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The challenges of prohibiting the use of steroid hormones in FTAI protocols and the resulting impact on South American cattle systems

Gabriel A Bó[12], Alejo Menchaca[34] and Pietro Baruselli[5]

[1] Instituto de Reproducción Animal Córdoba (IRAC), Zona Rural General Paz, (5145) Córdoba, Argentina, [2] Instituto de Ciencias Básicas, Medicina Veterinaria, Universidad Nacional de Villa María, Villa del Rosario, Córdoba, Argentina, [3] Plataforma de Salud Animal, Instituto Nacional de Investigación Agropecuaria (INIA), Montevideo, Uruguay, [4] Fundación IRAUy, Instituto de Reproducción Animal Uruguay, Montevideo, Uruguay, [5] Departamento de Reprodução Animal, Universidade de São Paulo, São Paulo, SP, Brasil

Abstract

The development of fixed-time artificial insemination (FTAI) protocols at the end of the 20th century has exponentially increased the number of beef cattle inseminated over the last 20 years in South America. The main reasons for this growth were the possibility of obtaining acceptable pregnancy rates without estrus detection at the beginning of the breeding season in herds with a high percentage of suckled cows in postpartum anestrus and prepubertal heifers. Most FTAI treatments in South America have been based on the use of progesterone (P4) releasing devices and estradiol to synchronize both follicular wave emergence and ovulation, with pregnancy rates ranging from 40 to 60%. The massive application of FTAI benefited farmers who use these protocols in genetic improvement and crossbreeding programs, that in turn, improved their profitability through increments in pregnancy rates, weaning weights, and the market price of their calves. It was also important for the veterinarians because it became an important source of income. Many of these practices are now apparently at risk from restrictions on the use of estradiol by the European Union (EU) and other countries. Therefore, it is imperative to develop alternative protocols that will allow us to adapt to the new times that are coming. The objective of the present review is to briefly summarize the main aspects of banning estradiol in livestock production, the negative impacts on reproductive efficiency, and to present some alternative FTAI protocols for dairy and beef cattle.

Keywords: *Estradiol, Fixed-time AI, GnRH, pregnancy rates.*

Introduction

The ban on the use of estradiol in livestock by the European Union (EU) is a long story that transcends technical reasons linked to bovine reproduction (Bó and Menchaca, 2023). Estradiol-based drugs (estradiol-17β and its esters) are routinely used in fixed-time artificial insemination (FTAI) programs in cattle in most countries outside Europe, particularly in Latin America. In EU countries its use is not allowed, as is the importation of food derived from animals that have received estradiol (Directives: 81/602/CE; 96/22/CE; 2003/74/CE, **2008/97/EC**), thus exerting pressure on the countries supplying beef and milk to the EU. Consequently, Uruguay, for example, suspended in January 2021 the use of estradiol in food-producing animals; Paraguay, Chile, and Argentina have adapted their regulations in recent years and finally the EU and the UK unilaterally decided to stop buying beef from Brazil.

The EU bases its position mainly on one very specific aspect: food safety. However, this argument by the European authorities lacks support since there is no scientific evidence that shows that the use of estradiol in FTAI protocols generates any risk for consumers. The objective of the present review is to briefly summarize the main aspects of the ban on estradiol in livestock production, the negative impacts on reproductive efficiency and to present some alternative FTAI protocols for dairy and beef cattle.

Manipulation of ovarian function for fixed-time AI (FTAI) with estradiol esters

The development of estradiol and P4-based FTAI protocols began in the 1990s after the publications that described the effect of estradiol on follicular dynamics (Bó *et al*., 1991, 1994, 1995). The protocols commonly used today involve the application of 2 mg of estradiol benzoate (EB) at the time of insertion of an intravaginal P4-releasing device (which is normally defined as Day 0 of the treatment) to induce follicle atresia and the emergence of a new follicular wave 2 to 5 days later (Martinez et al., 2005). The P4 device is removed 7, 8, or 9 days later, and cows or heifers also receive at the same time

Correspondência: gabrielbo62@gmail.com
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prostaglandin F2α ($PGF_{2\alpha}$) to induce luteal regression, equine chorionic gonadotropin (eCG) to stimulate the growth of the dominant follicle, and estradiol cipionate (ECP) to induce ovulation. This allowed the FTAI of large groups of cows and heifers (48 to 56 h after P4 device removal), with pregnancy rates ranging from 40 to 60% (Sales *et al*., 2012; Baruselli *et al*., 2017; Bó *et al*., 2019).

During the past two decades, this technology represented the greatest revolution that has occurred in the reproductive management of livestock, with an enormous impact in many countries. Before FTAI, in the 1990s, AI was done on estrus detection and no more than 2 or 3% of the breeding females were inseminated. Currently, more than 30,000,0000 bovine females receive FTAI every breeding season in Brazil, Argentina, Paraguay and Uruguay (Baruselli *et al*., 2017; Mapletoft *et al*., 2018). For the beef and dairy industry, the benefit is such that for every dollar that the producer invests in FTAI, it generates a return of 4 to 5 dollars for the country (Baruselli *et al*., 2017), which, transferred to the Mercosur scale, represents an annual gross income of more than 2 billion dollars for this region.

The bad reputation of estradiol

Although estradiol plays a fundamental role in FTAI protocols, the greatest difficulty when discussing the use of estradiol in livestock farming arises because two completely different indications for its use are considered in the same way: a) estradiol for ovarian control and b) estradiol as a growth promoter. Estradiol for ovarian control is used at very low doses (0.5 to 2 mg of ECP or EB), intramuscularly and in a single administration. These doses are extremely low in relation to the indicated use as a growth promoter in beef cattle, where it is used in doses 10 to 100 times higher, administered by prolonged-release subcutaneous implants for 60 to 120 days, and generally every animal receives several implants in succession (Smith and Johnson, 2020). This use as a growth promoter has led to questions about the safety of food derived from these animals. Although this has no connection with the use of estradiol in reproduction, the regulatory consequences have been the same.

In the 1980s, after several years of debate between government authorities from different countries, various commissions and specialized working groups, international organizations, the media, and the public, the EU prohibited the use of growth promoters, including estradiol. Shortly after, the importation of food derived from animals that had received these drugs was also banned. The EU measure came into force in 1989. Although in the first instance the European ban did not cover hormones for estrous cycle control, a few years later the regulation was expanded, and estradiol was also prohibited for this purpose.

There are no solid arguments that prove that the estradiol used in the doses indicated for FTAI and embryo transfer protocols affects food safety. Furthermore, there is no method available in practice to identify whether a cow received an estradiol dose for FTAI. The reason is that estradiol salts, after being injected, are hydrolyzed to estradiol-17β in a few hours, and this substance is the main estrogen produced naturally by the cow, reaching high levels during estrus or at the end of pregnancy. It is the same molecule that the cow has, and therefore with classical methods such as radioimmunoassay, ELISA, or chemiluminescence, it is not possible to identify between exogenous and endogenous estradiol, even when only a few hours have passed since the treatment. In recent years there have been advances combining other more precise methods, such as gas chromatography coupled with isotope ratio mass spectrometry, which seek to identify whether an animal has received synthetic estradiol from the determination of the ratio between the isotopes. Although promising, these methods are complex and expensive, they are not yet fully validated, they are not found in the official residue control programs for estradiol, and they are not effective for the determination of estradiol either, since the dose administered and the concentration in tissues are extremely low, and thus the sensitivity of the method makes the determination very difficult. It should also be considered that a cow that receives estradiol for FTAI or an embryo transfer is normally not sent to the market until after parturition and the calf has been weaned. Even for those that do not become pregnant, it takes several months from treatment to slaughter, because cows need to first being diagnosed as not pregnant, and they are then usually fattened. Finally, these animals that go to slaughter at the end of their productive life are generally old animals or animals that would not meet the conditions for the European market. The problem is that the EU prohibits the use of estradiol at any stage of the animal's life, and no waiting time, maximum residue limit, or acceptable daily intake values are considered for this product, which are the parameters that they are typically used for product registration and risk analysis. This makes it even more difficult to find a fair solution that considers the best interests of both parties.

To reinforce our argument, it has been shown that doses used in FTAI induce circulating estradiol levels similar to those of a cow in estrus 12 to 24 hours after treatment and then return to basal levels a few hours later, with no significant differences to the untreated controls by 48 or 72 hours (Souza *et al*., 2005; Bosolasco *et al*., 2021). For this reason, EB and ECP do not require a withdrawal period in beef or dairy cattle, as indicated by most of the registries approved by the regulatory agencies of each country outside of Europe. Even though it is used as a growth promoter in much higher doses and for much longer times than for ovarian control, in the USA the FDA does not require a waiting time for implants with estradiol, which indicates that this prestigious regulatory agency does not find any arguments that suggest a risk to consumers. While in various instances of the Codex Alimentarius Commission–another world reference body–it is reiterated that there is insufficient evidence to prohibit the use of these substances, the EU argues that the prohibition is because the public opposes the use of "hormones" for fattening animals (Codex Alimentarius, 1989, 2001). This then transcends the discussion based on scientific evidence and responds more to public preference and political reasons, which will be very difficult to modify. Therefore, it is necessary to develop alternatives to our farming practices to adapt them to the needs of the market, even when these respond to commercial or cultural interests or simply to consumer preferences. It is of little use that our animals live according to their natural condition in the field, feeding on grass and in the open air, without suffering, preserving the environment, and generating healthy and safe food, if we are not capable of measuring it, making it known and defending it.

Gonadotropin-releasing hormone (GnRH)-based protocols in *Bos taurus* beef cattle

Probably the best-known alternative to estradiol-based protocols for FTAI are those based on GnRH. Pursley *et al*. (1995) have developed an ovulation synchronization protocol for FTAI in lactating dairy cattle that uses GnRH, a protocol called Ovsynch, which with several modifications, is today the most widely used protocol in dairy cattle in the world (Consentini *et al*., 2021). In beef cattle, GnRH-based protocols are used in North America and Europe, and for a couple of years in Uruguay, due to the restrictions imposed by the EU. The variation of the OvSynch protocol that is mostly used for beef cattle is called Co-Synch, in which cows are FTAI and receive GnRH at the same time (Geary *et al*., 2001a). In addition, Co-Synch protocols include the insertion of a P4-releasing device in heifers (Martinez *et al*., 2002) and in postpartum anestrous cows (Lamb *et al*., 2001).

More recently, a modification of the Co-Synch was developed in which the period of insertion of the P4 device was shortened to 5 days and the period from P4 device removal to FTAI was prolonged to 72 hours, with the aim of increasing the period of preovulatory exposure to estradiol and improving uterine function and early embryo development (Bridges *et al*., 2008; 2012; 2014). Also, the greater exposure to preovulatory estradiol was related to lower embryonic losses in the period of time between the maternal recognition of pregnancy and the adhesion of the placental membranes (Madsen *et al*., 2015). The protocol was called the 5-day Co-Synch+P4 and resulted in greater pregnancy rates than the 7-day Co-Synch+P4 in beef cows (Bridges *et al*., 2008; Whittier *et al*., 2013).

Due to the shorter interval between the first GnRH and the induction of luteolysis in the 5-day Co-Synch+P4 protocol, it is recommended to use two doses of $PGF_{2\alpha}$ in cows with an interval of 6 to 24 h (Souto *et al*., 2009). In an experiment with 2,465 postpartum beef cows, the pregnancy rate was greater in cows that received 2 $PGF_{2\alpha}$ 8 hours apart (55%) than in those that received only one $PGF_{2\alpha}$ (48%), and those that received 2 $PGF_{2\alpha}$ administered at the same time had an intermediate pregnancy rate (51%; Bridges *et al*., 2012). Therefore, double $PGF_{2\alpha}$ administered 8 to 24 h apart appears to be necessary to maximize fertility with the 5-day protocol in cows. However, if herd management conditions do not allow for further manipulation, a double dose of $PGF_{2\alpha}$ administered at device removal would be an acceptable alternative.

In heifers, the 5-day Co-Synch+P4 protocol has also been tested with modifications (Day, 2015); for example, Colazo and Ambrose (2011) and Cruppe *et al.* (2014) showed that pregnancy rate did not differ in heifers that did not receive GnRH at the time of P4 device insertion. However, other authors found different results (Kasimanickam *et al*., 2014). Also in heifers, some found higher pregnancy rates when two doses of $PGF_{2\alpha}$ were used with intervals between 6 and 24 h (Peterson *et al*., 2011; Lima *et al*., 2013; Day, 2015), while others did not report differences (Rabaglino *et al*., 2010; Kasimanickam *et al.*, 2014; Garcia Pintos *et al*., 2022). In relation to the optimal time for FTAI, Kasimanickam *et al*. (2012) reported a greater pregnancy rate with Angus heifers inseminated at 56 h after device removal than those inseminated at 72 h, and Day (2015) suggested performing the FTAI at 60 to 66 h after P4 device removal or to inseminate 12 h post estrus using patches or paint and inseminate and administer GnRH to all those not in heat at 72 h. Indeed, estrus expression has been shown to influence pregnancy rates in cows (Richardson *et al*., 2016), and Colazo et al. (2017) have reported similar findings in heifers inseminated with sexed semen, suggesting the possibility of dividing the insemination based on the expression of estrus (i.e., delaying insemination in those animals that do not show estrus at the time of FTAI).

The 5-day Co-Synch protocol has also been extensively evaluated in Uruguay (Garcia Pintos *et al*., 2022), where it was also decided to slightly alter the original 5-day Co-Synch+P4 protocol by modifying the time for device removal and the FTAI (protocol called 5-day Split-Synch). In this way, the administration of $PGF_{2\alpha}$ is facilitated by giving the first $PGF_{2\alpha}$ when the device is removed and the eCG is administered on Day 5 PM. Then the cows remain in the corrals overnight and receive the second $PGF_{2\alpha}$ before releasing them to the pasture in the morning. Furthermore, tail paint is also placed at the base of the tail to detect those that are already in heat at the time of the first insemination, which is performed approximately 62 h after P4 device removal (i.e., Day 8 AM). Those that are not in estrus by that time (i.e., with <50% of the tail-paint rubbed off) receive a GnRH injection and are inseminated in the afternoon.

The same protocol was used in heifers, and it was reported that in this category only one dose of $PGF_{2\alpha}$ is necessary at the end of treatment to induce luteolysis. Most important of all, the results in heifers were similar to those obtained with the J-Synch protocol, and in cows they were similar to those obtained with the conventional estradiol-based protocol, with ECP as an ovulation inducer. With this scheme it is possible to inseminate animals all day, thus allowing the implementation of FTAI programs on a large scale without negatively affecting pregnancy rates.

GnRH-based protocols in *Bos indicus* beef cattle

The application of GnRH-based protocols has also been investigated in Bos indicus cattle (Abreu et al., 2022). In one study, a total of 1,111 heifers and 1,290 suckled cows from commercial farms in Brazil were used. On Day 0, cows received an intravaginal P4 device (Primer®; Agener União) and were randomized to 1 of 4 treatments in a 2 x 2 arrangement. 1) EB/ECP: 2 mg of EB (RIC BE®, Agener União) on Day 0 and 1 mg of ECP (Cipiotec®, Agener União) on Day 8; 2) EB/GnRH: 2 mg of EB on Day 0 and 25 µg of lecirelin (GnRH; Tec-Relin®, Agener União) on D10; 3) GnRH/ECP: 50 µg of GnRH on Day 0 and 1 mg of ECP on Day 8; and 4) GnRH/GnRH: 50µg of GnRH on Day 0 and 25µg of GnRH on Day 10. The experimental protocol was adjusted for heifers [0.265mg of $PGF_{2\alpha}$ (Estron®; Agener União) on Day 0 and 0.5 mg of ECP on Day 7 (7 days of P4 device insertion) instead of 1 mg of ECP on Day 8]. All animals received 0.530 mg of $PGF_{2\alpha}$ and eCG (200 IU in heifers and 300 IU in cows; Novormon®; Zoetis), concomitant with P4 device removal. At the same time, animals were painted with chalk on their tailheads, and removal of chalk on the day of FTAI was used as an indication of estrus. The FTAI was performed 48 hours after P4 device removal. When the treatment used on Day 0 was compared, cows treated with EB had a greater pregnancy rate compared to those that received GnRH [EB=44.0% (280/642) vs. GnRH=33.0% (216/648); P<0.0001], which was related to a poorer efficiency in the synchronization of a new follicular wave in animals treated with EB than those treated with GnRH. A similar effect was observed for heifers [BE=43.1% (201/466) vs. GnRH=37.2% (174/468); P=0.003]. When the hormones used as ovulation inducers were compared, the estrus detection rate was greater in animals that received ECP instead of GnRH [heifers: 89.8% vs. 83.7%, P=0.01, and cows 78.6% vs. 68.1%, P=0.02]. However, there were no significant differences in pregnancy rates between ECP and GnRH [heifers: 41.9% (234/560) vs. 38.4% (211/551); cows: 40.5% (265/655) vs. 36.4% (231/635)]. In conclusion, the removal of estradiol in the synchronization protocol for FTAI had a negative impact on reproductive efficiency in cows and heifers. The greater pregnancy rates in the estradiol protocols were related to a lower efficiency in synchronizing a follicular wave with GnRH than with EB. Furthermore, a follow-up study also found lower circulating concentrations of estradiol and a decrease in endometrial thickness in animals that received GnRH compared to those receiving ECP to induce ovulation, which has also been related to fertility (de Abreu et al., 2023).

The 5-day Co-Synch+P4 protocol has also been investigated in *Bos indicus* cows in Brazil, with a lower pregnancy rate in suckled Nelore cows than those treated with the conventional 8-day estradiol-based protocol (Ferraz Jr et al., 2016). One important difference was that 400 IU eCG was used in the estradiol and P4-based protocol, but not in the 5-day Co-Synch+P4 protocol. To confirm this notion, we have found a greater pregnancy rate in postpartum anestrus cows that received 400 IU eCG upon P4 device removal (5-day Co-Synch+P4: 46.3%, 120/259) than in cows treated with the 5-day Co-Synch+P4 protocol, but without eCG (26.8%, 71/265; P <0.05; Huguenine et al., 2013).

Also, we recently conducted an experiment to evaluate pregnancy rates to FTAI in *Bos indicus* crossbred cows synchronized with two Co-Synch protocols and the estradiol-based J-Synch protocol (Bó *et al*., 2023). Cross-bred *Bos indicus* mature suckled cows (n = 1,161) that were 60 to 90 d postpartum with a CL or at least one follicle ≥ 8 mm in diameter (detected by ultrasonography) and a body condition score between 2 and 4 (scale 1 to 5) were randomly allocated into one of three groups: J-Synch 7 d, Co-Synch 6 d, and Co-Synch 5 d. On Day 0, cows in the J-Synch 7 d group received 2 mg of EB (Gonadiol, Zoetis, Ecuador) and an intravaginal device with 0.5 g of P4 (DIB 0.5 g, Zoetis, Ecuador). Cows in the two Co-Synch groups received 100 µg of gonadorelin (GnRH, Gonasyn GDR, Zoetis, Ecuador) on Day 1 (Co-Synch 6 d) or on Day 2 (Co-Synch 5 d), respectively. On Day 7, all cows received 500 µg of cloprostenol sodium ($PGF_{2\alpha}$; Ciclase DL, Zoetis, Ecuador) and 300 IU of equine chorionic gonadotropin (eCG; Novormon 5000, Zoetis, Ecuador), with the difference that cows in the two Co-Synch groups also received a second dose of $PGF_{2\alpha}$ 8 h later. In addition, all the cows were tail painted for estrus determination at the time of FTAI. Cows that had their paint loss ≥50% by 70 h after P4 device removal were inseminated at that time, and cows without their tail-paint rubbed off received GnRH at that time and were inseminated 6 to 8 h later. The percentage of cows in estrus at AI was 68.1% (791/1161) and did not differ among groups (J-Synch 7 d: 70.1% 291/415, Co-Synch 6 d: 68.0% 252/370, and Co-Synch 5 d: 66.0% 248/376). However, the pregnancy rate was greater in cows in the J-Synch 7 d group (55.0%, 228/415) than those in the Co-Synch 6 d (45.0%, 167/370) and Co-Synch 5 d (38.5%, 145/376) groups. In summary, the estradiol-based synchronization protocol (J-Synch) resulted in greater P/AI than the two GnRH-based protocols evaluated in suckling *Bos indicus* beef cows. Lower pregnancy rates in the *Bos indicus* cows may be attributed to the lower effectiveness of GnRH than EB in synchronizing the emergence of a new follicle wave, and it may be necessary to double the dose of GnRH, since it has been reported that the magnitude of the LH surge produced by the administration of GnRH is lower in *Bos indicus* than in *Bos taurus*, especially in cows with a CL (Batista *et al*., 2017). Furthermore, it has been shown recently that duplicating the dosage of the GnRH analog buserelin (i.e., 8.4 vs 16.2 µg) significantly increased ovulation rate in Bos indicus cows, but not in heifers with high circulating progesterone concentrations (Silva et al., 2020). Obviously, further studies are required to thoroughly investigate this issue.

Long GnRH+P4-based protocols

As it was indicated in the previous section, one of the main limitations for the application of protocols with GnRH in beef cows and heifers is the low response to the first dose of GnRH (Geary *et al*., 2001b, Martinez *et al*., 2000). Recently, Bonacker *et al*. (2020a) developed a new synchronization protocol called 7 & 7 Synch, using previous knowledge generated by Small *et al*. (2009). This protocol consists of applying $PGF_{2\alpha}$ and a P4 device on Day -7 as a pre-synchronization treatment to develop a persistent follicle; on Day 0, GnRH is administered to ovulate the persistent follicle and synchronize the emergence of a new follicular wave; on Day 7, all cows receive $PGF_{2\alpha}$ and device removal; and finally, all cows are FTAI with a dose of GnRH 60 to 66 hours after device removal. The 7 & 7 Synch protocol demonstrated an improvement in the ovulatory response to the first GnRH administration (Bonacker et al., 2020a), and pregnancy rates to FTAI were increased, both with conventional semen and with sexed semen, when compared against a 7-day Co-Synch treatment + P4 in suckled beef cows (Andersen et al., 2021). In addition, it was an interesting alternative in recipients transferred at a fixed time with fresh and frozen embryos, improving estrus, utilization, and pregnancy rates per synchronized recipient when compared to the 7-day Co-Synch protocol (Bonacker et al., 2020b).

Based on this knowledge and given the restrictions on the use of estradiol in EU certified farms in Argentina, an alternative treatment based on GnRH was designed, which we called "Web-Synch" (Without Estradiol Benzoate). Briefly, this treatment is a slight modification of the 7 & 7 Synch (de la Mata et al., 2022). On Day -5 a pre-synchronization treatment is initiated with the administration of $PGF_{2\alpha}$ and a P4 device to generate a persistent follicle. On Day 0, GnRH is injected to induce ovulation of the persistent follicle and promote the emergence of a new follicular wave (36 hours later). Subsequently, on Day 6, the device is removed along with a dose of $PGF_{2\alpha}$ and eCG to induce follicular growth and promote a prolonged proestrus (as in the 5-day Co-Synch treatments), and tail paint is used for estrus detection. Finally, FTAI is performed 72-84 h after P4 device removal, with the application of GnRH only to animals that are not in estrus by that time. In most experiments carried out to evaluate the Web-Synch protocol in beef cows, pregnancy rates were comparable to those obtained with estradiol-based protocols (estradiol: 49.8% (214/430) vs. Web-Synch 50.6% (214/430) in cows with a moderate to high incidence of cyclicity (40 to 50 % of the cows with a CL on Day 0; reviewed in Bó et al., 2024). However, in another group of cows in which only 9.8% of them had the CL on Day 0, the pregnancy rate was greater in those receiving the conventional estradiol treatment (66.3%, 102/154) than those receiving the Web-Synch protocol (49.4%, 79/160; P=0.01; de la Mata *et al*., 2023). Although it was not evaluated in these studies, we speculate that differences may be due to a lower ovulation rate to the first GnRH in anestrus beef cows or to differences in the uterine environment due to lower estradiol in the proestrus period in the cows not treated with ECP at P4 device removal. Therefore, the application of this protocol warrants further modifications and investigation to improve pregnancy rates in cows in postpartum anestrus.

Equine Chorionic Gonadotropin (eCG)

A final paragraph is included to briefly mention the use of eCG. In its natural form, this hormone is a high-molecular-weight glycoprotein produced by the endometrial cups of the mare's uterus between 35 and 100 days of gestation, and it is extracted from the blood of pregnant mares, which has raised some animal welfare concerns in some European countries. In the mare, eCG has LH activity, but in the cow, eCG can have either FSH or LH activity, depending on the receptor populations in the ovarian follicles at the time. Although eCG was originally used to induce superovulation, today its use in cattle is more oriented towards stimulating the growth of the dominant follicle that results in greater pregnancy rates in FTAI and fixed-time embryo transfer (FTET; Bó *et al*., 2002; 2016; 2019; Baruselli *et al.*, 2004; 2012; 2017; Randi *et al*., 2021).

Although until recently 100% of the eCG used in bovines was produced through the bleeding of pregnant mares, today we have the possibility of producing this hormone in the laboratory. These hormones are generically called “recombinant”. Today we have at least one recombinant eCG in the Argentine market, and the experiments recently carried out showed that the addition of recombinant eCG increases the pregnancy rate in suckled cows (Villarraza et al., 2022; Cattaneo et al., 2024). Other recombinant eCG are about to appear on the market with similar results (de Abreu et al., 2023), and it is expected that in the future recombinant and/or synthetic hormones will replace those obtained from animals due to political pressure from the environmental groups.

Final comments

Undoubtedly, the advance in the knowledge of the reproductive physiology of the cow will allow us to face the next challenges in the implementation of reproductive technologies in beef and dairy cattle. Our obligation will always be to maximize productivity to produce food at low cost for a growing population, but we need to do that by creating efficient protocols and management strategies minimizing the negative impact on the environment. Furthermore, we must educate the public about it and show that we can feed the world with safe methodologies, with animal welfare, and by taking care of the environment.

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