DOI:
https://doi.org/10.61900/SPJVS.2025.04.07

CONTROL OF OVARIAN FUNCTION IN THE FERTILITY MANAGEMENT OF DAIRY CATTLE

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Abstract
Reproductive performance in dairy cows has become increasingly challenging due to the demands of intensified milk production. This surge in productivity has led to significant physiological strain on the animals, resulting in a notable decline in fertility rates. Thus, high-yielding cows are often predisposed to reproductive challenges, such as delayed resumption of ovarian cyclicity, cystic ovarian disease, and anovulation, which decrease conception rates. These disorders are closely linked to the metabolic stress and hormonal imbalances associated with intensive milk production. Controlling ovarian function through timed artificial insemination (TAI) protocols has become an essential strategy for addressing various challenges. Protocols like Ovsynch, Presynch, Double Ovsynch, and other TAI protocols allow precise synchronization of ovulation. This approach reduces the dependence on estrus detection. In addition, the incorporation of progestative devices further supports luteal function and enhances reproductive outcomes. In parallel, advanced assisted reproduction techniques, including embryo transfer and in vitro fertilization, expand the options available for genetic improvement and reduce the gap between generations. While metabolic status and individual variation in ovarian response can influence the outcomes of TAI protocols, continual advancements in protocol development and reproductive management strategies are enhancing cow fertility. Integrating TAI protocols with assisted reproduction techniques can significantly enhance fertility management in dairy cows, supporting farm profitability.

Keywords: ovarian activity; dairy cattle; estrus synchronization; fertility; assisted reproduction.

Reproductive performance in dairy cows is a cornerstone of farm profitability, directly impacting calving interval and lifetime productivity. However, in contemporary high-yielding breeds, particularly Holsteins, there has been a significant and challenging decline in fertility rates over the past few decades (López-Gatius, 2024;). This decline is largely attributed to the immense physiological strain associated with intensified milk production, which predisposes cows to extended periods of Negative Energy Balance (NEB) during the critical post-partum period.

The resulting metabolic stress profoundly disrupts the hypothalamic-pituitary-gonadal axis, leading to a notable increase in reproductive disorders. These clinical manifestations include delayed resumption of ovarian cyclicity (anestrus), the prevalence of cystic ovarian disease, and anovulation, all of which collectively decrease overall conception rates and lengthen the critical Days Open interval (Wiltbank et al., 2011).

To mitigate these systemic challenges and improve herd reproductive efficiency, controlling the ovarian function through precise hormonal interventions has become an indispensable strategy in modern dairy farms (Wiltbank et al., 2011). The main objective of these interventions is to manipulate the timing of follicular wave emergence and luteolysis, transforming the spontaneous, often unreliable, physiological event of estrus into a predictable, scheduled process.

Protocols utilizing Timely Artificial Insemination (TAI), such as Ovsynch and its numerous variations (e.g., Presynch, Double Ovsynch), represent the most effective and widely adopted strategies for achieving accurate synchronization (Bó et al., 2022; Bó et al., 2025). These regimens combine key hormones—GnRH (Gonadotropin-releasing hormone) to control follicular dynamics, and Prostaglandin F_2 alpha (PGF_2 alpha) to induce luteolysis— hereby reducing the reliance on visual estrus detection (Bó et al., 2022). Furthermore, the strategic incorporation of exogenous progestins via intravaginal devices (e.g., CIDR) has proven invaluable, particularly for initiating ovarian activity in anestrous and silent-heat cows (Colazo et al., 2024).

In parallel with TAI protocols, advancements in Assisted Reproduction Techniques (ART),

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including Embryo Transfer (ET) and in vitro fertilization (IVF), offer complementary options for genetic improvement and reduce the gap between generations.
The purpose of this review is to provide a critical and up-to-date synthesis of the literature regarding the strategies for controlling ovarian function in dairy cattle. We will evaluate the efficacy of various TAI protocols, analyze the important role of progesterone (P4) supplementation, ultimately highlight the necessary future directions to maximize reproductive performance in high-yielding dairy herds.

MATERIALS AND METHODS

The present review was developed through a focused synthesis of scientific publications addressing the regulation of ovarian function and its relevance to fertility management in dairy cattle. Literature was identified using targeted searches in the PubMed, Scopus, and Google Scholar databases, employing keywords such as "ovarian function," "dairy cattle," "estrous synchronization," "ovulation control," and "fertility management."
Studies were included if they provided data on bovine ovarian physiology, hormonal strategies for estrus or ovulation synchronization, or reproductive performance in dairy herds. Sources not directly related to dairy cattle reproduction, and publications lacking sufficient methodological or reproductive information were excluded. The selected studies were examined critically and organized thematically to outline the main physiological mechanisms, the principal hormonal protocols used in practice, and the major factors influencing reproductive efficiency in dairy cows.

RESULTS

Normal ovarian function in cattle is characterized by the fundamental process of follicular waves, with the estrous cycle typically consisting of two or three such waves. Each wave involves the recruitment of a cohort of antral follicles under the influence of FSH (Follicle Stimulating Hormone), followed by the selection of a single dominant follicle. This dominant follicle actively suppresses the growth of subordinate follicles via negative feedback, primarily through the production of estradiol and inhibin (Mapletoft et al., 2018).
The selection mechanism involves a critical shift: the dominant follicle acquires an increased density of LH receptors on its granulosa cells, making its continued growth dependent on LH (Luteinizing Hormone) support, while FSH concentrations decline (Mapletoft et al., 2009). The progression of the dominant follicle is tightly regulated by the P4 produced by the corpus luteum (CL). High concentrations of P4 suppress the frequency and amplitude of LH pulses, causing the dominant follicle of the non-ovulatory wave to regress. In contrast, luteal regression removes this inhibition, permitting the necessary increase in LH pulse frequency, which culminates in the pre-ovulatory LH surge and subsequent ovulation (Thatcher et al., 2007; Mapletoft et al., 2018).

Prostaglandin F2 alpha for luteal regression
PGF2 alpha is the elective agent for luteal regression, terminating the luteal phase. Critically, PGF2 alpha is ineffective on CLs younger than 5 days of age. Furthermore, PGF2 alpha alone does not control follicular development, leading to estrus occurring variably over 2 to 7 days.

GnRH for ovulation and follicular wave synchronization
GnRH induces an LH surge, serving two critical functions in TAI: (1) inducing the ovulation or luteinization of a dominant follicle (with a 6 to 70% success rate) and (2) synchronizing the emergence of a new follicular wave 1 to 2 days post-treatment (Mapletoft et al., 2009). The optimal response rate to the initial GnRH is achieved when administered between Days 5 and 9 of the cycle, a principle utilized by the Ovsynch protocol to ensure a higher percentage of cows respond favorably (Mapletoft et al., 2018).

Progestins (CIDR/PRID) for cycle initiation
Progesterone-releasing devices are essential for managing anestrous cows that lack a functional CL. Progesterone suppresses LH release, while not suppressing FSH secretion, thus allowing follicular waves to continue to emerge. Short-term use (7 to 8 days) followed by PGF2 alpha is recommended to normalize fertility and avoid the low fertility associated with persistent follicles caused by long-term P4 exposure. Progestin devices are well suited for synchronizing follicular development prior to GnRH treatment.

Hormonal Protocols
The Ovsynch protocol and its derivatives Presynch–Ovsynch and Double-Ovsynch represent the main framework for hormonal control of ovarian function in lactating dairy cows. These programs are based on sequential administration of GnRH and PGF2 alpha, with or without presynchronization, to manipulate follicular waves, luteal regression, and the timing of ovulation so that artificial insemination can be performed at a fixed time without estrus detection.

Classical Ovsynch: strengths and limitations

The original Ovsynch program consists of a GnRH injection on day 0, PGF2 alpha on day 7, and a second GnRH dose 48–56 h later, followed by TAI. By inducing ovulation of a dominant follicle at the first GnRH and luteolysis at PGF2alpha, Ovsynch creates a controlled window for synchronized ovulation at the second GnRH. Early studies demonstrated that Ovsynch allows acceptable conception rates while almost completely eliminating the need for estrus detection, thereby improving reproductive management in large herds (Rabiee et al., 2005).

A meta-analysis of 46 primary studies on the use of the Ovsynch protocol reported an average first-service conception rate of around 41%, with considerable variability among studies. According to the authors, this variation was mainly associated with geographic differences and the characteristics of the study populations. (Akçay et al., 2022). More recent field data confirm that in high-yielding herds, P/AI to a first Ovsynch-based TAI often lies around30% to 40%, especially when cows begin the protocol in suboptimal luteal status or deep negative energy balance (Juodžentis et al., 2022).

While Ovsynch is solid and simple to implement, its main limitation is that it does not control the stage of the estrous cycle at protocol initiation. Cows starting Ovsynch without a functional corpus luteum or with small follicles respond less consistently to GnRH, leading to incomplete synchronization and lower fertility. This limitation motivated the development of presynchronization strategies.

Presynch–Ovsynch

Presynchronization protocols were designed to place cows in a more favorable ovarian status when Ovsynch begins. The classic Presynch–Ovsynch system uses two PGF_2 alpha injections given 14 days apart (often starting around 30–40 days in milk), with Ovsynch initiated 11–14 days after the second PGF_2 alpha. By inducing estrus and luteal formation before Ovsynch, this approach increases the proportion of cows that enter Ovsynch in diestrus with a functional corpus luteum and a well-developed dominant follicle.

Randomized field trials have shown that Presynch–Ovsynch improves pregnancy per TAI compared with stand-alone Ovsynch and with TAI after observed estrus. For example, Strickland et al. (2024) reported that the Presynch-11–Ovsynch program increased P/AI relative to estrus + TAI strategies in first, second, and ≥3rd parity cows, with multiparous cows in the Presynch-11 group having >60% greater odds of pregnancy than cows bred after detected estrus.

Across multiple studies, Presynch–Ovsynch typically yields P/AI in the range of 38–45% at first service, i.e., several percentage points higher than standard Ovsynch, particularly in herds with moderate estrus detection efficiency (Mariol et al., 2024; Strickland et al., 2024). These improvements are largely attributed to a higher proportion of cows exhibiting luteolysis in response to PGF2alpha within Ovsynch and a more predictable follicular wave at the time of the first GnRH. However, Presynch–Ovsynch still relies on partial estrus expression and luteal function before Ovsynch, and some cows remain suboptimally prepared, especially those with health problems or profound metabolic stress.

Double-Ovsynch: presynchronization with a full Ovsynch protocol

To further increase control over ovarian dynamics, Double-Ovsynch (DO) was developed as a more intensive presynchronization strategy. In this program, cows receive a complete Ovsynch protocol (GnRH–PGF_2 alpha–GnRH) as presynchronization, followed approximately seven days later by a second full Ovsynch used for TAI. Thus, ovarian function is “reset” twice before insemination, producing a highly synchronized follicular wave at the time of TAI (Herlihy et al., 2013).

In a landmark trial, Herlihy et al. (2013) compared Double-Ovsynch with Presynch–Ovsynch in lactating cows bred by Ovsynch. Double-Ovsynch increased circulating progesterone concentrations at the second GnRH and at TAI and resulted in higher P/AI, especially in primiparous cows. Overall, Double-Ovsynch improved first-service fertility compared with Presynch–Ovsynch, with P/AI differences of around 5–8 % in favor of DO.

Subsequent work has reinforced these findings. Dirandeh et al. (2015) demonstrated that in heat-stressed lactating cows, Double-Ovsynch achieved higher ovulation rates to the first GnRH, better synchronization, larger preovulatory follicles, and superior P/AI compared with various presynchronization schemes using PGF_2 alpha with or without GnRH (Dirandeh et al., 2015). In economic and reproductive modeling studies, Double-Ovsynch is frequently associated with shorter time to pregnancy and lower cost per pregnancy than standard Ovsynch programs, despite higher hormone costs and handling requirements (Berean et al., 2015; Stangaferro et al., 2016).

A recent synthesis of fertility programs by Consentini et al. (2025) evaluated Double-Ovsynch against a novel presynchronization scheme-Double E-Synch (an intensified ovulation-synchronization protocol that applies two sequential eCG treatments together with GnRH/PGF_2 alpha to optimize follicular development and harmonize ovarian status before fixed-time AI, particularly in anestrous cows.) and showed that both protocols produced excellent synchronization rates and high fertility, confirming that the biological principle—presynchronization through repeated, well-timed hormonal control—is more important than the specific drug combination alone.

Furthermore, recent findings further illustrate how targeted modifications of established synchronization protocols can enhance fertility in low-performing herds. In a field study evaluating anestrous dairy cows, Borș et al. (2025) tested a modified Double-Ovsynch program that incorporated an additional GnRH administration on Day 5 after timed AI to support luteal development and early embryo survival. The modified protocol yielded markedly improved reproductive outcomes, increasing first-service pregnancy rate from 26.5% in the standard Double-Ovsynch group to 35.1% in the treated group, and raising cumulative pregnancy rate from 45.6% to 56.8%. These results suggest that strategic post-AI GnRH supplementation may enhance luteal sufficiency during the critical early luteal phase, offering a valuable refinement for herds experiencing reduced fertility or high prevalence of anestrus (Borș et al., 2025).

Taken together, evidence from controlled trials and meta-analyses supports a clear hierarchy of fertility outcomes under well-managed conditions: Ovsynch alone: P/AI typically 30–40% at first service, sensitive to cyclic status, health, and NEB; Presynch–Ovsynch: P/AI commonly 38–45%, with improved luteal function and better control of the cycle at Ovsynch start, especially in clinically normal cows; Double-Ovsynch: P/AI often 45–55%, particularly in primiparous and heat-stressed cows, plus shorter time to pregnancy and improved economic efficiency.

From a physiological perspective, Double-Ovsynch offers the most consistent control over ovarian function, because it standardizes both the preservice and breeding cycles, ensuring that cows arrive at AI with a mature preovulatory follicle and an optimal progesterone profile. Presynch–Ovsynch represents a compromise, enhancing luteal status at Ovsynch initiation while using fewer hormones and cow handlings than Double-Ovsynch. Ovsynch alone remains valuable where labor, infrastructure, or cost constraints limit the implementation of more complex programs, or where estrus detection aids can be used in combination with partial synchronization.

In practical terms, the choice among Ovsynch, Presynch–Ovsynch, and Double-Ovsynch should consider herd size and handling logistics, estrus detection efficiency and availability of activity monitors, prevalence of metabolic and uterine disease, heat stress conditions, and the economic trade-off between hormone cost and improved P/AI.

Nevertheless, for high-producing, intensively managed herds, current literature strongly supports Double-Ovsynch and equivalent high-control programs as the gold standard for first-service fertility and long-term reproductive performance.

Progesterone Supplementation via CIDR or PRID Devices

Progesterone supplementation has become an important component of ovarian function control in high-producing dairy cows, particularly in synchronization programs where luteal support is required to optimize follicular development and ovulatory timing. The most widely used devices are the Controlled Internal Drug Release (CIDR) insert and the Progesterone-Releasing Intravaginal Device (PRID), both designed to deliver controlled and sustained release of exogenous progesterone during the follicular phase of synchronization.

Progesterone supplementation through intravaginal devices such as CIDR and PRID has become an essential component of ovarian synchronization strategies due to its ability to create a controlled and physiologically stable luteal-phase hormonal environment. By providing a sustained release of exogenous P4, these devices suppress premature LH pulsatility and prevent early ovulation, thereby promoting the synchronized emergence of a new follicular wave at device removal (Hölper et al., 2023). This mechanism is particularly important in cows that begin synchronization with low endogenous P4, a condition frequently associated with early postpartum anestrus, NEB, or incomplete luteal development (Bruinjé et al., 2024).

When incorporated into protocols such as the 5-day CIDR-Synch or the 7-day Ovsynch + CIDR, progesterone supplementation improves the consistency of follicular turnover and increases the proportion of cows responding appropriately to GnRH-induced ovulation. Numerous field studies report that progesterone-augmented protocols yield a 5–10 percentage point increase in pregnancy per AI (P/AI) compared with identical synchronization programs implemented without a progesterone device (Hölper et al., 2023). These improvements reflect both enhanced synchronization accuracy and improved early luteal support, which contributes to higher embryo survival during the critical first weeks after conception.

Although CIDR and PRID differ slightly in their release profiles—PRID producing a higher initial progesterone output and CIDR maintaining a more stable release—comparative trials generally demonstrate similar fertility outcomes between the two devices. Consequently, the choice between CIDR and PRID is often determined by availability, regional preference, or farm management logistics rather than by substantial differences in reproductive efficacy.

Overall, progesterone supplementation strengthens the biological reliability of synchronization programs by improving ovarian readiness, enhancing ovulatory precision, and promoting a uterine environment supportive of early embryonic development. In high-production herds, where metabolic stress and cyclicity disorders are common, CIDR and PRID devices play an important role in achieving consistent reproductive performance and optimizing fertility outcomes(Monteiro et al., 2015).

Assisted Reproductive Technologies (ART)

Assisted reproductive technologies (ART) are now integral components of advanced reproductive programs in dairy herds. The two most impactful methods are embryo transfer (ET) and in vitro fertilization (IVF), both designed to overcome fertility barriers and accelerate genetic progress.

In embryo transfer, donor cows are hormonally stimulated to produce multiple oocytes, which are fertilized and transferred to synchronized recipients. When properly timed, ET can achieve pregnancy rates of 45–55% with fresh embryos and 35–40% with frozen ones. The synchronization of both donor and recipient cows is critical; thus, the combination of TAI-based protocols for both has proven particularly effective.

In vitro fertilization (IVF) allows for the recovery of oocytes via ovum pick-up (OPU), followed by fertilization and culture in controlled laboratory conditions. Modern IVF systems have achieved success rates comparable to ET, particularly when using fresh in vitro-produced embryos (Sirard et al., 2025).

The adoption of sexed semen in IVF programs enables herd managers to bias offspring sex, prioritizing female replacements or incorporating beef-on-dairy strategies for surplus animals (Holden, 2018).

ART also serves a therapeutic role, mitigating reproductive inefficiencies caused by uterine pathology or chronic subfertility. By bypassing early embryo mortality and optimizing genetic resource use, these technologies enhance both productivity and economic sustainability (Lonergan et al., 2001).

DISCUSSION

The comparative evaluation of synchronization protocols indicates that the degree of control exerted over ovarian physiology is the primary determinant of fertility outcomes in high-producing dairy cows. Although Ovsynch remains the foundational strategy for TAI, its effectiveness is limited by the ovarian status at protocol initiation. Cows beginning Ovsynch without a functional CL or with small, immature follicles show inconsistent responses to GnRH, leading to reduced synchronization and pregnancy rates typically around 30–40% P/AI (Akçay et al., 2022; Juodžentis et al., 2022).

Presynchronization protocols improve this limitation by ensuring that cows begin Ovsynch in a well-defined luteal phase, characterized by a functional corpus luteum and stable progesterone concentrations. As a result, P/AI commonly increases to 38–45%, with several studies confirming superior luteolysis and more synchronized follicular turnover when cows enter Ovsynch from diestrus (Strickland et al., 2024). These findings highlight the importance of preparing the ovaries in advance to optimize responsiveness to the Ovsynch sequence.

Among all evaluated protocols, Double-Ovsynch provides the most consistent improvements in fertility because it presynchronizes the cow using a complete hormonal sequence before the main breeding protocol. This dual synchronization improves the uniformity of follicular wave emergence, increases progesterone concentrations at AI, and enhances ovulatory precision. Consequently, Double-Ovsynch routinely achieves 45–55% P/AI, even under stressful metabolic or thermal conditions (Herlihy et al., 2013; Consentini et al., 2025).

Progesterone supplementation via CIDR or PRID devices further enhances synchronization performance, particularly in cows with low endogenous progesterone or postpartum anestrus. These devices stabilize LH pulsatility, improve dominant follicle quality, and support early embryo survival, contributing to modest but meaningful gains in fertility (Hölper et al., 2023).

Overall, the literature demonstrates a clear hierarchy in synchronization efficiency—Double-Ovsynch > Presynch–Ovsynch > Ovsynch alone—reflecting increasing levels of physiological control. Nevertheless, reproductive success remains influenced by metabolic status, uterine health, and environmental conditions such as heat stress. Sustainable improvements in fertility require integrating synchronization protocols with solid metabolic monitoring, transition cow management, and precision technologies.

ACKNOWLEDGMENTS

We are thankful to Mara Bălinișteanu (Tipa) for constructive criticism of the manuscript and English revision.

CONCLUSIONS

Reproductive efficiency in high-producing dairy cows is increasingly challenged by the metabolic and physiological pressures associated with intensive milk production. The evidence reviewed indicates that hormonal control of ovarian function through TAI protocols is essential for achieving predictable and efficient fertility outcomes in such herds.

Among synchronization strategies, Ovsynch provides acceptable performance, but presynchronization systems—particularly Double-Ovsynch—offer superior control of follicular and luteal dynamics and consistently higher pregnancy rates. Progesterone supplementation via CIDR or PRID further enhances synchronization accuracy and improves fertility, especially in anestrous or metabolically stressed cows.

Assisted reproductive technologies, including embryo transfer and IVF, complement these protocols by accelerating genetic progress and helping overcome reproductive limitations in subfertile animals.

Overall, integrating precise hormonal synchronization, adequate progesterone support, and selected ART applications provides the most effective framework for optimizing fertility and sustaining productivity in modern dairy herds.

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