Review Article
Journal of Veterinary Healthcare ISSN: 2575-1212
Freely Available Online

A Review of Attempts to Improve Cow Fertility Through Reproductive Management: Estrous Synchronisation

Mohammed A Elmetwally[1,*] Adel Hussien[1], Heba Sharawy[1], Amira Mostagir[1], Engy Risha[2], Wael Eldomany[1], Abdelrouf O Hegab[1], Madeha H Darwish[3], Samy M Zaabel[1]

[1]Departments of Theriogenology,
[2]Clinical Pathology, Faculty of veterinary medicine, Mansoura University, Mansoura 35516, Egypt
[3]Department of Animal and Poultry Behavior and Management, Faculty of Veterinary Medicine, Assiut University, 26, Egypt

Corresponding author:

Mohammed Elmetwally, Ph.D., Department of Theriogenology, Faculty of Veterinary Medicine, University of Mansoura, Mansoura, Egypt .ORCID:0000-0001-7486-7756

Keywords:
Dairy cows, Ovulation, Synchronisation, Reproductive management, Ovsynch

Received: Sep 24, 2021

Accepted: Nov 16, 2021

Published: Nov 29, 2021

Editor:
Yanzhou Yang, Ningxia Medical University

DOI: 10.14302/issn.2575-1212.jvhc-21-3973

Abstract

This review focused on the various methods for controlling estrous cycles in well-managed dairy cows. Because up to 70% of dairy cows may stay non-pregnant after an AI procedure, an effective approach for identifying and reinseminating open cows is essential for dairy herds to achieve optimal reproductive performance. Overall, well-managed dairy farms with effective estrus detection programs inseminate 50% or more of non-pregnant cows after behavioral estrus is detected. Cows not detected in estrus are admitted in a resynchronization of ovulation procedure to receive a timed AI (TAI) service to avoid a long interbreeding interval. In Egypt, a widely used program involves starting the Ovsynch protocol (GnRH-7 d-PGF2-56 h-GnRH-16 to 20 h-TAI) 32 days after an initial AI, regardless of pregnancy status. Previous studies have proven that there was no difference in pregnancy/artificial insemination (P/AI) between Ovsynch+P4 and Presynch-Ovsynch, both protocols were equally effective in improving the fertility of cows with a CL 15 mm. The review also addressed different methods for synchronization of ovulation and different factors affecting the selection of the management program.

Introduction

The profitability of dairy cows is depending mainly on reproductive performance [1]. Reproductive management is considered as one of the most important factors that should be taken into consideration to increase the profitability of dairy cows. Calving interval, milk production efficiency, and herd replacement dynamics, the timing of pregnancy during lactation affect the profitability of dairy herds [2]. Although insemination and the risk of conception after the end of the voluntary waiting period (VWP) are the two main determinants of time to pregnancy during lactation, the length of the VWP, which determines when cows are eligible for insemination, can also affect the timing of pregnancy. VWP has traditionally lasted 60 days in dairy farms [3]. Dairy farm revenue is affected by maximizing the number of female calves born for substitutions, minimizing replacement due to reproductive disorders, and optimizing the time that adult cows spend in the most efficient part of the lactation curve [1].

Although there are numerous reproductive management strategies available for dairy farms, determining the best management program to implement remains a major challenge for dairy producers owing to the complicated interactions of multiple biological and management factors affecting dairy herd dynamics and economics [4,5]. The dairy industry has recently approved hormonal protocols for synchronizing estrus and ovulation as reproductive management systems to increase the overall reproductive performance of lactating cows 6. Ovsynch protocols are important for increasing insemination risk but not fertility in dairy cattle because the conception rate (CR) of AI services after Ovsynch is typically within the reference range for cows inseminated after observed estrus [4,7]. Recently, new protocols, such as Presynch-Ovsynch and Double-Ovsynch, have recently been developed to improve not only the risk of insemination but also the fertility of timed AI (TAI) [7–9].

So, the present study aimed to evaluate how the application of different synchronization protocols such as Ovsynch, modified Ovsynch, presynch, and modified presynch protocols would be used to maximize the reproductive performance of Holstein dairy cows in Egypt.

The Estrous Cycle in Dairy Cows

In dairy cows, the estrous cycle is the time between two standing heats. The estrous cycle is a cyclical pattern of ovarian activity that allows female animals to go from a state of reproductive receptivity to one of reproductive non-receptivity, allowing for the formation of pregnancy after mating. An estrous cycle in cattle lasts 18–24 days on average [10,11]. The luteal phase (14–18 days; met-estrus and di-estrus) and the follicular phase (4–6 days; pro-estrus and estrus) are the two distinct periods of the cycle. The luteal phase begins after ovulation when the corpus luteum (CL) is created, and the follicular phase begins when the corpus luteum (CL) dies (luteolysis) and ends with ovulation [11–13]. During the follicular phase, the ovulatory follicle's final maturation and ovulation occur, resulting in the release of an egg (the female gamete) into the oviduct, allowing for fertilization.

GnRH starts a chain reaction of hormones that regulate the estrous cycle [14–16]. Follicle maturation is influenced by FSH, while LH acts on the ovarian tissues at the site of ovulation, changing them into corpus luteum (CL) [[15,17,18]. Furthermore, these hormones control the many stages of estrus, including the follicular phase, estrus, and luteal phase [19–22]. Ovulation is an inflammatory process characterized by an influx of leukocytes into the ovulatory follicle and changes in the translation profile of immune markers in the theca and granulosa tissue layers and has been defined as an inflammatory process [23].

Following ovarian stimulation with FSH and LH, estrogen and progesterone are generated. Because it produces prostaglandin F2, the uterus aids in reproductive control [24–26].

During the follicular, estrus, and luteal phases of the cycle, the combination of hormone secretion and metabolism maintains the correct hormonal balance [27–29]. The pre-ovulatory follicle and the later formed corpus luteum are the two main ovarian structures that govern the estrous cycle by secreting estradiol and progesterone, respectively [23,30,31].

During the ruminant estrous cycle, changes in a pre-ovulatory follicle and corpus luteum, patterns of LH, estrogen, and progesterone release, and changes in ovarian blood flow all occur [32 33–35].

Maximizing reproductive performance in high-producing cows is one of the top aims of dairy herd management [36]. Oestrus detection failure and artificial insemination timing error may occur in dairy cows with short and weakened estrous signals, resulting in low reproductive success [37]. Moreover, the difficulty of detecting oestrus and the resulting low heat detection rate may be major contributors to declining reproductive performance [38,39].

To attain an appropriate heat detection rate, cows must exhibit estrous symptoms for a significant amount of time, and estrous behaviors must be carefully observed by herdsmen. Due to delayed resumption of ovarian cyclicity and failure of oestrus expression, increased milk production and changes in management techniques can result in a longer duration of post-partum anoestrus [16,40,41]. The predominant estrous symptom in cattle is standing to be mounted by herd members. Mounting other cows, restlessness, enlargement, relaxation, and congestion of the vulva, clear mucus secretion, bleeding following oestrus, and a decrease in appetite and milk supply are all secondary estrous symptoms in cattle [42–44]. Standing oestrus in dairy cows is reported to last 12–18 hours [45,46]. Estrous detection failure and timing inaccuracy in artificial insemination (AI) might result from shorter oestrus length andweakened estrous signals without standing oestrus, resulting in a low conception rate [37]. In the majority of cows with standing oestrus, secondary estrous indicators such as sexual activity and changes to the external genitals were observed. Cows without standing oestrus who were detected in oestrus based on external genital changes as secondary estrous signs had a significantly lower percentage of secondary estrous behavior such as mounting and deviant mounting and chasing when compared to standing estrous cows [37,47–49]

Of note, the success of the artificial insemination program in most cases depends mainly on the detection of estrous. However, because peak estrus activity generally occurs at night, accurate control of the period of estrus is difficult, and determining the true commencement of standing estrus without 24 hours of observation may be challenging [45,50]

Regular observation of the cows is required for the successful detection of heat. These should be observed at least twice a day, once early in the morning and once later in the evening. At least 20 minutes should be spent on each observation. The more females on heat at the same time, the more heat activity there will be [48,51,52]. Estrus behavior is suppressed by high stocking rates and concrete or slippery flooring (as opposed to straw yards or grassland).

The optimal time to inseminate a heifer or cow is a few hours before ovulation, which happens about 24–38 hours after standing heat begins. This means cows or heifers should be inseminated in the latter two-thirds of a heat cycle or within a few hours after the cycle has ended [53–55]

The environment (temperature, season, and light), age and body weight, hormonal imbalance, diet, and amount of production are all aspects that influence the expression of estrus behavior in bovine species. The temperature has a significant impact on the expression of estrous in bovines since sexual activity is reduced in extreme cold and hot settings, resulting in poor conception. It also has an impact on the duration of the estrous cycle [48,56–58].

The ability to correctly identify cows in estrus and inseminate them at the right time is crucial in reproductive control. In recent decades, technology for recognizing cows in estrus has progressed from tail paint in the 1970s to automated activity monitors and mount detectors [33,59,60]. The gold standard indicator that a cow is in estrus is standing to be mounted. Cows have been reported to stand for 6 to 10 hours to be mounted, however standing estrus is usually missed due to either weak intensity of expression (cow effect) or insufficient observation (human effect), or both [60]. Between the 1990s and the early 2000s, automated estrus detection technologies such as mount detectors, pedometers, and accelerometers were validated and commercially available [61]. The effectiveness and accuracy of these devices have been proven, and they provide continuous, automated monitoring and analysis of mounting or moving behavior [50,62,63].

Understanding the endocrine and neurological processes that drive estrus in dairy cows makes it easier to devise tactics for increasing estrous behavior identification. A concept map on estrus in cattle has been created (Figure 1), which should be referred to frequently throughout the reading of this work to aid comprehension of the issues covered [64,65]. A preovulatory follicle forms on one of the two ovaries during proestrus. This follicle secretes estrogens in response to pituitary gonadotropins in high amounts, causing plasma concentrations of the major estrogen, estradiol, to reach peak levels [24,26,66].

Estrus is caused in the absence of progesterone by the action of estradiol on the hypothalamus (Figure 1). Estradiol has been shown to induce estrus in cattle, horses, sheep, and pigs with ovariectomies. Despite the presence of estrus-inducing serum concentrations of estradiol, vaccination of cattle and sheep against estradiol reduced the development of estrous behavior [24]. Estradiol appears to have "all or none" effects in inducing estrus (Figure 1). That is, once the concentration of plasma estradiol is high enough to induce estrus, additional amounts have no effect on the behavior's expression. Additional amounts, however, may be required for reproductive functions, such as the secretion of specific proteins needed to nourish the early embryo [67–69]. In both intact and ovariectomized cattle, this all-or-none effect has been demonstrated [70,71]. Furthermore, when low doses of estradiol are given and 50% of the ovariectomized cattle are induced into estrus, the cows in estrus exhibit a frequency of various behaviors that are similar to that of cows given much higher doses [72,73].

The size of the follicle at the time of GnRH-induced ovulation influenced the formation and maintenance of pregnancy in beef cattle [16,67,74]. In postpartum beef cows and beef heifers, GnRH-induced ovulation from a tiny dominant follicle (<11.33 mm) was linked with a lower pregnancy rate and late embryonic/fetal survival compared to GnRH-induced ovulation from a large dominant follicle [75–77].

The lower percentage of cows pregnant after GnRH-induced ovulation from a physiologically immature dominant follicle is likely related to oocyte competence difficulties and insufficient maternal tissue preparation for pregnancy [72,78]. A lower plasma 17-estradiol (E2) concentration before and after ovulation, as well as lower plasma progesterone (P4) concentration after ovulation, may result in insufficient preparation of the maternal tissues for pregnancy [79–81].

Reproduction Management of Dairy Cows: Estrus Synchronization

Estrus synchronization is a significant reproductive control method in the dairy cattle sector, where the majority of animals are bred through artificial insemination. Estrus synchronization lowers the cost of estrus detection and eliminates mistakes. Manipulation of the length of the luteal phase of the estrus cycle is the core premise of estrus synchronization [82,83.]

Although numerous synchronization programs involving one or more hormones have been created and deployed on commercial farms, the fundamental concept of estrus synchronization is to modify the length of the estrus cycle [84,85]. The luteal phase can be shortened or lengthened using prostaglandin F2 or its analogs, and it

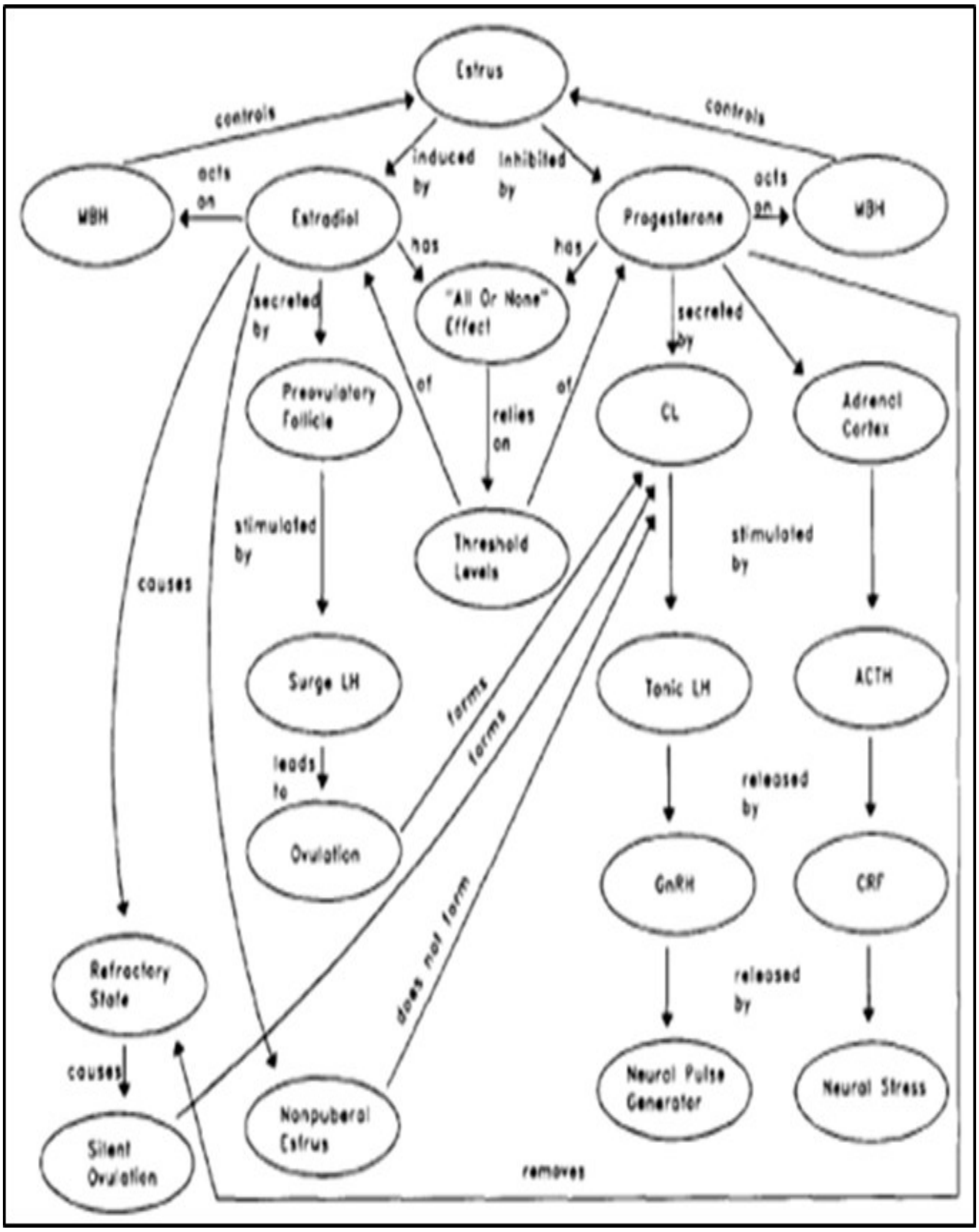

Figure 1. Concept map of estrus in dairy cattle. MBH=Medical basal hypochamismus, CL= corpus luteum and CRF= cortiocotroin realeasing hormone

can also be lengthened with exogenous progestogens. Furthermore, some programs have employed gonadotropin-releasing hormone (GnRH) and estrogens to increase conception rates by modifying follicular wave development and shortening the time between estrus and ovulation [86,87].

Despite the fact that estrus synchronization is associated with a reduced conception rate during the synchronized estrus, improvements in estrus detection efficiency and accuracy can improve practically all reproductive performance. [87,88]. The fundamental challenge in estrus synchronization research has been to achieve tight synchrony while minimizing the unfavorable effect on the conception rate during the synchronized estrus. Ovulation synchronization is the current trend, which allows for planned breeding without detecting estrus [89].

In fact, despite the advantages of estrus synchronization, commercial dairy producers have yet to implement it. When dairy farmers consider whether or not to use estrus synchronization, they consider the expense of drugs as well as the time it takes to implement the program. Detecting estrus in a large herd of synchronized cattle can be more difficult because so many animals are in estrus at the same time, making it impossible to tell which ones are in real estrus [89–91]. This problem can be solved by developing synchronization routines that allow insemination to occur at a precise time. Herd managers must have strong organizational skills as well as some technical knowledge of the program in order to run an effective estrus synchronization scheme. Herd managers, veterinarians, and AI technicians must all efficiently communicate and collaborate. Because the use of PG on pregnant animals causes abortion, meticulous record-keeping is required [4,92].

Principles of Estrus Synchronization

Since the introduction of the Ovsynch protocol two decades ago, significant progress has been made in the understanding and application of synchronization programs for the management of reproduction in dairy herds [4,92]. Dairy farmers have quickly adopted scheduled artificial insemination (AI) methods as a result of a better understanding of oestrus cycle regulation and its relationship to inadequate reproductive performance in dairy herds. Fixed-time AI has become an essential component of the management of reproduction in high-producing herds, according to recent assessments [93,94]. Moreover, due to their capacity to improve the insemination rate, timed AI procedures have shown benefits in pasture-based milk production systems. In order to use the Ovsynch protocol successfully, some basic physiological principles must be followed, such as inducing ovulation to synchronize follicle growth in the first two days of the program so that a young antral follicle is recruited; maintaining high progesterone concentrations during the development of the ovulatory follicle while also effectively lysing the ovulatory follicle [95, 96]

Furthermore, timed AI protocols have also demonstrated benefits in pasture-based milk production systems because of the ability to increase the insemination rate. In general, successful use of the Ovsynch protocol requires some fundamental physiological principles to be respected, including induction of ovulation to synchronize follicle growth in the first 2 days of the program such that a young antral follicle is recruited; maintenance of high concentrations of progesterone during the development of the ovulatory follicle. Having a good quality pre-ovulatory follicle of moderate diameter that is highly oestrogenic and responsive to gonadotropins to synchronously ovulate 12 to 18 hours after insemination, and having an active corpus luteum to result in very low progesterone concentration at AI, and having a healthy corpus luteum to result in very low progesterone concentration at AI. The present estrous and ovulation synchronization methods are inefficient, and future progress would almost probably demand new hormone composition and delivery technology, lowering the need for intervention and assuring producer acceptance [88].

The dairy industry's consolidation, combined with the steady increase in herd size, has necessitated the implementation of systematic reproduction management programs. The development of synchronized ovulation procedures, which provide artificial insemination at a predetermined period with acceptable fertility, has become an important part of breeding management in a variety of production systems [84]. In the last two decades, improvement of these programs has resulted from a greater understanding of ovarian biology in lactating cows, as well as improved control of follicle growth and luteal lifespan, providing unique opportunities to modify follicle development, optimize oocyte quality, and increase embryo survival [97].

Methods of Estrus Synchronization Application in Dairy Cows

For the selection and successful implementation of the estrus synchronization planned, knowledge of the hormonal profile and functional structures present in the ovaries at various stages of the estrous cycle is highly crucial [53,98]. The basic method is to manage the time when the estrus begins by managing the length of the estrous cycle. Different ways to the estrous cycle length control are Prostaglandin shots before natural luteolytic time, for the recovery of the animal's corpus luteum (CL), is by employing gonadotropin release hormones or analogs that cause ovulation of a dominant follicle or ovulation of a larger follicle causing the ovulation of a larger follicle [99,100].

Prostaglandins Based Protocol Approach

The hormones that exist spontaneously are prostaglandin (PG). PGF will be released from the womb within 16 to 18 days of the heat of the animal during the regular estrous cycle of a non-pregnant animal. This PGF release works to damage the corpus luteum (CL). The CL is an ovarian structure producing the hormone progesterone and avoiding the return of the animal to the estrus. The release of PGF from the uterus causes the animal to return to the estrus every 21 days [101, 102]. PGF2α (Lutalyse, Estrumate, Prostamate), which is commercially available, allows the cattle owner the possibility to remove CL concurrently from all the animals at an advantageous moment for warmth detection and raising [53]. PGF2α has a key drawback in that it is ineffective in animals that do not have a CL. This comprises animals who have been in heat for 6 to 7 days, prepubertal heifers, and postpartum anestrous cows [103,104].

Despite these drawbacks, using prostaglandins to synchronize estrus in cattle is the easiest way. These products can synchronize estrus and fertility in cyclic females, such as virgin heifers, but they can't produce estrous cycles in non-cycling cows [105,106,107,108].

One-Shot Prostaglandin F2α

In dairy cows with a functioning corpus luteum, prostaglandin F2 is often utilized to synchronize estrus. When dairy cows are given PGF2, around 50–60% of the treated cows go into estrus within 2–6 days [92 4]. Following artificial insemination after estrous detection, subsequent conception rates have been reported to reach [30–42] percent, resulting in a pregnancy rate of around 20% per treated cow [95]. As a result, the large time intervals between PGF2 injection and estrus/ovulation, as well as the failure to detect estrus, are important practical drawbacks. To optimize the efficacy of timed AI (TAI), a procedure that closely synchronizes PGF2 therapy and estrus/ovulation is required [50,84].

Two Shot Prostaglandin

Once the stage of the estrous cycle in the cows is identified, two injections of prostaglandins are administered at 10-to-14-day intervals. Before or between injections, estrus detection is not required. Regardless of where they were in their estrous cycle when the first injection was given, all cycling cows should respond to the second. All females experiencing estrus after the initial PGF2 injection can be bred, which can change the program [109,110]. Then only the females that haven't been bred receive the second injection. This option saves money and time, but it results in two synchronized groups rather than one, and it takes longer to breed.

Recent studies used intravaginal (IVG) prostaglandins instead of intramuscular or subcutaneous. of notes, Wijma et al. (2016) found that IVG delivery of two doses of 25 mg dinoprost (a natural form of PGF2α) 12 hours apart successfully produced complete luteal regression and resulted in circulating progesterone (P4) profile similar to that of milking dairy cows given a single 25-mg IM dosage of PGF2α. Circulating P4 concentrations in cows treated with IVG or IM PGF2α did not differ 48, 60, or 72 hours after therapy, and a similar proportion of cows in both groups exhibited complete CL reduction by 60 and 72 hours following treatment [111]. Similarly, were the results for the application of GnRH intravaginal in automated synchronization systems [112].

Wijma et al. (2016) also found that giving two 25-mg dinoprost doses 12 hours apart was the most effective way to get complete CL regression compared to smaller or larger doses (i.e., 25 and 125 mg) or a similar dose (i.e., 50 mg) given as a single therapy. P4 concentration dynamics in cows given two 25-mg PGF2α doses 12 hours apart were similar to those in cows given a single 25-mg IM dosage of dinoprost, suggesting that this dose and treatment frequency for intravaginal infusion is a feasible choice for future investigations examining CL regression and ovulation synchronization [111].

Progesterone Base Protocol Approach

Even after the corpus luteum has regressed, synchronization of estrus with progestogens maintains high amounts of progesterone in the female's system. Estrus synchrony occurs 2 to 5 days after progestin withdrawal. Melengesterol acetate (oral feeding), Syncro-Mate-B (Ear Implant), and CIDR are commercial products that fit within this category (Intra-vaginal device). Only 48% of cows treated on day 3 had their estrus synchronized, but when treatment began on day 9 of the estrous cycle, the synchronization was 100%. The longer cattle were given progestin, the higher the rate of estrous synchronization, but the lower the fertility of the synchronized animals [113–116]. In addition to PGF2α, inserting a progesterone-impregnated intravaginal insert (progesterone-releasing intravaginal device (PRID) or controlled internal drug release (CIDR) insert) during a 5- or 7-day period efficiently synchronizes estrus. When injected at the time of insert removal, PGF2α lyses any functioning corpus luteum. Inseminations usually take place two to five days after estrus is recognized and removed [117,118].

This therapeutic regimen was used to develop the Syncro-mate B commercial product, as well as the PRID (Progesterone releasing intravaginal device) and CIDR (Controlled intra vaginal drug release device). Although the corpus luteum has shrunk, increased pulsatile secretion of gonadotropin during the period when exogenous progestin is preventing estrus leads the persistent follicle to grow [119]. The use of an intravaginal device for 10 to 14 days during any synchronization program increases the risk of local vaginal infection, which, in the worst-case scenario, leads to an ascending infection to the uterus, producing endometritis-pyometra. At the time of CIDR application and withdrawal, strict cleanliness must be kept. For each CIDR application, new latex gloves should be worn, and the applicator should be sanitized between uses. Over the CIDR and applicator, a disinfecting ointment is also applied. When the CIDR devices are removed, the next CIDR is performed with a new glove. When injecting eCG, take care to ensure that the female receives the whole amount [119].

The decreased fertility of cows bred at synchronized estrus after long-term progestin administration is attributed to early ovarian meiosis or aberrant embryo development produced from persisting follicle ova. The use of progestogens in cattle for less than 14 days did not lower the percentage of calves conceived. Furthermore, short-term progestogen exposure induces some anestrus (postpartum or prepubertal) heifers to cycle [120,121].

GnRH – Based Protocol Approach Synchronization Systems

Ovsynch, a GnRH and PGF2α regimen, was created to synchronize ovulation in dairy calves, with the goal of synchronizing ovulation within an 8-hour interval (from 24 to 32 hours after the second GnRH treatment), allowing TAI without detection of estrus and pregnancy rates of 30 to 40% [4,122]. GnRH was injected on day 0 of the Ovsynch regimen, then by PGF2 after 7 days, and the second infusion of GnRH after 48 hours, with TAI 72 hours following PGF2α. Synchronization with the Ovsynch procedure was successful in detecting estrus, facilitating artificial insemination, and assisting producers in improving reproductive efficiency by causing precise ovulations [92,122,4]. Although PGF2α is particularly successful at promoting luteolysis from days 6 to 16 of the estrous cycle, the time between therapy and estrus and ovulation is rather variable [123]. Early investigations of PGF2α for estrus synchronization were aimed to ensure the presence of a responding CL, either by providing a single PGF2α infusion after palpating a CL per rectum or by giving two PGF2α treatments, 11 or 14 days apart. While fertility in response to a PGF-induced estrus has been shown to be comparable to that of a spontaneous estrus, pregnancy outcomes in PGF-based protocols using timed-AI (TAI; without estrus detection) have been considered unacceptably low [124]. Timed artificial insemination (TAI) following ovulation synchronization is a technology that is critical for reproductive success in many dairy and beef cow enterprises in North America and around the world [4,92,125]. Synchronization of ovulation procedures entails using a sequence of two or more hormonal therapies to control follicular wave dynamics, corpus luteum (CL) regression, and ovulation [4]. In the dairy cows industry, breeders can choose from a variety of simple hormonal treatment protocols that vary in form, number, and sequence, all with the goal of assuring quick insemination after the voluntary waiting period or a failure in AI treatment [126]. Finally, ovulation timing is synchronized within a short time frame, allowing for insemination of groups of cows by a fixed time, regardless of estrus expression and detection [127].

Fertility to AI in dairy heifers is frequently regarded as the gold standard to obtain in lactating dairy cows, and that such fertile responses in heifers should be achieved in TAI programs for both heifers and lactating cows. Lactating dairy cows have a number of problems, including the biological responses and demands of lactation, metabolism, and production disorders include metabolic, mammary, and uterine diseases, all of which reduce fertility. Due to basic reproductive differences, however, developing a fertile TAI program in heifers has proven difficult. Application of a simple OvSynch-program [48] in the early stages of TAI development [81,128,129]

Presynch techniques that include gonadotropin-releasing hormone (GnRH) and prostaglandin (PG) F2 induce ovulation in anovulatory cattle and increase the proportion of cows that synchronize during an Ovsynch procedure maximize pregnancies per A.I. In a seven-day Ovsynch protocol, adding a second PGF2α injection 24 hours after the first boost luteal regression, which leads to more pregnancies per A.I. especially in multiparous cows [130,9,131].

The intervals between PGF2α therapy and estrus and ovulation relied on the stage of development of the dominant follicle at the time of treatment, according to preliminary research involving estrus monitoring and following comprehensive ultrasound analyses of ovarian follicular wave patterns [122,124]. PGF2α given 5 or 8 days after ovulation caused the dominant follicle of the first follicular wave to ovulate in 2 or 3 days, but PGF given 12 days after ovulation caused the dominant follicle of the subsequent follicular wave to ovulate in 5 days [132].

There was a rise in the number of synchronized animals and a reduction in the variability in the time to estrus in beef cows and heifers when a GnRH analog was administered 6 days before injection of PGF2. This reduction in time variability could be explained by the commencement of a new follicular wave in response to GnRH, resulting in the presence of a new dominant follicle at the time of PGF2α injection [4,92].

GnRH-induced follicle turnover or the initiation of a new follicular wave would be most useful if ovulation was prompted in response to the first administration of GnRH, resetting follicular development, and producing a new dominant follicle containing at least 25.8% of the dairy cattle in the Ovsynch group had insufficient luteal regression [133–135].

Pregnant Mare Serum Gonadotropins (PMSG) and Estrous Synchronization

Late embryonic and early fetal mortality, which average 13 percent and 11 percent, respectively, impair breastfeeding dairy cows' reproductive effectiveness [136,137]. In breastfeeding dairy cows, low plasma progesterone levels are a primary cause of poor embryo development and higher pregnancy losses. In fact, cows with a higher number of corpora lutea than embryos (extra corpus luteum) were less likely to lose a fetus. As a result, increasing progesterone levels in plasma by inducing auxiliary corpora lutea or administering progesterone decreased late embryonic and early fetal mortality [138,139].

In Bos indicus cows, intervention with intravaginal P4 devices coupled with eCG at device removal enhanced ovulation rates, plasma P4 concentrations, and pregnancy rates in suckled beef cattle with a higher incidence of anestrous or a poor body condition score [140–142].

The efficiency of TAI procedures is limited in postpartum anestrous cows because their pulsatile release of LH is insufficient to support the final phases of ovarian follicular growth and ovulation [143]. Exogenous progestins caused ovulation by increasing LH pulse frequency during and after treatment [144]. Despite progestin-induced postpartum cyclicity, the efficacy of such treatment may be hampered in populations with a high number of anestrous cattle, poor body condition scores, or both [144] In order to boost LH support, gonadotropins could be added in synchronization methods.

Because of its cost-effectiveness, pregnant mare serum gonadotropin (PMSG) is commonly used for estrus synchronization programs in small and large ruminants [141,145]. PMSG enhances follicular development and ovulation in cattle by acting like FSH but also like LH. Its parenteral injection stimulates follicular growth and ovulation in cattle [146,147]. PMSG is given to cows either the ovaries produce a pool of little follicles or cause ovulation of big follicles. Following that, PGF2 was given to help with corpus luteum regression. On day 14 postpartum, PMSG treatment improves follicular development and plasma estradiol levels in cattle without influencing subsequent reproductive function [147].

Treatment with PMSG is thought to improve ovarian follicular development and fertility in dairy cows at the end of the estrus synchronization program [122][148–150]. In the dairy cows' estrous cycle, on Day 4 of the first follicular wave of the estrous cycle, when LH receptors are first discovered in granulosa cells of the dominant follicle [151], maturing ovarian follicles have the highest amount of FSH receptors. After gaining LH receptors in granulosa cells, dominant follicles react to both FSH and LH or eCG [151]. In nulliparous beef heifers, injection of eCG at the same time as PGF2 increased the size of the pre-ovulatory ovarian follicle [143] and raised circulating estradiol levels in suckled cattle. On day 14 postpartum, PMSG treatment improves follicular development and plasma estradiol levels in cattle without influencing subsequent reproductive function [122,148]. PMSG is used to either increase the number of small follicles or triggers ovulation in large follicles on the ovaries, followed by PGF2 to reduce corpus luteum growth [152].

Detection of Oestrus is Suboptimal in Dairy Cows

The rate of submission to insemination and P/AI define the rate of pregnancy in dairy herds once the voluntary waiting period has ended. The reduced rate of oestrus detection and, as a result, reduced submission to insemination found in nursing dairy cows is one of the constraints to optimal reproduction in many dairy farms [84,122]. Cows are usually eligible for insemination when they have completed the voluntary waiting period and are not pregnant. Because the oestrus cycle of dairy cows is estimated to last 21 days, appropriate cows should show oestrus and be eligible for insemination every three weeks [85]. As a result, the proportion of eligible cows inseminated for each 21-day interval out of the total eligible cattle in the same period is commonly used to compute oestrus diagnosis. Because oestrus identification is the only way to inseminate cows, pregnancy rates decrease when compared to management programs that allow for systematic AI control [4,92,153]. The delaying in first postpartum insemination and the longer period between re insemination in non-pregnant cows are to account for the reduction in the conception rate [154].

Cows should be Chosen Based on the following Criteria

Sufficient time has passed between calving and the start of synchronization treatments; a minimum of 40 days postpartum is recommended at the start of therapy. On a scale of 1 to 9, a body condition score of at least 5 is considered average or above average. Calving issues are minimal [155].

Replacement to avoid issues during synchronization, heifers are grown to a pre-breeding target weight of at least 65 percent of their predicted mature weight, and reproductive tract scores of 2 or higher on a scale of 1 to 5 are assigned to heifers two weeks before synchronization treatment begins [156,157]. To improve the likelihood of responding to a synchronization program, heifers must reach puberty before being synchronized. In addition, compared to her pubertal estrus, a heifer's third estrus results in a 21% increase in fertility [158,159].

Factors Affecting Estrus Synchronization

Several factors have been proven to alter the length of the estrous cycle, including age, species, and body weight, amount of nourishment, time of the year, hormonal changes, lactation, suckling, and degree of milk yield [160]. The effects of herd conflict and stress on the estrous cycle are well established. The duration of oestrus in the farmyard is likely to vary depending on breed, management, and a variety of environmental factors: The average duration of the hot spell is 12-16 hours, with a larger range of 3-28 hours seen across the board [65,160].

Ovulation has been observed to occur 10-12 hours after the heat cycle has ended [4,26,161]. Because sperm cells have a short life in the female reproductive system, the moment of ovulation is critical if maximal breeding success is to be achieved [162]. The research findings on the timing of ovulation in cattle have been inconsistent, and the number of animals employed in the studies has been limited. According to Foot [163], ovulation happens spontaneously in cows between 24 and 48 hours following the commencement of estrus, based on his own research and that of others. Ovulation occurs 27 hrs from the commencement or just after the conclusion of estrus [37,164]

Body Condition of the Animal

On a scale of one to five, a score of one suggests that the cow is malnourished, while a score of five means that the cow is overweight. A BCS of 3 indicates that the animal has adequate energy stores to support a pregnancy around the time of breeding; a BCS of less than 3 suggests that the animal does not have enough energy reserves to maintain a pregnancy. Because the cow has mobilized body fat stores to fulfill the energy requirements for milk yield in early lactation, negative feeling balance (NEB) is indicated by a drop in BCS [165,166].

The state of a cow's body has a direct impact on one's ability to reproduce. In dairy cows, there is a lot of evidence that body condition affects reproductive performance. Low body condition can have a detrimental impact on female fertility for a variety of reasons, including a prolonged interval between parturition and the commencement of ovarian activity [167]. The single most critical element determining when beef heifers and cows will begin cycling after calving is their body condition at the time of calving [168].

Undernutrition can affect pituitary activity, which includes gonadotropin production and release, as well as the responses of target organs to gonadotropin-releasing hormone or gonadal hormones. The capacity of an animal to maintain a high-frequency mode of pulsatile LH release has been related to its metabolic status. One important way that energy limitation impairs reproductive activity appears to be suppression of an increase in luteinizing hormone pulse the frequency that has been necessary for the growth of ovarian follicles inhibits pulsatile release by the hypothalamus [167,169,170].

The Parity Effects

The time between calving and first ovulation in primiparous cows has been shown to be longer than in multiparous cows. Because of the requirements for growth other than lactation, this link is related to more nutritional shortages being imposed on young cows. According to recent research, primiparous cows' first ovulation postpartum was postponed under optimal management compared to multiparous cows. [171].

Multiparous cows have superior reproductive performance than primiparous cows [93]. Others discovered that primiparous cows performed equally well or better than multiparous cows. Reduced incidence of metabolic problems in early lactation could be one factor for primiparous cows' better fertility[94].

Breed of the Cows' Effects

The breed plays an important role in the response of cows to the synchronization program. There are considerable differences in the effects of estrus synchronization between zebu and taurine breeds due to their different estrus cycles. There has been documented diversity in the length, duration, and severity of the estrus cycle within and across breeds [172–174]. Estrus lasts 4.8 and 7.4 hours in zebu and their crossbreeds, respectively. Crossbreeding has also been demonstrated to improve estrus appearance and allow calves to reach puberty 6 to 12 months longer than Bos taurus cows [175].

Recently, slight changes in ovarian follicular dynamics that could affect the use of assisted reproduction like synchronization or superovulation have been addressed. [176]. Because of the differences in the estrus cycle or the duration of the estrus cycle, synchronization techniques for one do not always work for the other[171]

Lactation/Suckling and Level of Milk Production

Because prolactin function peaks during intense lactation, and sensory cues from sucking decrease the prolactin inhibiting factor (PIF), which comprises dopamine and GnRH-related peptide, lactation has been demonstrated to diminish ovarian activity. Because dopamine and GnRH have essential interactions with gonadotropins, the GnRH component is important. Because the LH releasing factor is blocked, no LH is released, and hence no final follicle maturation, oestrus, or ovulation occurs [177,178]. When compared to low-producing cows, high-producing cows have worse oestrus behavior and a shorter oestrus duration. It's been claimed that heavy producer cows don't have oestrus cycles for 3 to 4 months after giving birth [87,178].

Stress

Even in the presence of estrus-inducing doses of estradiol, stress has been shown to delay, shorten, or entirely block the manifestation of estrus in cows [179]. The proper operation of the cow's endocrine system is known to be influenced by several forms of stress, whether caused by poor feeding, management, or environmental conditions [31,173]. Many ordinary husbandry procedures can cause a rise in plasma glucocorticoids, and stress in the cow can result in elevated concentrations of progesterone of adrenal origin. Increased cortisol release has been observed in cattle in response to a number of acute stresses [180,181].

The Influence of Estrous Synchronization Protocol on the Conception Rates in Dairy Cows

Breeding at Fixed-Time Artificial Insemination (FTAI)

Larson and Ball (1992) found that pregnancy rates from fixed TAI after synchronization with PGF2 were varied, especially in lactating dairy cows compared to heifers, owing to changes in the time of ovulation in response to AI, resulting in varying estrous cycle duration in cows [182]. Estrus detection accuracy is a critical management issue [183]. Approximately half of all estrous episodes go undetected. As a result, the number of insemination possibilities is extremely limited, resulting in increased days open and financial loss. Because of inaccuracies in estrous identification, many cows are inseminated at periods when pregnancy is unlikely [184].

Pursley et al. (1995 and 1997) developed Ovsynch to build a TAI program that put less emphasis on detecting estrus because all cows were inseminated at a specific time relative to hormone injection [92, 4]. According to some sources, a fixed-time insemination scheme could revolutionize dairy cow reproductive management by eliminating the requirement for estrus detection [89,94,134]. Others found that cows getting AI at observed estrus after GnRH–PGF2 had higher conception rates than those receiving Ovsynch with the FTAI program [185].

TAI methods minimized the annoyances of ovulation synchronization and AI on detected estrus, and they suggested that they could provide an efficient and effective means of capturing selecting genetic features with economic implications in a fixed time insemination program. They also noted that changes in pasture and diet, breed composition, physical condition, postpartum interval, climate, and geographic location will impact TAI protocol performance [186]. All of these obstacles have prompted scientists to develop a number of estrous synchronization regimens with TAI that are tailored to the needs of each region.

Conception Rate

The initial service pregnancy rate was a useful metric for assessing fertility, with 60-70 % being considered ideal in well-managed herds [187]. Several previous studies have looked at the fertility of postpartum dairy cows using the Ovsynch procedure, with fertility rates ranging from 27 to 39 percent each AI [4,188,189]. Pursley et al. (1995) found that when PGF2 was given 48 and 24 hours before the second GnRH, the rates of conception were 55 and 46 percent, respectively. They also discovered that pregnancy rates varied from 37, 40, 44, 40, and 32 percent in cows inseminated at fixed times of 0, 8, 16, 24, and 32 hours following the second injection of GnRH in the Ovsynch procedure [4]. Burke et al. (1996) examined the efficiency of TAI and AI in nursing dairy cows with identified estrus after the Ovsynch protocol and found that conception rates were 30.5 and 29.0 percent, respectively [185].

Progesterone and Estrogen Changes and Estrous Synchronization

The progesterone hormone is in charge of stimulating cyclicity, follicular growth, and pregnancy maintenance. The plasma protein, cholesterol, and mineral profiles of animals indicate their nutritional status and are associated with their fertility [190, 191]. Cholesterol, as a major contributor of steroid hormones, is important in steroidogenesis, while calcium tones up the genitalia, and protein and inorganic phosphorus are implicated in metabolic pathways at the cellular level. Several metabolic and environmental factors disrupt these hormonal and nutritional statuses, impairing normal physiology in the animal body [191].

PGF2 therapy resulted in a decrease in progesterone levels on day 9 (48 hours later) in all controlled breeding programs (Ovsynch and CIDR synch) due to PGF2's luteolytic action on the corpus luteum [191,192].

Significant increase in plasma P4 profile observed on day 7 of treatments with CIDR and Ovsynch protocols (4.97 ±1.68 and 3.75 ±0.47 ng/ml) over initial (0 days) values, with dramatic fall to almost basal values on induced estrus within 48-60 h after PG injection has previously been identified in anestrus cows using CIDR and Ovsynch protocols [190,193].

Some researchers reported lower first service conception rates (CR) in targeted breeding programs compared to spontaneous oestrus breeding [194]. Reducing the estrous cycle repeatedly may interrupt corpus luteum function and reduce fertility in high-yielding dairy cows. Rosenberg et al. (1990) hypothesized that the amount of progesterone produced during the cycle preceding artificial insemination could influence conception [195]. Ovulatory failure has been blamed for dairy cows' inability to develop luteal tissue after synchronization [196,197]. The significance of follicular wave dynamics in the onset of oestrus and ovulation timing after synchronization was proven [198]

Additionally, serum P4 levels are higher 14 days later than they were at the time of the first treatment. At any given time, a certain percentage of cycling cows have physiologically low progesterone levels. During lactation, the percentage of cows with consistently low P4 levels in serum (1 ng/ml) decreased. Inactive ovaries or cystic ovarian disease are associated with low progesterone levels at PG shots of the ovsynch protocol [194].

Regarding the level of estrogen (E2) during the ovsynch programs, it was reported that GnRH-induced ovulation of small follicles (11.3 mm) in beef cows was associated with lower P/AI and serum E2 concentrations at AI, as well as higher pregnancy loss [199]. Moreover, in cows, proestrus estradiol concentration is positively related to the size of the preovulatory follicle, subsequent CL size, serum P4 concentration, and, as a result, pregnancy rate 200. of notes, on days 0 and 7, estrogen levels in various animals treated with Ovsynch protocols were nearly identical [200].

References

1. Giordano JO, Fricke PM, Wiltbank MC, et al. An economic decision-making support system for selection of reproductive management programs on dairy farms. J Dairy Sci 2011;94:6216–6232.
2. Giordano JO, Kalantari AS, Fricke PM, et al. A daily herd Markov-chain model to study the reproductive and economic impact of reproductive programs combining timed artificial insemination and estrus detection. J Dairy Sci 2012;95:5442–5460.
3. Miller RH, Norman HD, Kuhn MT, et al. Voluntary waiting period and adoption of synchronized breeding in dairy herd improvement herds. J Dairy Sci 2007;90:1594–1606.
4. Pursley JR, Mee MO, Wiltbank MC. Synchronization of ovulation in dairy cows using PGF2α and GnRH. Theriogenology 1995;44:915–923.
5. Souza AH, Ayres H, Ferreira RM, et al. A new presynchronization system (Double-Ovsynch) increases fertility at first postpartum timed AI in lactating dairy cows. Theriogenology 2008;70: 208–215.
6. Olynk NJ, Wolf CA. Economic analysis of reproductive management strategies on US commercial dairy farms. J Dairy Sci 2008;91:4082–4091.
7. Fricke PM, Giordano JO, Valenza A, et al. Reproductive performance of lactating dairy cows managed for first service using timed artificial insemination with or without detection of estrus using an activity monitoring system. J Dairy Sci 2014;97:2771–2781.
8. Voelz BE, Rocha L, Scortegagna F, et al. Response of lactating dairy cows with or without purulent vaginal discharge to gonadotropin-releasing hormone and prostaglandin F2α. J Anim Sci 2018;96:56–65.
9. Stangaferro ML, Wijma RW, Giordano JO. Profitability of dairy cows submitted to the first service with the Presynch-Ovsynch or Double-Ovsynch protocol and different duration of the voluntary waiting period. J Dairy Sci 2019;102:4546–4562.
10. Silva LOE, Valenza A, Alves RLOR, et al. Progesterone release profile and follicular development in Holstein

cows receiving intravaginal progesterone devices. Theriogenology 2021;172:207–215.

11. Perez Marquez HJ, Ambrose DJ, Schaefer AL, et al. Evaluation of infrared thermography combined with behavioral biometrics for estrus detection in naturally cycling dairy cows. Animal 2021;15:100205.
12. Motta JCL, Madureira G, Silva LO, et al. Interactions of circulating estradiol and progesterone on changes in endometrial area and pituitary responsiveness to GnRH†. Biol Reprod 2020;103:643–653.
13. Veronese A, Marques O, Peñagaricano F, et al. Genomic merit for reproductive traits. II: Physiological responses of Holstein heifers. J Dairy Sci 2019;102:6639–6648.
14. Savio JD, Thatcher WW, Badinga L, et al. Regulation of dominant follicle turnover during the oestrous cycle in cows. J Reprod Fertil 1993;97:197–203.
15. Webb R, Nicholas B, Gong JG, et al. Mechanisms regulating follicular development and selection of the dominant follicle. Reprod Suppl 2003;61:71–90.
16. Elmetwally MA. Uterine involution and ovarian activity in postpartum holstein dairy cows. A review. JVHC 2018;1:29–40.
17. Webb R, Campbell BK, Garverick HA, et al. Molecular mechanisms regulating follicular recruitment and selection. J Reprod Fertil Suppl 1999;54:33–48.
18. Riccetti L, Sperduti S, Lazzaretti C, et al. The cAMP/PKA pathway: steroidogenesis of the antral follicular stage. Minerva Ginecol 2018;70:516–524.
19. Luo X, Chang H-M, Yi Y, et al. Bone morphogenetic protein 2 upregulates SERPINE2 expression through noncanonical SMAD2/3 and p38 MAPK signaling pathways in human granulosa-lutein cells. FASEB J 2021;35:e21845.
20. Meier S, Kuhn-Sherlock B, Amer PA, et al. Positive genetic merit for fertility traits is associated with superior reproductive performance in pasture-based dairy cows with seasonal calving. J Dairy Sci 2021;104:10382–10398.
21. Basavaraja R, Drum JN, Sapuleni J, et al. Down regulated luteolytic pathways in the transcriptome of early pregnancy bovine corpus luteum are mimicked by interferon-tau in vitro. BMC Genomics 2021;22:452.
22. Mahé C, Zlotkowska AM, Reynaud K, et al. Sperm migration, selection, survival, and fertilizing ability in the mammalian oviduct†. Biol Reprod 2021;105: 317–331.
23. Abdulrahman Alrabiah N, Evans ACO, Fahey AG, et al. Immunological aspects of ovarian follicle ovulation and corpus luteum formation in cattle. Reproduction 2021;162:209–225.
24. Ginther OJ. Switching of follicle destiny so that the second largest follicle becomes dominant in monovulatory species. Theriogenology 2021;171: 147–154.
25. Garcia-Ispierto I, Llobera-Balcells M, López-Gatius F. Inducing ovulation with human chorionic gonadotrophin improves the pregnancy rate in lactating dairy cows receiving an in vitro-produced embryo. Reprod Domest Anim 2021;56:1145–1147.
26. Pereira de Moraes F, Amaral D'Avila C, Caetano de Oliveira F, et al. Prostaglandin F2α regulation and function during ovulation and luteinization in cows. Theriogenology 2021;171:30–37.
27. Piccinno M, Sciorsci RL, Masciopinto V, et al. Effects of d-cloprostenol on different layers and regions of the bovine uterus during the follicular and luteal phases. Theriogenology 2017;96:92–96.
28. Sakaguchi K, Yanagawa Y, Yoshioka K, et al. Relationships between the antral follicle count, steroidogenesis, and secretion of follicle-stimulating hormone and anti-Müllerian hormone during follicular growth in cattle. Reprod Biol Endocrinol 2019;17:88.
29. Nishimura R, Okuda K. Multiple roles of hypoxia in bovine corpus luteum. J Reprod Dev 2020;66: 307–310.

30. Oosthuizen N, Cooke RF, Schubach KM, et al. Effects of estrous expression and intensity of behavioral estrous symptoms on variables associated with fertility in beef cows treated for fixed-time artificial insemination. Anim Reprod Sci 2020;214:106308.

31. Sakai S, Yagi M, Fujime N, et al. Heat stress influences the attenuation of prostaglandin synthesis by interferon tau in bovine endometrial cells. Theriogenology 2021;165:52–58.

32. Batista EOS, Vieira LM, Freitas BG, et al. Anti-Mullerian hormone and its relationship to ovulation response and fertility in timed AI Bos indicus heifers. Reprod Domest Anim 2020;55:753–758.

33. Schweinzer V, Gusterer E, Kanz P, et al. Comparison of behavioral patterns of dairy cows with natural estrus and induced ovulation detected by an ear-tag based accelerometer. Theriogenology 2020;157:33–41.

34. Ramachandran R, Vinothkumar A, Sankarganesh D, et al. Detection of estrous biomarkers in the body exudates of Kangayam cattle (Bos indicus) from interplay of hormones and behavioral expressions. Domest Anim Endocrinol 2020;72:106392.

35. Schweinzer V, Gusterer E, Kanz P, et al. Evaluation of an ear-attached accelerometer for detecting estrus events in indoor housed dairy cows. Theriogenology 2019;130:19–25.

36. López-Gatius F. Is fertility declining in dairy cattle? A retrospective study in northeastern Spain. Theriogenology 2003;60:89–99.

37. Yoshida C, Nakao T. Some characteristics of primary and secondary oestrous signs in high-producing dairy cows. Reprod Domest Anim 2005;40:150–155.

38. Neglia G, de Nicola D, Esposito L, et al. Reproductive management in buffalo by artificial insemination. Theriogenology 2020;150:166–172.

39. Kunii H, Kubo T, Asaoka N, et al. Loop-mediated isothermal amplification (LAMP) and machine learning application for early pregnancy detection using bovine vaginal mucosal membrane. Biochem Biophys Res Commun 2021;569:179–186.

40. Steeneveld W, Hogeveen H. Characterization of Dutch dairy farms using sensor systems for cow management. J Dairy Sci 2015;98:709–717.

41. Richardson BN, Hill SL, Stevenson JS, et al. Expression of estrus before fixed-time AI affects conception rates and factors that impact expression of estrus and the repeatability of expression of estrus in sequential breeding seasons. Anim Reprod Sci 2016;166: 133–140.

42. García-Guerra A, Kirkpatrick BW, Wiltbank MC. Follicular waves and hormonal profiles during the estrous cycle of carriers and non-carriers of the Trio allele, a major bovine gene for high ovulation and fecundity. Theriogenology 2017;100:100–113.

43. Díaz R, Galina CS, Rubio I, et al. Resumption of ovarian function, the metabolic profile and body condition in Brahman cows (Bos indicus) is not affected by the combination of calf separation and progestogen treatment. Anim Reprod Sci 2017;185:181–187.

44. Zhang S, Mao W, Li Q, et al. Concentration effect of prostaglandin E2 on the growth factor expression and cell proliferation in bovine endometrial explants and their kinetic characteristics. Reprod Domest Anim 2018;53:143–151.

45. Cunha TO, Martinez W, Walleser E, et al. Effects of GnRH and hCG administration during early luteal phase on estrous cycle length, expression of estrus and fertility in lactating dairy cows. Theriogenology 2021;173:23–31.

46. Held-Montaldo R, Cartes D, Sepúlveda-Varas P. Behavioral changes in dairy cows with metritis in seasonal calving pasture-based dairy system. J Dairy Sci 2021.

47. Fricke PM, Carvalho PD, Giordano JO, et al. Expression and detection of estrus in dairy cows: the role of new technologies. Animal 2014;8 Suppl 1:134–143.

48. Madureira AML, Silper BF, Burnett TA, et al. Factors affecting expression of estrus measured by activity monitors and conception risk of lactating dairy cows. J Dairy Sci 2015;98:7003–7014.

49. Reith S, Hoy S. Review: Behavioral signs of estrus and the potential of fully automated systems for detection of estrus in dairy cattle. Animal 2018;12:398–407.

50. Tippenhauer CM, Plenio JL, Madureira AML, et al. Factors associated with estrous expression and subsequent fertility in lactating dairy cows using automated activity monitoring. J Dairy Sci 2021;104:6267–6282.

51. Marques O, Veronese A, Merenda VR, et al. Effect of estrous detection strategy on pregnancy outcomes of lactating Holstein cows receiving artificial insemination and embryo transfer. J Dairy Sci 2020;103:6635–6646.

52. Burnett TA, Polsky L, Kaur M, et al. Effect of estrous expression on timing and failure of ovulation of Holstein dairy cows using automated activity monitors. J Dairy Sci 2018;101:11310–11320.

53. Wood SL, Lucy MC, Smith MF, et al. Improved synchrony of estrus and ovulation with the addition of GnRH to a melengestrol acetate-prostaglandin F2alpha synchronization treatment in beef heifers. J Anim Sci 2001;79:2210–2216.

54. Meng Chao L, Sato S, Yoshida K, et al. Comparison of oestrous intensity between natural oestrus and oestrus induced with ovsynch based treatments in Japanese black cows. Reprod Domest Anim 2010;45:168–170.

55. Denis-Robichaud J, LeBlanc SJ, Jones-Bitton A, et al. Pilot study to evaluate the association between the length of the luteal phase and estrous activity detected by automated activity monitoring in dairy cows. Front Vet Sci 2018;5:210.

56. Schindler H, Eger S, Davidson M, et al. Factors affecting response of groups of dairy cows managed for different calving-conception intervals. Theriogenology 1991;36:495–503.

57. Yániz JL, Santolaria P, Giribet A, et al. Factors affecting walking activity at estrus during postpartum period and subsequent fertility in dairy cows. Theriogenology 2006;66:1943–1950.

58. Madureira AML, Polsky LB, Burnett TA, et al. Intensity of estrus following an estradiol-progesterone-based ovulation synchronization protocol influences fertility outcomes. J Dairy Sci 2019;102:3598–3608.

59. Stevenson JS, Britt JH. A 100-Year Review: Practical female reproductive management. J Dairy Sci 2017;100:10292–10313.

60. Moore SG, Aublet V, Butler ST. Monitoring estrous activity in pasture-based dairy cows. Theriogenology 2021;160:90–94.

61. Stevenson JS, Hill SL, Nebel RL, et al. Ovulation timing and conception risk after automated activity monitoring in lactating dairy cows. J Dairy Sci 2014;97:4296–4308.

62. Tippenhauer CM, Plenio JL, Madureira AML, et al. Timing of artificial insemination using fresh or frozen semen after automated activity monitoring of estrus in lactating dairy cows. J Dairy Sci 2021;104: 3585–3595.

63. Schilkowsky EM, Granados GE, Sitko EM, et al. Evaluation and characterization of estrus alerts and behavioral parameters generated by an ear-attached accelerometer-based system for automated detection of estrus. J Dairy Sci 2021;104:6222–6237.

64. Cardinali DP, Vacas MI, Lowenstein PR, et al. [Neurohumoral control of the pineal gland. A model for the study of neuroendocrine integrative processes]. Acta Physiol Lat Am 1979;29:291–304.

65. Allrich RD. Endocrine and neural control of estrus in dairy cows. J Dairy Sci 1994;77:2738–2744.

66. Etchevers L, Belotti EM, Díaz PU, et al. MC2R/MRAP2 activation could affect bovine ovarian steroidogenesis potential after ACTH treatment. Theriogenology 2021;174:102–113.

67. Manuel Palomino J, Grand F-X, Vigneault C, et al. Effects of follicular ablation and GnRH on synchronization of ovulation and conception rates in embryo recipient heifers. Anim Reprod Sci 2020;221:106596.

68. Bai Y, Zhang F, Zhang H, et al. Follicular Fluid Metabolite Changes in Dairy Cows with Inactive Ovary Identified Using Untargeted Metabolomics. Biomed Res Int 2020;2020:9837543.

69. Agarwal S, Gupta HP, Prasad S, et al. Effect of various hCG treatment protocols on luteal characteristics, plasma progesterone concentration, and pregnancy in normal cyclic Indian crossbred dairy cows. Trop Anim Health Prod 2021;53:220.

70. Ray DE. Oestrous response of ovariectomized beef heifers to oestradiol benzoate and human chorionic gonadotrophin. J Reprod Fertil 1965;10:329–335.

71. Walton JS, Veenhuizen LP, King GJ. Relationships between time of day, estrous behavior, and the preovulatory luteinizing hormone surge in Holstein cows after treatment with cloprostenol. J Dairy Sci 1987;70:1652–1663.

72. Jinks EM, Smith MF, Atkins JA, et al. Preovulatory estradiol and the establishment and maintenance of pregnancy in suckled beef cows. J Anim Sci 2013;91:1176–1185.

73. Ciernia LA, Perry GA, Smith MF, et al. Effect of estradiol preceding and progesterone subsequent to ovulation on proportion of postpartum beef cows pregnant. Anim Reprod Sci 2021;227:106723.

74. Stevenson JS. Spatial relationships of ovarian follicles and luteal structures in dairy cows subjected to ovulation synchronization: Progesterone and risks for luteolysis, ovulation, and pregnancy. J Dairy Sci 2019;102:5686–5698.

75. de Carvalho NAT, de Carvalho JGS, de Souza DC, et al. Lack of effect of melatonin on ovarian function and response to estrous synchronization and fixed-time AI during the nonbreeding season in lactating dairy buffalo (Bubalus bubalis). Anim Reprod Sci 2021;231:106796.

76. Garcia-Ispierto I, Pando M, Llobera-Balcells M. Inducing Ovulation with hCG Improves Fertility Outcomes of Co-Dominant Follicle Drainage to Avoid Twin Pregnancy in Dairy Cows. Animals (Basel) 2021;11.

77. Mahdavi-Roshan H, Niasari-Naslaji A, Vojgani M, et al. Size and number of corpora lutea and serum progesterone concentrations when administering two doses of eCG in an estrous synchronization treatment regimen for dairy cattle. Anim Reprod Sci 2020;222:106620.

78. Atkins JA, Smith MF, Wells KJ, et al. Factors affecting preovulatory follicle diameter and ovulation rate after gonadotropin-releasing hormone in postpartum beef cows. Part II: Anestrous cows. J Anim Sci 2010;88:2311–2320.

79. Macmillan KL, Segwagwe BVE, Pino CS. Associations between the manipulation of patterns of follicular development and fertility in cattle. Anim Reprod Sci 2003;78:327–344.

80. Hori K, Matsuyama S, Nakamura S, et al. Age-related changes in the bovine corpus luteum function and progesterone secretion. Reprod Domest Anim 2019;54:23–30.

81. Madureira AML, Burnett TA, Borchardt S, et al. Plasma concentrations of progesterone in the preceding estrous cycle are associated with the intensity of estrus and fertility of Holstein cows. PLoS ONE 2021;16:e0248453.

82. Knight TW, Lambert MG, Devantier BP, et al. Calf survival from embryo transfer-induced twinning in dairy-beef cows and the effects of synchronised calving. Anim Reprod Sci 2001;68:1–12.

83. Osawa T, Honjou S, Nitta H, et al. Effect of synchronisation of ovulation on ovarian profile and days open in holstein cows diagnosed as nonpregnant 26 days after timed artificial insemination. J Reprod Dev 2009;55:163–169.

84. Masello M, Ceglowski B, Thomas MJ, et al. A reproductive management program aimed at increasing reinsemination of nonpregnant dairy cows at detected estrus resulted in similar reproductive

performance to a program that favored timed artificial insemination. J Dairy Sci 2020;103:3719–3729.

85. Pérez MM, Wijma R, Scarbolo M, et al. Lactating dairy cows managed for second and greater artificial insemination services with the Short-Resynch or Day 25 Resynch program had similar reproductive performance. J Dairy Sci 2020;103:10769–10783.

86. Lee M-S, Rahman MS, Kwon W-S, et al. Efficacy of four synchronization protocols on the estrus behavior and conception in native Korean cattle (Hanwoo). Theriogenology 2013;80:855–861.

87. Carvalho PD, Santos VG, Giordano JO, et al. Development of fertility programs to achieve high 21-day pregnancy rates in high-producing dairy cows. Theriogenology 2018;114:165–172.

88. Giordano JO, Thomas MJ, Catucuamba G, et al. Reproductive management strategies to improve the fertility of cows with a suboptimal response to resynchronization of ovulation. J Dairy Sci 2016;99:2967–2978.

89. Lopes G, Johnson CR, Mendonça LGD, et al. Evaluation of reproductive and economic outcomes of dairy heifers inseminated at induced estrus or at fixed time after a 5-day or 7-day progesterone insert-based ovulation synchronization protocol. J Dairy Sci 2013;96:1612–1622.

90. Busch W, Klinsky JD, Slucka R, et al. [Planned control of reproduction processes in industrialized cattle production]. Arch Exp Veterinarmed 1977;31: 799–808.

91. Cavalieri J, Macmillan KL. Synchronisation of oestrus and reproductive performance of dairy cows following administration of oestradiol benzoate or gonadotrophin releasing hormone during a synchronised pro-oestrus. Aust Vet J 2002;80: 486–493.

92. Pursley JR, Wiltbank MC, Stevenson JS, et al. Pregnancy rates per artificial insemination for cows and heifers inseminated at a synchronized ovulation or synchronized estrus. J Dairy Sci 1997;80:295–300.

93. Thomas JM, Poock SE, Ellersieck MR, et al. Delayed insemination of non-estrous heifers and cows when using conventional semen in timed artificial insemination. J Anim Sci 2014;92:4189–4197.

94. Abel JM, Bishop BE, Thomas JM, et al. Comparing strategies to synchronize estrus before fixed-time artificial insemination in primiparous 2-year-old beef cows. Theriogenology 2017;87:306–315.

95. Jeong JK, Kang HG, Hur TY, et al. Synchronization using PGF(2α) and estradiol with or without GnRH for timed artificial insemination in dairy cows. J Reprod Dev 2013;59:97–101.

96. Santos JEP, Bartolome JA, Cerri RLA, et al. Effect of a deslorelin implant in a timed artificial insemination protocol on follicle development, luteal function and reproductive performance of lactating dairy cows. Theriogenology 2004;61:421–435.

97. Bilby TR, Bruno RGS, Lager KJ, et al. Supplemental progesterone and timing of resynchronization on pregnancy outcomes in lactating dairy cows. J Dairy Sci 2013;96:7032–7042.

98. Anon. Unable to find information for 11601145.

99. Overton TR, McArt JAA, Nydam DV. A 100-Year Review: Metabolic health indicators and management of dairy cattle. J Dairy Sci 2017;100:10398–10417.

100. Moore SG, Hasler JF. A 100-Year Review: Reproductive technologies in dairy science. J Dairy Sci 2017;100:10314–10331.

101. Borchardt S, Haimerl P, Heuwieser W. Effect of insemination after estrous detection on pregnancy per artificial insemination and pregnancy loss in a Presynch-Ovsynch protocol: A meta-analysis. J Dairy Sci 2016;99:2248–2256.

102. Bonacker RC, Stoecklein KS, Locke JWC, et al. Treatment with prostaglandin F2α and an intravaginal progesterone insert promotes follicular maturity in advance of gonadotropin-releasing hormone among postpartum beef cows. Theriogenology 2020;157: 350–359.

103.de Souza LB, Dupras R, Mills L, et al. Effect of synchronization of follicle-wave emergence with estradiol and progesterone and superstimulation with follicle-stimulating hormone on milk estrogen concentrations in dairy cattle. Can J Vet Res 2013;77:75–78.

104.Madureira AML, Burnett TA, Pohler KG, et al. Short communication: Greater intensity of estrous expression is associated with improved embryo viability from superovulated Holstein heifers. J Dairy Sci 2020;103:5641–5646.

105.Stevenson JS, Hoffman DP, Nichols DA, et al. Fertility in estrus-cycling and noncycling virgin heifers and suckled beef cows after induced ovulation. J Anim Sci 1997;75:1343–1350.

106.Wright PJ, Malmo J. Pharmacologic manipulation of fertility. Vet Clin North Am Food Anim Pract 1992;8:57–89.

107.Kohram H, Poorhamdollah M. Relationships between the ovarian status and superovulatory responses in dairy cattle. Anim Reprod Sci 2012;131:123–128.

108.Sato T, Nakada K, Uchiyama Y, et al. The effect of pretreatment with different doses of GnRH to synchronize follicular wave on superstimulation of follicular growth in dairy cattle. J Reprod Dev 2005;51:573–578.

109.Machado VS, Neves RC, Lima FS, et al. The effect of Presynch-Ovsynch protocol with or without estrus detection on reproductive performance by parity, and the long-term effect of these different management strategies on milk production, reproduction, health and survivability of dairy cows. Theriogenology 2017;93:84–92.

110.Noronha IM, Cooke RF, Martins CFG, et al. Administering an additional prostaglandin F2α injection to Bos indicus beef cows during a treatment regimen for fixed-time artificial insemination. Anim Reprod Sci 2020;219:106535.

111.Wijma R, Stangaferro ML, Giordano JO. Circulating progesterone dynamics after intravaginal instillation of prostaglandin-F2α to lactating dairy cows. Theriogenology 2016;85:1660–1668.

112.Wijma R, Stangaferro ML, Masello M, et al. Intravaginal instillation of gonadotropin-releasing hormone analogues with an absorption enhancer induced a surge of luteinizing hormone in lactating dairy cows. J Dairy Sci 2017;100:7626–7637.

113.Sahu SK, Cockrem JF, Parkinson TJ, et al. Effects of progesterone inclusion in a gonadotropin-prostaglandin-gonadotropin programme on follicular dynamics and ovulation synchronisation of pasture-based dairy cows with anoestrous. Res Vet Sci 2015;102:200–205.

114.Edwards SAA, Boe-Hansen GB, Satake N, et al. A field investigation of a modified intravaginal progesterone releasing device and oestradiol benzoate based ovulation synchronisation protocol designed for fixed-time artificial insemination of Brahman heifers. Anim Reprod Sci 2015;160:105–111.

115.Sahu SK, Cockrem JF, Parkinson TJ, et al. Effects of GnRH, a progesterone-releasing device, and energy balance on an oestrus synchronisation program in anoestrous dairy cows. Aust Vet J 2017;95:281–288.

116.de la Mata JJ, Núñez-Olivera R, Cuadro F, et al. Effects of extending the length of pro-oestrus in an oestradiol- and progesterone-based oestrus synchronisation program on ovarian function, uterine environment and pregnancy establishment in beef heifers. Reprod Fertil Dev 2018;30:1541–1552.

117.Swelum AA-A, Saadeldin IM, Moumen A, et al. Efficient follicular wave synchronization using a progesterone-releasing intravaginal device (PRIDΔ) in Camelus dromedarius. Theriogenology 2018;118: 203–211.

118.Macan RC, Camargo CE, Zielinski BL, et al. Timed artificial insemination in crossbred mares: Reproductive efficiency and costs. Reprod Domest Anim 2021;56:459–466.

119.Fernandez-Novo A, Santos-Lopez S, Pesantez-Pacheco JL, et al. Effects on Synchronization and Reproductive

Efficiency of Delaying the Removal of the Intravaginal Progesterone Device by 24 h in the 5d Co-Synch Protocol in Heifers. Animals (Basel) 2021;11.

120. van Werven T, Waldeck F, Souza AH, et al. Comparison of two intravaginal progesterone releasing devices (PRID-Delta vs CIDR) in dairy cows: blood progesterone profile and field fertility. Anim Reprod Sci 2013;138:143–149.

121. Edwards SAA, Atkinson PC, Satake N, et al. Ovarian dynamics in response to two modified intravaginal progesterone releasing device and oestradiol benzoate based ovulation synchronisation protocols designed for use in Brahman heifers. Anim Reprod Sci 2014;148:18–25.

122. Hussien A, Sharawy H, Lenis Y, et al. The impact of different estrus synchronization programs on postpartum holstein dairy cow reproductive performance. Mans Vet Med J 2021;22:124–130.

123. Roche JF. Synchronization of oestrus and fertility following artificial insemination in heifers given prostaglandin F 2 alpha. J Reprod Fertil 1974;37: 135–138.

124. Martínez MF, Kastelic JP, Mapletoft RJ. The use of estradiol and/or GnRH in a two-dose PGF protocol for breeding management of beef heifers. Theriogenology 2004;62:363–372.

125. Yousuf MR, Martins JPN, Ahmad N, et al. Presynchronization of lactating dairy cows with PGF2α and GnRH simultaneously, 7 days before Ovsynch have similar outcomes compared to G6G. Theriogenology 2016;86:1607–1614.

126. Wijma R, Pérez MM, Masello M, et al. A resynchronization of ovulation program based on ovarian structures present at nonpregnancy diagnosis reduced time to pregnancy in lactating dairy cows. J Dairy Sci 2018;101:1697–1707.

127. Ruelle E, Shalloo L, Butler ST. Economic impact of different strategies to use sex-sorted sperm for reproductive management in seasonal-calving, pasture-based dairy herds. J Dairy Sci 2021.

128. Randi F, Kelly AK, Parr MH, et al. Effect of ovulation synchronization program and season on pregnancy to timed artificial insemination in suckled beef cows. Theriogenology 2021;172:223–229.

129. Kasimanickam R, Kasimanickam V, Kappes A. Timed artificial insemination strategies with or without short-term natural service and pregnancy success in beef heifers. Theriogenology 2021;166:97–103.

130. Karakaya-Bilen E, Yilmazbas-Mecitoglu G, Keskin A, et al. Fertility of lactating dairy cows inseminated with sex-sorted or conventional semen after Ovsynch, Presynch-Ovsynch and Double-Ovsynch protocols. Reprod Domest Anim 2019;54:309–316.

131. Stevenson JS, Sauls JA, Mendonça LGD, et al. Dose frequency of prostaglandin F2α administration to dairy cows exposed to presynchronization and either 5- or 7-day Ovsynch program durations: Ovulatory and luteolytic risks. J Dairy Sci 2018;101:9575–9590.

132. Kaneko K, Mungthong K, Noguchi M. Day of prostaglandin F2α administration after natural ovulation affects the interval to ovulation, the type of ovulated follicle, and the failure to induce ovulation in cows. J Vet Med Sci 2020;82:590–597.

133. Zuluaga JF, Saldarriaga JP, Cooper DA, et al. Presynchronization with gonadotropin-releasing hormone increases the proportion of Bos indicus-influenced females ovulating at initiation of synchronization but fails to improve synchronized new follicular wave emergence or fixed-time artificial insemination conception rates using intravaginal progesterone, gonadotropin-releasing hormone, and prostaglandin F2alpha1. J Anim Sci 2010;88: 1663–1671.

134. Perry GA, Perry BL, Krantz JH, et al. Influence of inducing luteal regression before a modified fixed-time artificial insemination protocol in postpartum beef cows on pregnancy success. J Anim Sci 2012;90:489–494.

135. Satheshkumar S, Subramanian A, Devanathan TG, et al. Follicular and endocrinological turnover associated

with GnRH induced follicular wave synchronization in Indian crossbred cows. Theriogenology 2012;77: 1144–1150.

136.Santos JEP, Thatcher WW, Chebel RC, et al. The effect of embryonic death rates in cattle on the efficacy of estrus synchronization programs. Anim Reprod Sci 2004;82–83:513–535.

137.López-Gatius F, Santolaria P, Yániz J, et al. Factors affecting pregnancy loss from gestation Day 38 to 90 in lactating dairy cows from a single herd. Theriogenology 2002;57:1251–1261.

138.Thatcher WW, Moreira F, Pancarci SM, et al. Strategies to optimize reproductive efficiency by regulation of ovarian function. Domest Anim Endocrinol 2002;23:243–254.

139.López-Gatius F, Santolaria P, Yániz JL, et al. Progesterone supplementation during the early fetal period reduces pregnancy loss in high-yielding dairy cattle. Theriogenology 2004;62:1529–1535.

140.Baruselli PS, Reis EL, Marques MO, et al. The use of hormonal treatments to improve reproductive performance of anestrous beef cattle in tropical climates. Anim Reprod Sci 2004;82–83:479–486.

141.Carvalho NAT, Soares JG, Porto Filho RM, et al. Equine chorionic gonadotropin improves the efficacy of a timed artificial insemination protocol in buffalo during the nonbreeding season. Theriogenology 2013;79:423–428.

142.Sá Filho MF, Torres-Júnior JRS, Penteado L, et al. Equine chorionic gonadotropin improves the efficacy of a progestin-based fixed-time artificial insemination protocol in Nelore (Bos indicus) heifers. Anim Reprod Sci 2010;118:182–187.

143.Sá Filho MF, Ayres H, Ferreira RM, et al. Equine chorionic gonadotropin and gonadotropin-releasing hormone enhance fertility in a norgestomet-based, timed artificial insemination protocol in suckled Nelore (Bos indicus) cows. Theriogenology 2010;73:651–658.

144.Meneghetti M, Sá Filho OG, Peres RFG, et al. Fixed-time artificial insemination with estradiol and progesterone for Bos indicus cows I: basis for development of protocols. Theriogenology 2009;72:179–189.

145.Anon. Unable to find information for 11534410.

146.Anon. Unable to find information for 11534415.

147.Kamomae H, Kaneda Y, Domeki I, et al. Blood LH level and induced ovulation after hCG and PMSG treatment in ovarian quiescent cattle. Nippon Juigaku Zasshi 1989;51:467–473.

148.Souza AH, Viechnieski S, Lima FA, et al. Effects of equine chorionic gonadotropin and type of ovulatory stimulus in a timed-AI protocol on reproductive responses in dairy cows. Theriogenology 2009;72: 10–21.

149.Anon. Unable to find information for 11534423.

150.Pulley SL, Wallace LD, Mellieon HI, et al. Ovarian characteristics, serum concentrations of progesterone and estradiol, and fertility in lactating dairy cows in response to equine chorionic gonadotropin. Theriogenology 2013;79:127–134.

151.Ireland JJ, Roche JF. Development of antral follicles in cattle after prostaglandin-induced luteolysis: changes in serum hormones, steroids in follicular fluid, and gonadotropin receptors. Endocrinology 1982;111:2077–2086.

152.Sheldon IM, Dobson H. Effect of administration of eCG to postpartum cows on folliculogenesis in the ovary ipsilateral to the previously gravid uterine horn and uterine involution. J Reprod Fertil 2000;119:157–163.

153.Middleton EL, Pursley JR. Short communication: Blood samples before and after embryonic attachment accurately determine non-pregnant lactating dairy cows at 24 d post-artificial insemination using a commercially available assay for pregnancy-specific protein B. J Dairy Sci 2019;102:7570–7575.

154.Tenhagen BA, Drillich M, Surholt R, et al. Comparison of timed AI after synchronized ovulation to AI at estrus: reproductive and economic considerations. J Dairy Sci 2004;87:85–94.

155.Meier S, Kay JK, Kuhn-Sherlock B, et al. Effects of far-off and close-up transition cow feeding on uterine health, postpartum anestrous interval, and reproductive outcomes in pasture-based dairy cows. J Anim Sci Biotechnol 2020;11:17.

156.Schmidt C, Gajewski Z, Wehrend A. [Strategic hormonal reproductive programs in cows. Part 1: overview, Ovsynch and its modifications]. Tierarztl Prax Ausg G Grosstiere Nutztiere 2013;41:45–54.

157.El-Zarkouny SZ, Shaaban MM, Stevenson JS. Blood metabolites and hormone-based programmed breeding treatments in anovular lactating dairy cows. J Dairy Sci 2011;94:6001–6010.

158.Roth Z, Kressel YZ, Lavon Y, et al. Administration of GnRH at Onset of Estrus, Determined by Automatic Activity Monitoring, to Improve Dairy Cow Fertility during the Summer and Autumn. Animals (Basel) 2021;11.

159.Ataide Junior GA, Kloster A, de Moraes ÉG, et al. Early resynchronization of follicular wave emergence among Nelore cattle using injectable and intravaginal progesterone for three timed artificial inseminations. Anim Reprod Sci 2021;229:106759.

160.Shiferaw Y, Tenhagen BA, Bekana M, et al. Reproductive disorders of crossbred dairy cows in the central highlands of Ethiopia and their effect on reproductive performance. Trop Anim Health Prod 2005;37:427–441.

161.Bó GA, Baruselli PS, Chesta PM, et al. The timing of ovulation and insemination schedules in superstimulated cattle. Theriogenology 2006;65: 89–101.

162.Walker WL, Nebel RL, McGilliard ML. Time of ovulation relative to mounting activity in dairy cattle. J Dairy Sci 1996;79:1555–1561.

163.Foote RH. Review: dairy cattle reproductive physiology research and management—past progress and future prospects. J Dairy Sci 1996;79:980–990.

164.Nowicki A, Barański W, Baryczka A, et al. OvSynch Protocol and its Modifications in the Reproduction Management of Dairy Cattle Herds - an Update. J Vet Res 2017;61:329–336.

165.Scipioni RL, Foote RH, Lamb SV, et al. Electronic probe measurements of cervico-vaginal mucus for detection of ovulation in dairy cows: sanitation, clinical observations and microflora. Cornell Vet 1982;72: 269–278.

166.Talukder S, Kerrisk KL, Ingenhoff L, et al. Infrared technology for estrus detection and as a predictor of time of ovulation in dairy cows in a pasture-based system. Theriogenology 2014;81:925–935.

167.Cardoso Consentini CE, Wiltbank MC, Sartori R. Factors That Optimize Reproductive Efficiency in Dairy Herds with an Emphasis on Timed Artificial Insemination Programs. Animals (Basel) 2021;11.

168.Roche JR, Friggens NC, Kay JK, et al. Invited review: Body condition score and its association with dairy cow productivity, health, and welfare. J Dairy Sci 2009;92:5769–5801.

169.Alkan H, Karaşahin T, Dursun Ş, et al. Evaluation of the factors that affect the pregnancy rates during embryo transfer in beef heifers. Reprod Domest Anim 2020;55:421–428.

170.Tríbulo P, Balzano-Nogueira L, Conesa A, et al. Changes in the uterine metabolome of the cow during the first 7 days after estrus. Mol Reprod Dev 2019;86:75–87.

171.Bayemi PH, Leinyuy I, Nsongka MV, et al. Effect of cow parity and synchronization method with PGF2α on conception rates of Bos indicus cows in Cameroon. Trop Anim Health Prod 2015;47:159–162.

172.Forro A, Tsousis G, Beindorff N, et al. Factors affecting the success of resynchronization protocols with or without progesterone supplementation in dairy cows. J Vet Sci 2015;16:121–126.

173.Macmillan KL. Recent advances in the synchronization of estrus and ovulation in dairy cows. J Reprod Dev 2010;56 Suppl:S42-7.

174.Bisinotto RS, Ribeiro ES, Santos JEP. Synchronisation of ovulation for management of reproduction in dairy cows. Animal 2014;8 Suppl 1:151–159.

175.Burnett TA, Madureira AML, Silper BF, et al. Integrating an automated activity monitor into an artificial insemination program and the associated risk factors affecting reproductive performance of dairy cows. J Dairy Sci 2017;100:5005–5018.

176.Nogueira É, Silva AS da, Amaral TB, et al. Follicular dynamics and production of oocytes in young Nellore heifers with energetic supplementation. R Bras Zootec 2012;41:2012–2017.

177.Niozas G, Tsousis G, Steinhöfel I, et al. Extended lactation in high-yielding dairy cows. I. Effects on reproductive measurements. J Dairy Sci 2019;102: 799–810.

178.Lucy MC. Reproductive loss in high-producing dairy cattle: where will it end? J Dairy Sci 2001;84: 1277–1293.

179.Dobson H, Routly JE, Smith RF. Understanding the trade-off between the environment and fertility in cows and ewes. Anim Reprod 2020;17:e20200017.

180.Nanda AS, Dobson H, Ward WR. Relationship between an increase in plasma cortisol during transport-induced stress and failure of oestradiol to induce a luteinising hormone surge in dairy cows. Res Vet Sci 1990;49:25–28.

181.Dobson H, Smith RF. What is stress, and how does it affect reproduction? Anim Reprod Sci 2000; 60–61:743–752.

182.Larson LL, Ball PJ. Regulation of estrous cycles in dairy cattle: A review. Theriogenology 1992;38: 255–267.

183.Ball PJ, Cowpe JE, Harker DB. Evaluation of tail paste as an oestrus detection aid using serial progesterone analysis. Vet Rec 1983;112:147–149.

184.Guner B, Erturk M, Yilmazbas-Mecitoglu G, et al. Effect of delaying the time of insemination with sex-sorted semen on pregnancy rate in Holstein heifers. Reprod Domest Anim 2020;55:1411–1417.

185.Burke JM, sal Sota RL, de la Risco CA, et al. Evaluation of timed insemination using a gonadotropin-releasing hormone agonist in lactating dairy cows. J Dairy Sci 1996;79:1385–1393.

186.Lamb GC, Stevenson JS, Kesler DJ, et al. Inclusion of an intravaginal progesterone insert plus GnRH and prostaglandin F2alpha for ovulation control in postpartum suckled beef cows. J Anim Sci 2001;79:2253–2259.

187.Yildiz A. Effect of administering ovsynch protocol plus postbreeding infusionon first service pregnancy outcome in cows. J of Animal and Veterinary Advances 2010;9:1345–1350.

188.Bisinotto RS, Castro LO, Pansani MB, et al. Progesterone supplementation to lactating dairy cows without a corpus luteum at initiation of the Ovsynch protocol. J Dairy Sci 2015;98:2515–2528.

189.Lima FS, Bisinotto RS, Ribeiro ES, et al. Effect of one or three timed artificial inseminations before natural service on reproductive performance of lactating dairy cows not observed for detection of estrus. Theriogenology 2012;77:1918–1927.

190.Nak Y, Tuna B, Nak D, et al. The effects of ovsynch, ovsynch with progestin and progestin plus double TAI on pregnancy rates in unobserved oestrus dairy cows and heifers. Kafkas Üniversitesi Veteriner Fakültesi Dergisi 2011.

191.Dhami AJ, Nakrani BB, Hadiya KK, et al. Comparative efficacy of different estrus synchronization protocols on estrus induction response, fertility and plasma progesterone and biochemical profile in crossbred anestrus cows. Vet World 2015;8:1310–1316.

192.Bhoraniya HL, Dhami AJ, Naikoo M, et al. Effect of estrus synchronization protocols on plasma progesterone profile and fertility in postpartum anestrous Kankrej cows. Trop Anim Health Prod 2012;44:1191–1197.

193.Kumar L, Phogat JB, Pandey AK, et al. Estrus induction and fertility response following different treatment protocols in Murrah buffaloes under field conditions. Vet World 2016;9:1466–1470.

194.Tenhagen BA, Birkelbach E, Heuwieser W. Serum progesterone levels in post-partum dairy cows after repeated application of the prostaglandin F2 alpha analogue D (+) cloprostenol sodium. J Vet Med A Physiol Pathol Clin Med 2000;47:213–220.

195.Rosenberg M, Kaim M, Herz Z, et al. Comparison of methods for the synchronization of estrous cycles in dairy cows. 1. Effects on plasma progesterone and manifestation of estrus. J Dairy Sci 1990;73: 2807–2816.

196.Mohammadi A, Seifi HA, Farzaneh N. Effect of prostaglandin F2α and GnRH administration at the time of artificial insemination on reproductive performance of dairy cows. Vet Res Forum 2019;10:153–158.

197.Uslu BA, Kocyigit A, Sendag S, et al. The effect of GnRH on the pregnancy ratio in low-yielding local race cows: comparison of different injection times. Trop Anim Health Prod 2020;52:497–502.

198.Dias FCF, Costa E, Adams GP, et al. Effect of duration of the growing phase of ovulatory follicles on oocyte competence in superstimulated cattle. Reprod Fertil Dev 2013;25:523–530.

199.Perry GA, Swanson OL, Larimore EL, et al. Relationship of follicle size and concentrations of estradiol among cows exhibiting or not exhibiting estrus during a fixed-time AI protocol. Domest Anim Endocrinol 2014;48:15–20.

200.Geary TW, Smith MF, MacNeil MD, et al. Triennial Reproduction Symposium: influence of follicular characteristics at ovulation on early embryonic survival. J Anim Sci 2013;91:3014–3021.