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## Review

## Control of estrus and ovulation: Fertility to timed insemination of gilts and sows

F. De Rensis<sup>a,\*</sup>, R.N. Kirkwood<sup>b</sup><sup>a</sup> Department of Medical-Veterinary Science, University of Parma, Parma, Italy<sup>b</sup> School of Animal and Veterinary Sciences, University of Adelaide, Roseworthy, SA, Australia

## ARTICLE INFO

## Article history:

Received 22 February 2016

Received in revised form 22 April 2016

Accepted 22 April 2016

## Keywords:

Swine

Gonadotrophins

Estrus

Ovulation

Synchronization

## ABSTRACT

It is possible to control follicular development in gilts and sows with the use of hormones including the progestogen altrenogest, GnRH, eCG, hCG, and porcine luteinizing hormone (pLH). These hormones can be used to develop protocols for control of estrus with artificial insemination (AI) timed to estrus detection (timed artificial insemination; TAI) or to control estrus and ovulation with insemination at a fixed time without the requirement of estrus detection (fixed-timed artificial insemination; FTAI). In cyclic gilts, double TAI after protocols based on altrenogest and eCG plus hCG administration can achieve a 70% of farrowing rate. Valuable results can be obtained in weaned sows by the utilization of protocols based on eCG administration at weaning and then GnRH or pLH at estrus onset followed by single or double TAI. In cyclic gilts, single or double FTAI regardless of estrus expression can be applied after protocols based on altrenogest administration followed by eCG and then GnRH, hCG, or pLH some hours later; farrowing rates are similar to control animals inseminated at estrus detection. With sows, a protocol based on eCG administration at weaning and hCG, GnRH, or pLH some hours later followed by single or double FTAI can give fertility rates comparable to control animal inseminated at estrus. Most recently, injection or vaginal deposition of GnRH 96 hours after weaning followed by a single FTAI 24 to 30 hours later is resulting in reproductive performance not different to animals subject to multiple inseminations after natural estrus. It is possible to apply FTAI in lactating sows. The protocols are based on eCG during lactation followed by hCG and FTAI. These protocols will induce ovulation during lactation, but pregnancy rates are reduced. However, in the future, a better knowledge on the effect of hormone administration on follicular dynamics during lactation may allow the development of more effective protocols.

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## 1. Introduction

It is important for the swine industry to develop new technologies that effectively decrease labor costs, increase throughput, and optimize utilization of farm facilities. A technology of recent interest is artificial insemination (AI) at predetermined times after induction of a synchronized estrus (timed artificial insemination; TAI). This has been further refined by inclusion of control of ovulation with

insemination at a fixed time without the requirement of estrus detection (fixed-timed artificial insemination; FTAI).

Control of estrus and ovulation has become more important in recent years because of batch flow management that requires a pool of service-ready females available for AI at scheduled times. Timed artificial insemination and FTAI systems were not fully developed until recently but, thanks to a better understanding of mechanisms controlling follicular development and ovulation, there are new perspectives on control of swine reproduction.

A variety of exogenous hormones can be used to control follicular development and synchronize ovulation in gilts

\* Corresponding author. Tel.: 00393392172315; fax: 00390521902798.  
E-mail address: [fabio.derensis@unipr.it](mailto:fabio.derensis@unipr.it) (F. De Rensis).

and sows. Estrus can be induced by administration of eCG with or without concurrent hCG, the latter being an LH analog. Protocols that include hCG are likely to be relatively more effective under conditions of limited endogenous LH, such as in younger females, because in swine it is LH that is the primary driver of follicular development from the 4 or 5-mm medium follicle stage to the point of ovulation [1]. The subsequent use of hCG, LH, or GnRH analogues can effectively induce a timed ovulation in gilts and in weaned sows [2–7]. The response to controlled ovulation protocols depends on the degree of follicular development at the time of treatment. The response to TAI improves when estrus onset is made more predictable by controlling the time of estrus onset with the oral administration of the progestogen, altrenogest.

For this review, we will first briefly describe the hormones available to control follicular development and ovulation, focusing on induction of estrus and ovulation. In the second part, we will describe and discuss some protocols that can be used for TAI or FTAI in gilts and in sows after weaning, in sows returning to estrus after insemination, or during lactation.

### 1.1. Hormones used to control follicular development and estrus

Exogenous hormones known to stimulate follicular development are eCG and a combination of eCG and hCG or porcine luteinizing hormone (pLH) [8–10]. Although eCG is frequently considered as a substitute for FSH, it also has some variable batch-dependant LH-like activity. When using eCG to induce estrus, an injection of 500 to 1000 IU of eCG was used to induce estrus in gilts. A dose of 500 to 750 IU is usually effective for weaned multiparous sows where endogenous LH is likely not limiting [5,11–13]. Administering 500 to 750 IU of eCG within 24 hours after weaning stimulates and synchronizes follicular growth [13–15]. The administration of eCG can also stimulate follicular development to the preovulatory stage in lactating sows [16,17] lending itself to the possibility to control follicular development during lactation. This could be interesting for modern sows that are weaned after 28 days of lactation, have a better lactation feed intake, and have a genotype that allows these animals to “escape” from suckling inhibition of ovarian function earlier compared to previous genotypes. Although eCG increases the control of weaning-to-estrus interval, it does not control the estrus-to-ovulation interval [6]. The latter requires control of ovulation, which is discussed in the following section.

The eCG dose should be increased to 900 to 1000 IU when eCG is used to stimulate estrus in gilts and in primiparous sows in which endogenous LH may be low, especially in the hotter months [5]. The improved response at higher dosages likely reflects the dose-dependent LH-like activity. Therefore, with gilts and younger sows, a combination of 400 IU of eCG with 200 IU of hCG is preferred because of the LH-like activity of the hCG.

In regularly cycling females, estrus can be controlled and synchronized by blocking follicular growth at the medium-sized follicle stage by suppression of endogenous LH achieved by feeding the progestogen altrenogest [18]. This

effectively stops the follicular phase, and on withdrawal of altrenogest, the follicular phase is initiated. It is established that feeding altrenogest at 15–20 mg/day for 14 or 18 days results in approximately 85% of females displaying estrus 4 to 8 days after its withdrawal [19]. The range in days to estrus reflects the innate variability in duration of the follicular phase. Similar to outcomes with exogenous gonadotrophin injection, the variability in time of ovulation after altrenogest withdrawal is too great to allow a predetermined time of insemination unless ovulation is also controlled.

## 2. Hormones used to control ovulation

When treatment with eCG at weaning is followed by administration of GnRH [2], hCG [2,20], or pLH [14,15,21–25], follicles ovulate within a period that is not dissimilar to that for ovulation after an endogenous LH surge. The control of ovulation has been the subject of recent reviews [5,7,26]. However, for completeness we will briefly describe available treatments.

### 2.1. GnRH analogues

Exogenous GnRH acts at the level of the pituitary to induce an endogenous ovulatory LH surge. As such, its efficacy may be constrained by available pituitary stores of LH. Although ovulation does not require a particularly large LH surge [27], an attenuated surge may negatively affect the quality of follicular luteinization [28]. It has been demonstrated that GnRH analogues are able to induce ovulation in gilts [2] and sows [2,29–31]. For example, a single injection of the GnRH analogue lecorelin at estrus onset induced ovulation within 40 hours in 70.9% of treated sows compared with 48.2% of nontreated control sows with a tendency for more lecorelin sows (92.7%) to ovulate by 48 hours compared to controls (82.4%) [32]. The GnRH treatment also reduced estrus duration and the interval between estrus onset and ovulation; farrowing rates and litter sizes were not affected by treatment. More recently, the administration of the GnRH analogue buserelin 86 hours after weaning induced ovulation 32 to 44 hours after treatment in most multiparous sows, but in only about 50% of primiparous sows, possibly reflecting a parity effect on follicle maturity at the time of treatment [3].

### 2.2. Human chorionic gonadotrophin

Being an LH analogue, hCG acts at the ovarian level and is not constrained by endogenous pituitary LH stores. After injection, hCG induces a predictable ovulation at about 42 hours (range 39–49 hours) in 85% to 90% of treated sows [33]. Therefore, if sows are likely to be late ovulators (i.e., more than 42 hours after estrus onset) such as in sows having short wean-to-estrus intervals (WEIs), injection of hCG 80 hours after weaning will allow for fixed time breeding of sows 24 to 36 hours after injection.

### 2.3. Luteinizing hormone

Similar to hCG, exogenous porcine LH acts at the level of the ovary and so is not constrained by endogenous pituitary

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