ellersieck. 1986. The effect of duration of boar exposure on the frequency of gilts reaching first estrus. *J. Anim. Sci.* 62:1210–1214. doi:10.2527/jas1986.6251210x

- Chen, T. Y., P. Stott, R. Z. Athorn, E. G. Bouwman, and P. Langendijk. 2012. Undernutrition during early follicle development has irreversible effects on ovulation rate and embryos. *Reprod. Fertil. Dev.* 24:886–892. doi:10.1071/RD11292
- Christenson, R. K., J. J. Ford, and D. A. Redmer. 1985. Maturation of ovarian follicles in the prepubertal gilt. *J. Reprod. Fertil. Suppl.* 33:21–36.
- Clutter, A. 2009. Genetic selection for lifetime reproductive performance. In: H. Rodriguez-Martinez, J. L. Vallet and A. J. Ziecik, editors, *Control of pig reproduction VIII*. 66. Nottingham University Press, Nottingham, UK. p. 293–302.
- Cronin, G. M., P. H. Hemsworth, C. G. Winfield, B. Muller, and W. A. Chamley. 1983. The incidence of, and factors associated with, failure to mate by 245 days of age in the gilt. *Anim. Reprod. Sci.* 5:199–205. doi:10.1016/0378-4320(83)90027-1
- De Rensis, F., A. J. Ziecik, and R. N. Kirkwood. 2017. Seasonal infertility in gilts and sows: Aetiology, clinical implications and treatments. *Theriogenology* 96:111–117. doi:10.1016/j.theriogenology.2017.04.004
- Da Silva, C. L. A., M. L. W. J. Broekhuijse, B. F. A. Laurensen, H. A. Mulder, E. F. Knol, B. Kemp, and N. M. Soede. 2017a. Relationship between ovulation rate and embryonic characteristics in gilts at 35 d of pregnancy. *J. Anim. Sci.* 95:3160–3172. doi:10.2527/jas.2017.1577
- Da Silva, C. L. A., B. F. A. Laurensen, E. F. Knol, B. Kemp, and N. M. Soede. 2017b. Validation of transrectal ultrasonography for assessment of corpora lutea characteristics in pregnant sows and its relationship with litter characteristics at birth. *Transl. Anim. Sci.* 1:507–517. doi:10.2527/tas2017.0057
- Diekmann, M. A., J. A. Clapper, M. L. Green, and D. K. Stouffer. 1991. Reduction in age of puberty in gilts consuming melatonin during decreasing or increasing daylength. *J. Anim. Sci.* 69:2524–2531. doi:10.2527/1991.6962524x
- Dufour, J. J., M. H. Fahmy, and P. M. Flipot. 1985. Follicular development during the prepubertal period of different morphological types of ovaries in Hampshire and Yorkshire gilts fed two planes of nutrition. *J. Anim. Sci.* 61:1201–1210. doi:10.2527/jas1985.6151201x
- Eastham, P. R., G. W. Dyck, and D. J. A. Cole. 1984. Reproduction in the gilt. 5. The effect of the presence of the mature male during rearing on puberty attainment. *Anim. Sci.* 39:277–282. doi:10.1017/S000335610004191X
- Eastham, P. R., G. Dyck, and D. Cole. 1986. The effect of age at stimulation by relocation and first mature boar contact on the attainment of puberty in the gilt. *Anim. Reprod. Sci.* 12:31–38. doi:10.1016/0378-4320(86)90014-X
- Einarsson, S., Y. Brandt, N. Lundeheim, and A. Madej. 2008. Stress and its influence on reproduction in pigs: a review. *Acta Vet. Scand.* 50:48. doi:10.1186/1751-0147-50-48
- Eissen, J. J., E. J. Apeldoorn, E. Kanis, M. W. A. Verstegen, and K. H. de Greef. 2003. The importance of a high feed intake during lactation of primiparous sows nursing large litters. *J. Anim. Sci.* 81:594–603. doi:10.2527/2003.813594x
- Eliasson, L. 1991. Relationships between puberty and production traits in the gilt. 2. Oestrous symptoms at puberty. *Anim. Reprod. Sci.* 25:255–264. doi:10.1016/0378-4320(91)90020-Z
- Elsaesser, F. 1982. Endocrine control of sexual maturation in the female pig and sexual differentiation of the stimulatory oestrogen feedback mechanism. In: D. J. A. Cole and G. R. Foxcroft, editors, *Control of Pig Reproduction* Butterworth Scientific, London. p. 93–116.
- Flowers, B., T. C. Cantley, M. J. Martin, and B. N. Day. 1989. Effect of elevated ambient temperatures on puberty in gilts. *J. Anim. Sci.* 67:779–784. doi:10.2527/jas1989.673779x
- Flowers, B., and B. N. Day. 1990. Alterations in gonadotropin secretion and ovarian function in prepubertal gilts by elevated environmental temperature. *Biol. Reprod.* 42:465–471. doi:10.1095/biolreprod42.3.465
- Flowers, W. L., and K. L. Esbenshade. 1993. Optimizing management of natural and artificial matings in swine. In: G. R. Foxcroft, M. G. Hunter and C. Doberska, editors, *Control of pig reproduction IV. The Journals of Reproduction and Fertility Ltd*, Cambridge, UK. p. 217–228.
- Foxcroft, G. R., F. Almeida, J. L. Patterson, and H. J. Willis. 2001. Age and weight at puberty in relation to lifetime performance. *Proc. VIth Int. Conf. Pig Reprod.* p. 1–5.
- Foxcroft, G. R., and M. G. Hunter. 1985. Basic physiology of follicular maturation in the pig. In: D. J. A. Cole, G. R. Foxcroft and B. J. Weir, editors, *Control of pig reproduction II*. 33. The Journals of Reproduction and Fertility Ltd, Cambridge, UK. p. 1–19.
- Foxcroft, G. R., H. J. Shaw, M. G. Hunter, P. J. Booth, and R. T. Lancaster. 1987. Relationships between luteinizing hormone, follicle-stimulating hormone and prolactin secretion and ovarian follicular development in the weaned sow. *Biol. Reprod.* 36:175–191. doi:10.1095/biolreprod36.1.175
- Foxcroft, G. R., and D. F. van de Wiel. 1982. Endocrine control of the oestrus cycle. In: D. J. A. Cole and G. R. Foxcroft, editors, *Control of pig reproduction*. Butterworth Scientific, London, UK. p. 161–177.
- Gerritsen, R., B. F. A. Laurensen, W. Hazeleger, P. Langendijk, B. Kemp, and N. M. Soede. 2014. Cystic ovaries in intermittently-suckled sows: follicle growth and endocrine profiles. *Reprod. Fertil. Dev.* 26:462–468. doi:10.1071/RD12382
- Grasso, F., F. Castonguay, E. Daviault, P. Matton, F. Minvielle, and J. J. Dufour. 1988. Study of follicular development and heredity of morphological types of ovaries in prepubertal gilts. *J. Anim. Sci.* 66:923–931. doi:10.2527/jas1988.664923x
- Guthrie, H. D. 2005. The follicular phase in pigs: Follicle populations, circulating hormones, follicle factors and oocytes. *J. Anim. Sci.* 83:E79–89. doi:10.2527/2005.8313_supplE79x
- Guthrie, H. D., and B. S. Cooper. 1996. Follicular atresia, follicular fluid hormones, and circulating hormones during the midluteal phase of the estrous cycle in pigs. *Biol. Reprod.* 55:543–547. doi:10.1095/biolreprod55.3.543
- Guthrie, H. D., R. W. Grimes, B. S. Cooper, and J. M. Hammond. 1995. Follicular atresia in pigs: measurement and physiology. *J. Anim. Sci.* 73:2834–2844. doi:10.2527/1995.7392834x
- Guthrie, H. D., and C. Polge. 1976. Luteal function and oestrus in gilts treated with a synthetic analogue of prostaglandin F-2 α (ICI 79,939) at various times during the oestrous cycle. *J. Reprod. Fertil.* 48:423–425. doi:10.1530/jrf.0.0480423
- Heinonen, M., A. Leppävuori, and S. Pyörälä. 1998. Evaluation of reproductive failure of female pigs based on slaughterhouse material and herd record survey. *Anim. Reprod. Sci.* 52:235–244. doi:10.1016/S0378-4320(98)00105-5
- Hughes, P. E. 1982. Factors affecting the natural attainment of puberty in the pig. In: D. J. A. Cole and G. R. Foxcroft, editors, *Control of Pig Reproduction* Butterworth Scientific, London. p. 93–116.

- editors, *Control of Pig Reproduction* Butterworth Scientific, London. p. 117–138.
- Hughes, P. E., G. P. Pearce, and A. M. Patterson. 1990. Mechanisms mediating the stimulatory effects of the boar on gilt reproduction. *Control of pig reproduction III*. In: D.J.A. Cole, G. R. Foxcroft, and B. J. Weir, editors, *J. Reprod. Fert. (Suppl.)*. 40. Journals of Reproduction and Fertility Ltd., Great Britain. p. 323–341.
- Hunter, M. G., and T. Wiesak. 1990. Evidence for and implications of follicular heterogeneity in pigs. *J. Reprod. Fert. Suppl.* 40:163–177.
- Hurtgen, J. P., and A. D. Leman. 1980. Seasonal influence on the fertility of sows and gilts. *J. Am. Vet. Med. Assoc.* 177:631–635.
- Kaneko, M., and Y. Koketsu. 2012. Gilt development and maturing in commercial swine herds with varying reproductive performance. *Theriogenology* 77:840–846. doi:10.1016/j.theriogenology.2011.09.006
- Karlbom, I., S. Einarsson, and L. E. Edqvist. 1982. Attainment of puberty in female pigs: Clinical appearance and patterns of progesterone, oestradiol-17 β and LH. *Anim. Reprod. Sci.* 4:301–312. doi:10.1016/0378-4320(82)90044-6
- Kemp, B., and N. M. Soede. 1996. Relationship of weaning-to-estrus interval to timing of ovulation and fertilization in sows. *J. Anim. Sci.* 74:944–949. doi:10.2527/1996.745944x
- Kemp, B., and N. M. Soede. 2012. Should weaning be the start of the reproductive cycle in hyper-prolific sows? A physiological view. *Reprod. Dom. Anim.* 47:320–326. doi:10.1111/j.1439-0531.2012.02092.x
- Kirkwood, R. N., J. M. Forbes, and P. E. Hughes. 1981. Influence of boar contact on attainment of puberty in gilts after removal of the olfactory bulbs. *J. Reprod. Fert.* 61:193–196. doi:10.1530/jrf.0.0610193
- Knox, R. V. 2005. Recruitment and selection of ovarian follicles for determination of ovulation rate in the pig. *Domest. Anim. Endocrinol.* 29:385–397. doi:10.1016/j.domaniend.2005.02.025
- Knox, R. V., S. M. Breen, K. L. Willenburg, S. Roth, G. M. Miller, K. M. Ruggiero, and S. L. Rodriguez-Zas. 2004. Effect of housing system and boar exposure on estrus expression in weaned sows. *J. Anim. Sci.* 82:3088–3093. doi:10.2527/2004.82103088x
- Knox, R. V., K. C. Esparza-Harris, M. E. Johnston, and S. K. Webel. 2017. Effect of numbers of sperm and timing of a single, post-cervical insemination on the fertility of weaned sows treated with OvuGel®. *Theriogenology* 92:197–203. doi:10.1016/j.theriogenology.2017.01.033
- Knox, R. V., G. M. Miller, K. L. Willenburg, and S. L. Rodriguez-Zas. 2002. Effect of frequency of boar exposure and adjusted mating times on measures of reproductive performance in weaned sows. *J. Anim. Sci.* 80:892–899. doi:10.2527/2002.804892x
- Knox, R., and S. Probst-Miller. 2004. Evaluation of transrectal real-time ultrasound for use in identifying sources of reproductive failure in weaned sows. *J. Swine Health Prod.* 12:71–74.
- Knox, R. V., and S. L. Rodriguez-Zas. 2001. Factors influencing estrus and ovulation in weaned sows as determined by transrectal ultrasound. *J. Anim. Sci.* 79:2957–2963. doi:10.2527/2001.79122957x
- Knox, R. V., S. L. Rodriguez Zas, N. L. Slotter, K. A. McNamara, T. J. Gall, D. G. Levis, T. J. Safranski, and W. L. Singleton. 2013. An analysis of survey data by size of the breeding herd for the reproductive management practices of North American sow farms. *J. Anim. Sci.* 91:433–445. doi:10.2527/jas.2012-5189
- Knox, R. V., J. Shen, L. L. Greiner, and J. F. Connor. 2016. Effect of timing of relocation of replacement gilts from group pens to individual stalls before breeding on fertility and well-being. *J. Anim. Sci.* 94:5114–5121. doi:10.2527/jas.2016-0799
- Knox, R. V., K. R. Stewart, W. L. Flowers, M. E. Swanson, S. K. Webel, and R. R. Kraeling. 2018. Design and biological effects of a vaginally administered gel containing the GnRH agonist, triptorelin, for synchronizing ovulation in swine. *Theriogenology* 112:44–52. doi:10.1016/j.theriogenology.2017.08.021
- Knox, R. V., K. W. Tudor, S. L. Rodriguez-Zas, and J. A. Robb. 2000. Effect of subcutaneous vs intramuscular administration of P.G. 600 on estrual and ovulatory responses of prepubertal gilts. *J. Anim. Sci.* 78:1732–1737. doi:10.2527/2000.7871732x
- Knox, R. V., G. Vatzias, C. H. Naber, and D. R. Zimmerman. 2003. Plasma gonadotropins and ovarian hormones during the estrous cycle in high compared to low ovulation rate gilts. *J. Anim. Sci.* 81:249–260. doi:10.2527/2003.811249x
- Knox, R. V., and D. R. Zimmerman. 1993. Effect of administration of porcine follicular fluid to gilts during the luteal phase of the estrous cycle on plasma gonadotropins, follicular development, and ovulation rate. *J. Anim. Sci.* 71:1546–1551. doi:10.2527/1993.7161546x
- Koketsu, Y., and G. D. Dial. 1997. Factors influencing the post-weaning reproductive performance of sows on commercial farms. *Theriogenology* 47:1445–1461. doi:10.1016/S0093-691X(97)00135-0
- Koketsu, Y., G. D. Dial, J. E. Pettigrew, and V. L. King. 1996. Feed intake pattern during lactation and subsequent reproductive performance of sows. *J. Anim. Sci.* 74:2875–2884. doi:10.2527/1996.74122875x
- Kraeling, R. R., P. J. Dziuk, V. G. Pursel, G. B. Rampacek, and S. K. Webel. 1981. Synchronization of estrus in swine with allyl trenbolone (RU-2267). *J. Anim. Sci.* 52:831–835. doi:10.2527/jas1981.524831x
- Kummer, R., M. L. Bernardi, A. C. Schenkel, W. S. Amaral Filha, I. Wentz, and F. P. Bortolozzo. 2009. Reproductive performance of gilts with similar age but with different growth rate at the onset of puberty stimulation. *Reprod. Dom. Anim.* 44:255–259. doi:10.1111/j.1439-0531.2007.01050.x
- Langendijk, P., H. van den Brand, N. M. Soede, and B. Kemp. 2000. Effect of boar contact on follicular development and on estrus expression after weaning in primiparous sows. *Theriogenology* 54:1295–1303. doi:10.1016/S0093-691X(00)00436-2
- Langendijk, P., N. M. Soede, and B. Kemp. 2006. Effect of boar stimuli on the follicular phase and on oestrous behaviour in sows. In: C. J. Ashworth and R. R. Kraeling, editors, *Control of pig reproduction VII*. Nottingham University Press, Nottingham, UK. p. 219–230.
- Liu, J., A. T. Koenigsfeld, T. C. Cantley, C. K. Boyd, Y. Kobayashi, and M. C. Lucy. 2000. Growth and the initiation of steroidogenesis in porcine follicles are associated with unique patterns of gene expression for individual components of the ovarian insulin-like growth factor system. *Biol. Reprod.* 63:942–952. doi:10.1095/biolreprod63.3.942

- Lopes, T. P., J. Sanchez-Osorio, A. Bolarin, E. A. Martinez, and J. Roca. 2014. Relevance of ovarian follicular development to the seasonal impairment of fertility in weaned sows. *Vet. J.* 199:382–386. doi:10.1016/j.tvjl.2013.11.026
- Lucy, M. C., J. Liu, C. K. Boyd, and C. J. Bracken. 2001. Ovarian follicular growth in sows. In: R. D. Geisert, H. Niemann and C. Doberska, editors, *Control of pig reproduction VI*. 58. Society for Reproduction and Fertility, Cambridge, UK. p. 31–45.
- Magnabosco, D., M. L. Bernardi, I. Wentz, E. C. P. Cunha, and F. P. Bortolozzo. 2016. Low birth weight affects lifetime productive performance and longevity of female swine. *Livest. Sci.* 184:119–125. doi:10.1016/j.livsci.2015.12.008
- Melrose, D. R., H. C. Reed, and R. L. Patterson. 1971. Androgen steroids associated with boar odour as an aid to the detection of oestrus in pig artificial insemination. *Br. Vet. J.* 127:497–502.
- Miller, P. S., R. Moreno, and R. K. Johnson. 2011. Effects of restricting energy during the gilt developmental period on growth and reproduction of lines differing in lean growth rate: Responses in feed intake, growth, and age at puberty. *J. Anim. Sci.* 89:342–354. doi:10.2527/jas.2010-3111
- Nissen, A., N. Soede, P. Hyttel, M. Schmidt, and L. D'hoore. 1997. The influence of time of insemination relative to time of ovulation on farrowing frequency and litter size in sows, as investigated by ultrasonography. *Theriogenology* 47:1571–1582. doi:10.1016/S0093-691X(97)00162-3
- Noguchi, M., K. Yoshioka, S. Itoh, C. Suzuki, S. Arai, Y. Wada, Y. Hasegawa, and H. Kaneko. 2010. Peripheral concentrations of inhibin A, ovarian steroids, and gonadotropins associated with follicular development throughout the estrous cycle of the sow. *Reproduction* 139:153–161. doi:10.1530/rep-09-0018
- Paterson, A. M. 1982. The controlled induction of puberty. In: D. J. A. Cole and G. R. Foxcroft, editors, *Control of Pig Reproduction* Butterworth Scientific, London. p. 139–160.
- Paterson, A. M., P. E. Hughes, and G. P. Pearce. 1989. The effect of season, frequency and duration of contact with boars on the attainment of puberty in gilts. *Anim. Reprod. Sci.* 21:115–124. doi:10.1016/0378-4320(89)90122-X
- Paterson, A. M., and D. R. Lindsay. 1981. Induction of puberty in gilts. *Anim. Prod.* 32:51–54. doi:10.1017/S0003356100024624
- Paterson, A. M., C. A. Maxwell, and A. Foldes. 1992. Seasonal inhibition of puberty in domestic gilts is overcome by melatonin administered orally, but not by implant. *J. Reprod. Fertil.* 94:97–105. doi:10.1530/jrf.0.0940097
- Pearce, G. P., and P. E. Hughes. 1987. The influence of boar-component stimuli on puberty attainment in the gilt. *Anim. Prod.* 44:293–302. doi:10.1017/S0003356100018663
- Pearce, G. P., and A. M. Paterson. 1992. Physical contact with the boar is required for maximal stimulation of puberty in the gilt because it allows transfer of boar pheromones and not because it induces cortisol release. *Anim. Reprod. Sci.* 27:209–224. doi:10.1016/0378-4320(92)90059-M
- Pearce, G. P., and A. N. Pearce. 1992. Contact with a sow in oestrus or a mature boar stimulates the onset of oestrus in weaned sows. *Vet. Rec.* 130:5–9. doi:https://doi.org/10.1136/vr.130.1.5
- Peltoniemi, O. A., and J. V. Virolainen. 2006. Seasonality of reproduction in gilts and sows. In: C. J. Ashworth and R. R. Kraeling, editors, *Control of pig reproduction VII*. 62. Nottingham University Press, Nottingham, UK. p. 205–218.
- Pope, W. F., M. H. Wilde, and S. Xie. 1988. Effect of electrocautery of nonovulated day 1 follicles on subsequent morphological variation among day 11 porcine embryos. *Biol. Reprod.* 39:882–887. doi:10.1095/biolreprod39.4.882
- Pope, W. F., S. Xie, D. M. Broermann, and K. P. Nephew. 1990. Causes and consequences of early embryonic diversity in pigs. In: D. J. A. Cole, G. R. Foxcroft and B. J. Weir, editors, *Control of pig reproduction III*. Journals of Reproduction and Fertility Ltd., Cambridge, UK. p. 251–260.
- Rhodes, M. T., D. L. Davis, and J. S. Stevenson. 1991. Flushing and altrenogest affect litter traits in gilts. *J. Anim. Sci.* 69:34–40. doi:10.2527/1991.69134x
- Romoser, M. R., B. J. Hale, J. T. Seibert, K. L. Bidne, M. J. Dickson, T. J. Gall, L. H. Baumgard, A. F. Keating, and J. W. Ross. 2017. 038 Assessment of methods for accurate reproductive tract scoring by vulva width as a tool for gilt selection. *J. Anim. Sci.* 95:18–18. doi:10.2527/asasmw.2017.038
- Rydmer, L., L. Eliasson-Selling, K. Johansson, S. Stern, and K. Andersson. 1994. A genetic study of estrus symptoms at puberty and their relationship to growth and leanness in gilts. *J. Anim. Sci.* 72:1964–1970. doi:10.2527/1994.7281964x
- Schilling, E., and F. Cerne. 1972. Induction and synchronization of estrus in prepuberal gilts and anestrus sows by a PMS/hCG-compound. *Vet. Rec.* 91:471–474.
- Signoret, J. P., F. Martinat-Botte, F. Bariteau, Y. Forgerit, C. Macar, A. Moreau, and M. Terqui. 1990. Control of oestrus in gilts I. Management-induced puberty. *Anim. Reprod. Sci.* 22:221–225. doi:10.1016/0378-4320(90)90062-K
- Soede, N., W. Hazeleger, and B. Kemp. 1998. Follicle size and the process of ovulation in sows as studied with ultrasound. *Reprod. Dom. Anim.* 33:239–244. doi:10.1111/j.1439-0531.1998.tb01350.x
- Soede, N. M., and B. Kemp. 1993. In synchronized pigs, the duration of ovulation is not affected by insemination and is not a determinant for early embryonic diversity. *Theriogenology* 39:1043–1053. doi:10.1016/0093-691X(93)90005-P
- Soede, N. M., P. Langendijk, and B. Kemp. 2011. Reproductive cycles in pigs. *Anim. Reprod. Sci.* 124:251–258. doi:10.1016/j.anireprosci.2011.02.025
- Soede, N. M., J. P. T. M. Noordhuizen, and B. Kemp. 1992. The duration of ovulation in pigs, studied by transrectal ultrasonography, is not related to early embryonic diversity. *Theriogenology* 38:653–666. doi:10.1016/0093-691X(92)90028-P
- Sporke, J., J. L. Patterson, E. Beltranena, and G. R. Foxcroft. 2005. Gilt development unit management using Matrix and PG600 in a commercial swine operation. *Proc. Allen D. Leman Swine Conf.* p. 72–100.
- Stevenson, J. S., and D. L. Davis. 1982. Estrous synchronization and fertility in gilts after 14- or 18-day feeding of altrenogest beginning at estrus or diestrus. *J. Anim. Sci.* 55:119–123. doi:10.2527/jas1982.551119x
- Terry, R., K. L. Kind, P. E. Hughes, D. J. Kennaway, P. J. Herde, and W. H. E. J. van Wettere. 2013. Split weaning increases the incidence of lactation oestrus in boar-exposed sows. *Anim. Reprod. Sci.* 142:48–55. doi:10.1016/j.anireprosci.2013.08.010
- Town, S. C., J. L. Patterson, C. Z. Pereira, G. Gourley, and G. R. Foxcroft. 2005. Embryonic and fetal development in a commercial dam-line genotype. *Anim. Reprod. Sci.* 85:301–316. doi:10.1016/j.anireprosci.2004.05.019
- Tummaruk, P., N. Lundeheim, S. Einarsson, and A. M. Dalin. 2001. Effect of birth litter size, birth parity number, growth rate, backfat thickness and age at first mating of gilts on their reproductive performance as sows. *Anim. Reprod. Sci.* 66:225–237. doi:10.1016/S0378-4320(01)00095-1

- Ulguim, R. R., F. P. Bortolozzo, I. Wentz, M. Johnston, S. K. Webel, L. Arend, and R. V. Knox. 2018. Ovulation and fertility responses for sows receiving once daily boar exposure after weaning and OvuGel® followed by a single fixed time post cervical artificial insemination. *Theriogenology* 105:27–33. doi:10.1016/j.theriogenology.2017.09.005
- Weitze, K. F., H. Wagner-Rietschel, D. Waberski, L. Richter, and J. Krieter. 1994. The onset of heat after weaning, heat duration, and ovulation as major factors in AI timing in sows. *Reprod. Dom. Anim.* 29:433–443. doi:10.1111/j.1439-0531.1994.tb00590.x
- Werlang, R. F., L. E. Argenti, H. C. C. Fries, M. L. Bernardi, I. Wentz, and F. P. Bortolozzo. 2011. Effects of breeding at the second oestrus or after post-weaning hormonal treatment with altrenogest on subsequent reproductive performance of primiparous sows. *Reprod. Dom. Anim.* 46:818–823. doi:10.1111/j.1439-0531.2010.01747.x
- van Wettere, W. H. E. J., M. Mitchell, D. K. Revell, and P. E. Hughes. 2011. Nutritional restriction of pre-pubertal liveweight gain impairs ovarian follicle growth and oocyte developmental competence of replacement gilts. *Theriogenology* 75:1301–1310. doi:10.1016/j.theriogenology.2010.12.001
- van Wettere, W. H. E. J., D. K. Revell, M. Mitchell, and P. E. Hughes. 2006. Increasing the age of gilts at first boar contact improves the timing and synchrony of the pubertal response but does not affect potential litter size. *Anim. Reprod. Sci.* 95:97–106. doi:10.1016/j.anireprosci.2005.09.009
- van de Wiel, D. F. M., and P. Booman. 1993. Post-weaning anoestrus in primiparous sows: LH patterns and effects of gonadotropin injection and boar exposure. *Vet Q.* 15:162–166. doi:10.1080/01652176.1993.9694398
- Williams, A. M., T. J. Safranski, D. E. Spiers, P. A. Eichen, E. A. Coate, and M. C. Lucy. 2013. Effects of a controlled heat stress during late gestation, lactation, and after weaning on thermoregulation, metabolism, and reproduction of primiparous sows. *J. Anim. Sci.* 91:2700–2714. doi:10.2527/jas.2012-6055
- Yen, H. W., J. J. Ford, D. R. Zimmerman, and R. K. Johnson. 2005. Follicular development and maturation in gilts selected for an index of high ovulation rate and high prenatal survival. *J. Anim. Sci.* 83:130–135. doi:10.2527/2005.831130x
- Young, M. G., M. D. Tokach, F. X. Aherne, S. S. Dritz, R. D. Goodband, J. L. Nelssen, and T. M. Loughin. 2008. Effect of space allowance during rearing and selection criteria on performance of gilts over three parities in a commercial swine production system. *J. Anim. Sci.* 86:3181–3193. doi:10.2527/jas.2007-0600
- Zimmerman, D. R., T. McGargill, and N. Rohda. 1998. Efficacy of once (1x) vs twice (2x) daily physical or fence-line contact with boars for stimulating earlier puberty in gilts. *Nebraska Swine Report*. University of Nebraska-Lincoln, pp. 4–5. Available from http://digitalcommons.unl.edu/coopext_swine/159/?utm_source=digitalcommons.unl.edu%2Fcoopext_swine%2F159&utm_medium=PDF&utm_campaign=PDFCoverPages