The advantages of using **prostaglandins** postpartum

This article reviews the most important reproductive failures on pig farms and presents the advantages of using postpartum prostaglandins to minimize their consequences.

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For years, improvements made in the world of pig production have been oriented towards developing techniques to study the factors affecting fertility.

We could even mention several branches of research responsible for identifying parameters related to the fertility of boars. This leads us to the fact that, although oriented towards different fields, all these studies target a common goal: improving the reproductive pattern of farms.

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Factors affecting fertility

These factors include:

- Management practices and adaptation of the gilts on the farm.
- Supplementation and nutrition processes in the different phases.
- Reduction of environmental stress.
- Genetic selection to improve prolificacy on the farm.

Reproductive failures

For various reasons, farms replace around 50% of their stock annually. A third of these replacements are because of reproductive failure, with the main causes of elimination being: anestrus (44%), vaginal discharges (20.5%), repetitions (15.5%), pregnancy loss (10%) and indeterminate causes (10%; Engblom *et al.*, 2007; Tummaruk *et al.*; 2009; *table 1*).

Post-weaning anestrus

Post-weaning anestruses are one of the reproductive problems with the biggest economic impact on farms because they increase the number of non-productive days (NPDs; *table 2*).

Thus, the shorter the Interval between farrows (IBF), the greater the number of farrowings per sow/year. One NPD can mean a 0.007 reduction in the number of litters/sow-year and, although this figure is only a few decimals, it will impact the eventual production of the farm (Estevez, 2010).

Under normal conditions, sows will return to heat approximately 4–7 days after weaning (*figure 1*): sows that come into heat earlier reduce the number of NPDs and those that come into heat later increase the number of NPDs.

Non-productive days

We must consider the following:

- Non-repeating sows: 100% of the NPDs are the result of the weaning–mating interval.
- Repeating sows: the weaning-to-service interval (WTSI) can account for up to 25% of the NPDs.

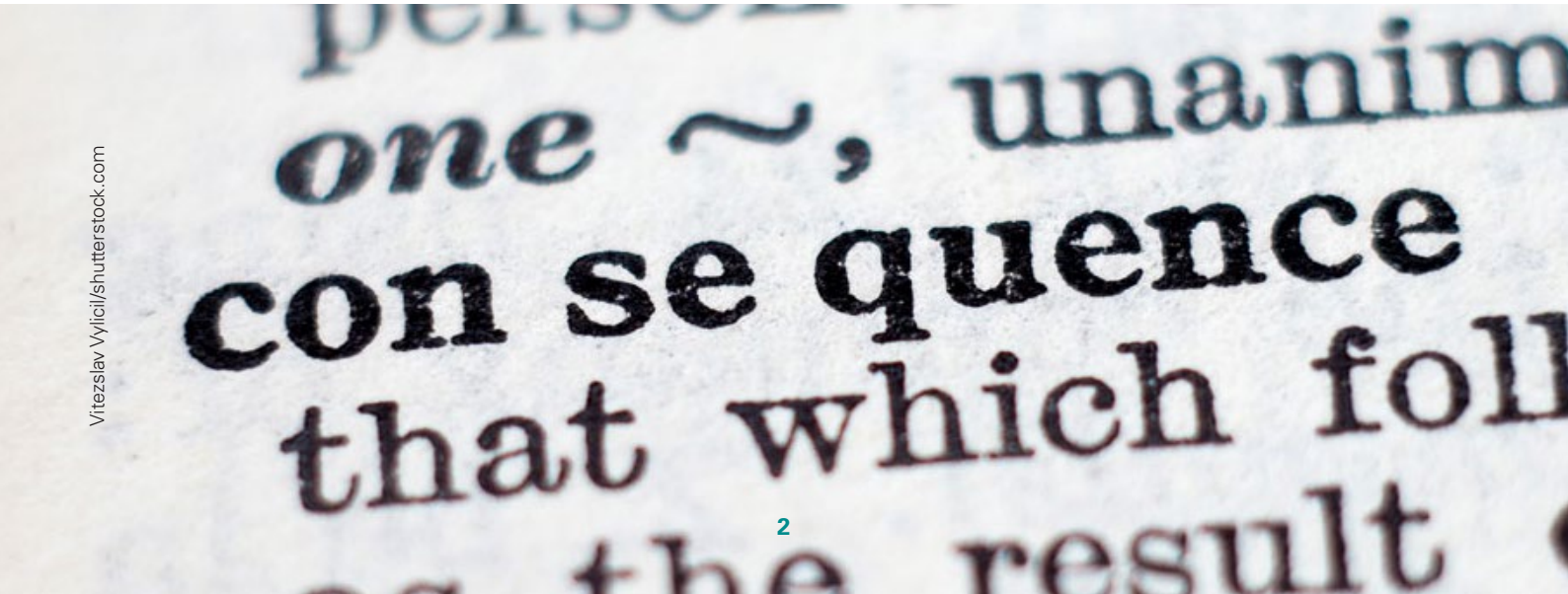
An NPD can reduce the number of litters/sow-year by 0.007.

Reference	Anestrus (%)	Conception failures[2] (%)	Farrowing failures[3] (%)	Abortions (%)	Country (year)
Koketsu, *et al.* (1997)	25.2	37.1	30.4	7.4	USA (1991)
Sehested and Schjerve (1996)	23.4	31.7	36.8	8.0	Norway (1992–1994)
Lucia, *et al.* (2000)[1]	27.0	39.7	33.3[4]	-	USA (1992)
Heinonen, *et al.* (1998)	22.3	77.5[5]	-	-	Finland (1992–1993)
D'Allaire, *et al.* (1987)[1]	21.0	75.0	-	4.0	USA (1986)
Stone (1981)[1]	45.8	53.3	-	0.9	Canada (1980–1981)
Stalder *et al.* (2007)[1.5]	41.7	58.3	-	-	USA (2006)
Dagom and Aumaitre (1977)[5]	13.8	75.1[6]	-	7.1	France (1975–1976)
Tummaruk and Tantilertcharoen (2008)[7]	51.2	39.2	-	9.6	Thailand (2005–2007)

[1]Includes gilts. [2]Normal return to heat (18–25 days after mating). [3]Abnormal return to heat (> 25 days after mating). [4]Includes abortions. [5]Includes farrowing failures and miscarriages. [6]Includes repetitions, negative pregnancy diagnoses, and empty sows at farrowing. [7]Only nulliparous.

Source: Sara Crespo.

Table 1. Causes of sow removal on commercial farms within the category of reproductive failures.



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NPD components	Mean	25% best (high-productivity farms)	Remaining farms
Total number of NPDs	57.90	42.30	63.40
Nulliparous: 1st mating to conception*	5.69 (9.24%)	3.37 (8.00%)	6.52 (9.68%)
Nulliparous: 1st mating to removal*	4.83 (7.82%)	2.76 (6.41%)	5.57 (8.32%)
Weaning to removal	4.00 (6.85%)	3.20 (7.49%)	4.27 (6.62%)
Weaning to 1st mating*	14.90 (27.90%)	14.20 (34.00%)	15.10 (25.70%)
Sow: 1st mating to conception*	11.50 (18.90%)	6.92 (16.30%)	13.10 (19.90%)
Sow: 1st mating to removal*	17.00 (29.30%)	11.90 (27.80%)	18.80 (29.80%)
Subgroups			
NPDs nulliparous*	10.52 (17.10%)	6.13 (14.40%)	12.09 (18.00%)
NPDs sows*	47.33 (82.90%)	36.21 (85.60%)	51.30 (82.00%)
NPDs before removal*	25.82 (43.90%)	17.89 (41.70%)	28.65 (44.75%)
NPDs until conception*	17.14 (28.20%)	10.29 (29.60%)	19.59 (24.30%)
*Indicates significant differences ($p < 0.05$) between high production farms and the remaining farms.			

Source: Koketsu (2005).

Table 2. Comparison between the NPDs for a total of 95 farms, divided by high production farms (weaned piglets per sow/year) and the remaining farms.

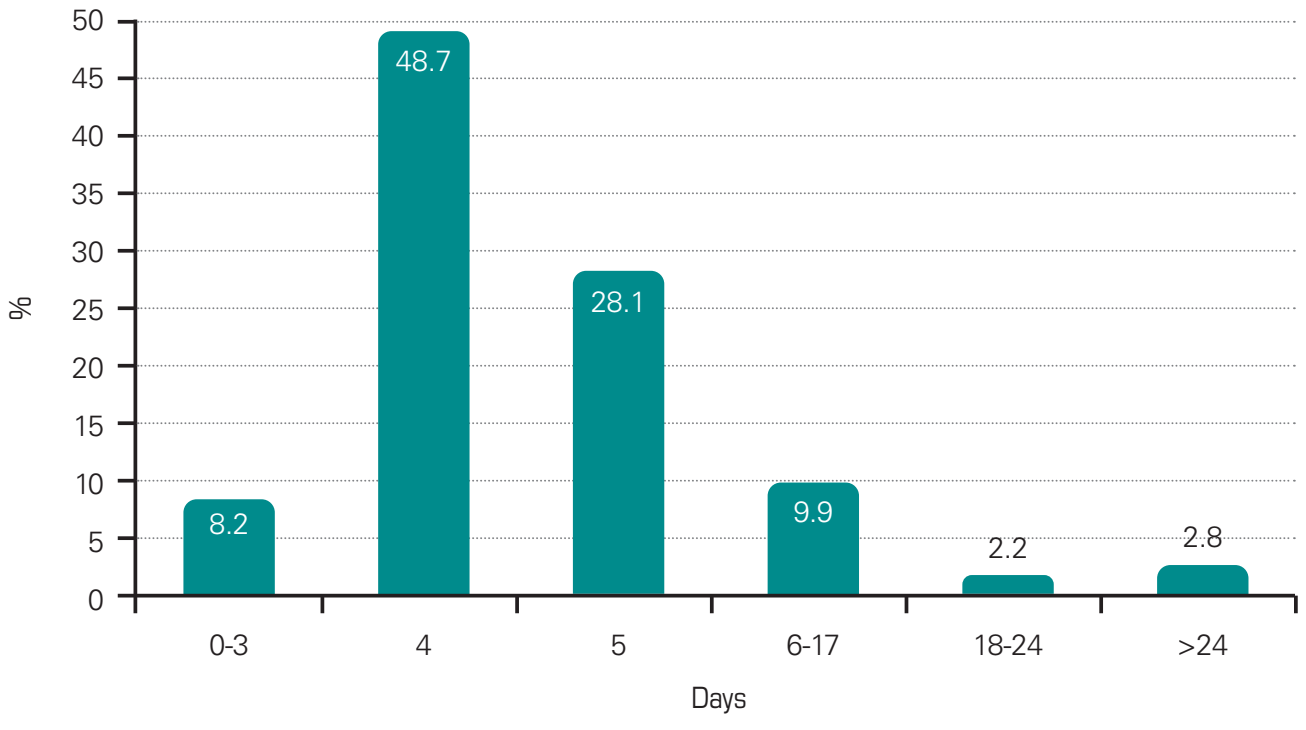

Figure 1. WTSI distribution under normal conditions.

Weaning–mating interval

In our sector, the weaning-to-service interval (WTSI) parameter strongly influences the productivity of farms because it impacts two factors (Estevez, 2010):

1 Number of matings in the batch

Delaying matings will result in maladjustment of the number of sows mated per batch, which can lead to:

- A deficit in matings in the batch they are removed from.
- Excess numbers of matings in the following batch.

We must remember that failure to achieve the number of matings per batch is one of the most frequent and costly problems on pig farms.

2 Organization of the farm

Most small farms choose to wean one day a week (Thursday) so that most returns to heat do not fall on weekends. Thus, most matings will be carried out on Mondays and Tuesdays and the subsequent farrowings, theoretically, will fall on Wednesdays and Thursdays. Consequently, delays in the return-to-estrus will shift the farrowings to weekends.

With day-to-day improvements in the sector, sow gestation is approaching an average of 116 days in association with an increase in prolificacy. Consequently, a short WTSI and matings become more important because they allow better farm management. Hence, hormones are used to decrease this interval (Roongsitthichain *et al.*, 2015).

A decrease in the WTFFSI implies a direct decline in the WTSI of the farm.

However, one cannot talk about the WTSI without considering the weaning-to-first-fertile-service interval (WTFFSI). In other words, the mating that gives rise to a farrowing.

Weaning-to-first-fertile-service interval

The WTFFSI is a parameter that indirectly indicates pregnancy losses. Therefore, this value is more directly related to farm productivity.

A farm that mates almost all its sows 4–5 days after weaning can have a good weaning-first mating interval but, at the same time, might have a bad WTFFSI if it has poor farrowing fertility.

However, this parameter varies because it directly depends on the farm's gestation losses (Piñeiro *et al.*, 2008, *3tres3*).

A decrease in the WTFFSI implies a direct decline in the WTSI of the farm.

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The importance of nutrition

In addition to the importance of reducing unproductive periods, the WTSI and the percentage of time spent in anestrus, nutrition is also of great importance. Weaned sows are usually fed *ad libitum* to ensure a:

- Good return-to-estrus.
- Optimal subsequent implantation of the embryos.

The care of weaned sows, their monitoring, and not taking full advantage of the facilities has a significant cost: in Spain, the average cost per NPD is estimated to be around 3 euros per day.

In summary...

Once the problems caused by production-level alterations in farm reproductive processes become known, the search for solutions to try to maximize their profitability become the key to their production success and profitability.

Use of postpartum prostaglandins

In postpartum sows, and within the context of the entire hormonal complex, we will focus on the hormones that are crucially important during lactation for:

- Good uterine involution.
- A normal return to heat in weaned sows.
- Good milk production.

These are: prostaglandins, progesterone, and prolactin (*table 3*).

Hormone	Released in...	Action
Prostaglandin $F_{2\alpha}$	Endometrium	Luteolysis Stimulation of uterine contractility
Progesterone	Ovary (corpora lutea)	Maintenance of pregnancy
Prolactin	Pituitary (anterior)	Maternal character Lactation

Table 3. Action and release of prostaglandin $F_{2\alpha}$, progesterone, and prolactin.

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Cloprostenol has a higher affinity for PGF_2 receptors and a longer half-life in the bloodstream.

The reproductive cycle of sows

The reproductive cycle of sows is controlled through a major neuro-endocrine-gonadal axis (*figure 2*; Estevez, 2010), regulated by different factors such as:

- External stimuli.
- Hormones
- Nutritional factors.

The hypothalamus and pituitary are the neuronal structures responsible for synthesizing gonadotropin and gonadotropin releasing factors, respectively. On the other hand, the gonads, in this case the ovaries, are responsible for synthesizing steroids.

Keep in mind that:

- This whole system is controlled by a complex mechanism that allows hormonal feedback at the different levels already mentioned.
- The control of this system is influenced by many factors whose study is ongoing.

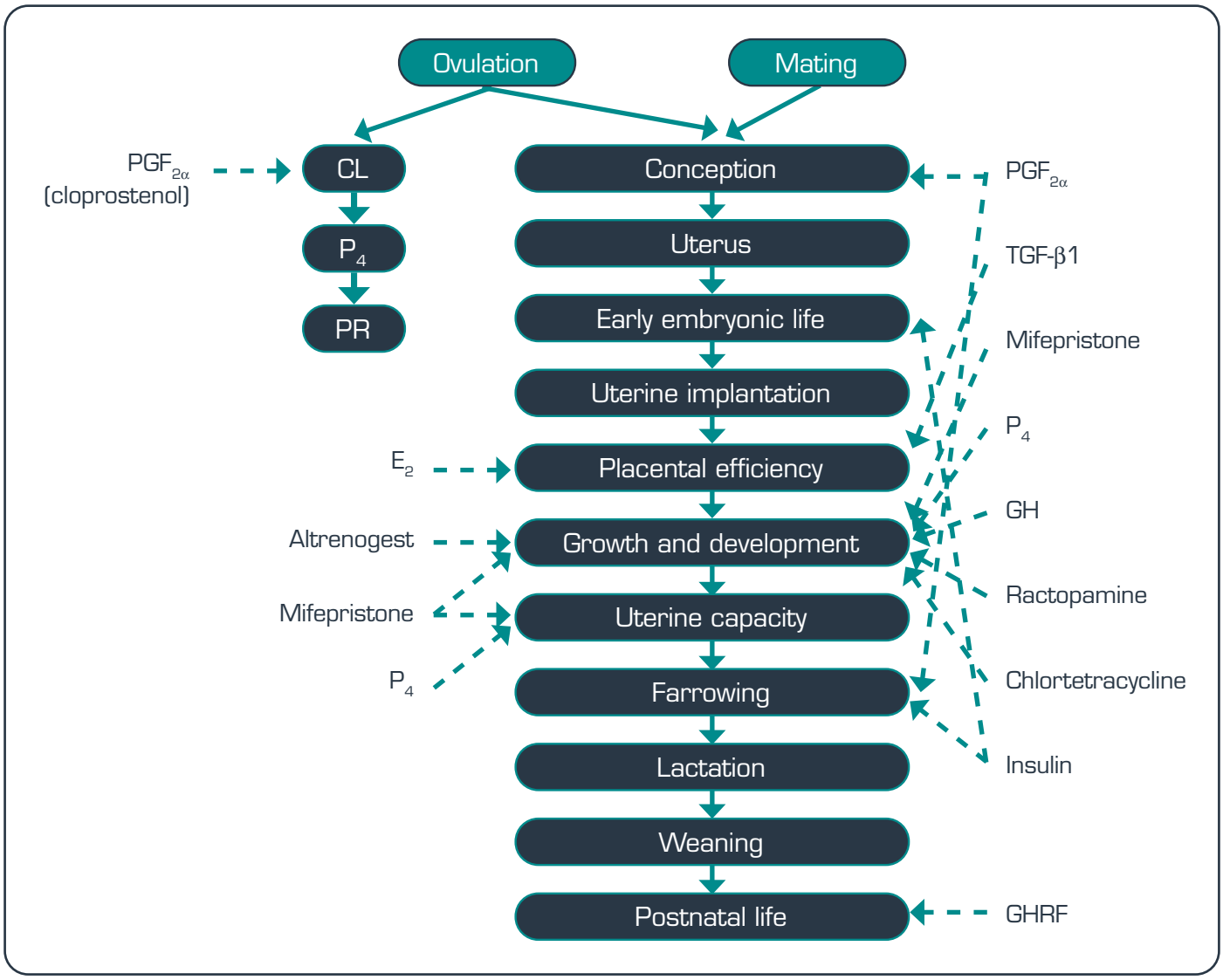


Figure 2. Summary of the drugs that can be used in each of the phases.

Prostaglandins

Although the practical application of prostaglandins and their analogues is usually related to their ovarian action, they have three main effects on the reproductive function of sows (*figure 3*; Dial, 1984):

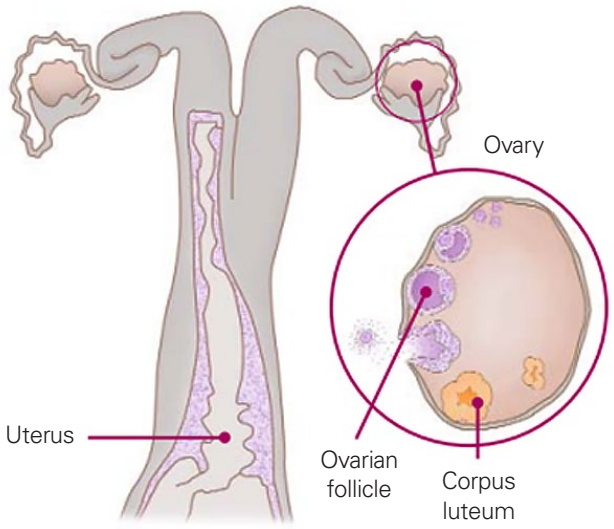
- Induction of luteolysis.
- Smooth muscle stimulation.
- Hormonal stimulation of endocrine tissues.

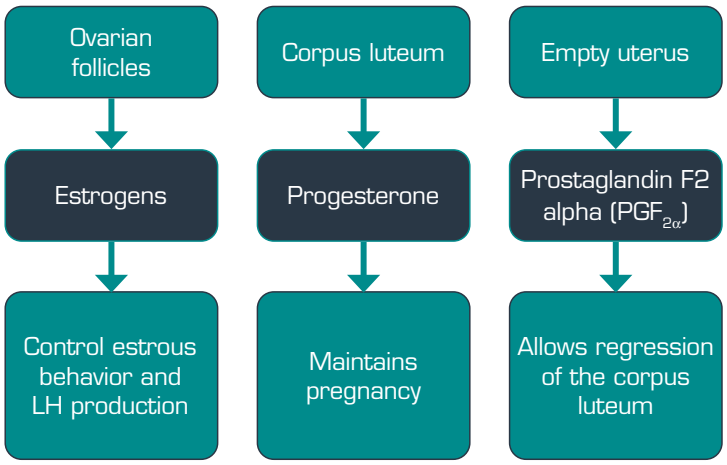
Postpartum endometrial regeneration and uterine involution occur after approximately 15 to 21 days (Bazer *et al.*, 1993) and are conditioned by an increase in prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) concentrations.

Uterine involution

When this uterine involution is affected, the natural prostaglandin cascade is insufficient to prevent regression of the corpus luteum. This conditions maintenance of progesterone production and can promote infectious processes (Bazer *et al.*, 1993).

Uterine infections and associated postpartum endometritis increase the WTSI by reducing fertility and reducing prolificacy in the next cycle. In addition, these are one of the main causes of sow removal due to reproductive failure (Sanders and Bilkei, 2004).





Source: Sara Crespo.

Figure 3. Reproductive cycle of the sow.

The first $PGF_{2\alpha}$ was discovered in 1979; shortly after, several $PGF_{2\alpha}$ agonists and generic products appeared. The main difference between them is that some are chemically analogous to uterine $PGF_{2\alpha}$ and others, such as cloprostenol sodium are chemical analogs of agonists.

Compared to $PGF_{2\alpha}$ analogs, cloprostenol has a higher:

- Affinity for PGF_2 receptors (Kimbal, 1976).
- A half-life in the bloodstream of 3 hours versus a few minutes (EMEA).

Cloprostenol use

Cloprostenol application early postpartum can:

- Improve the average daily gain in a litter.
- Reduce mortality during lactation resulting from rapid regression of the corpus luteum and the *negative feedback* effect caused by progesterone in relation to milk production (prolactin) (Vanderhaeghe *et al.*, 2008; *table 4*).

Postpartum cloprostenol can achieve an improvement in uterine involution similar to the effect of endogenous prostaglandins.

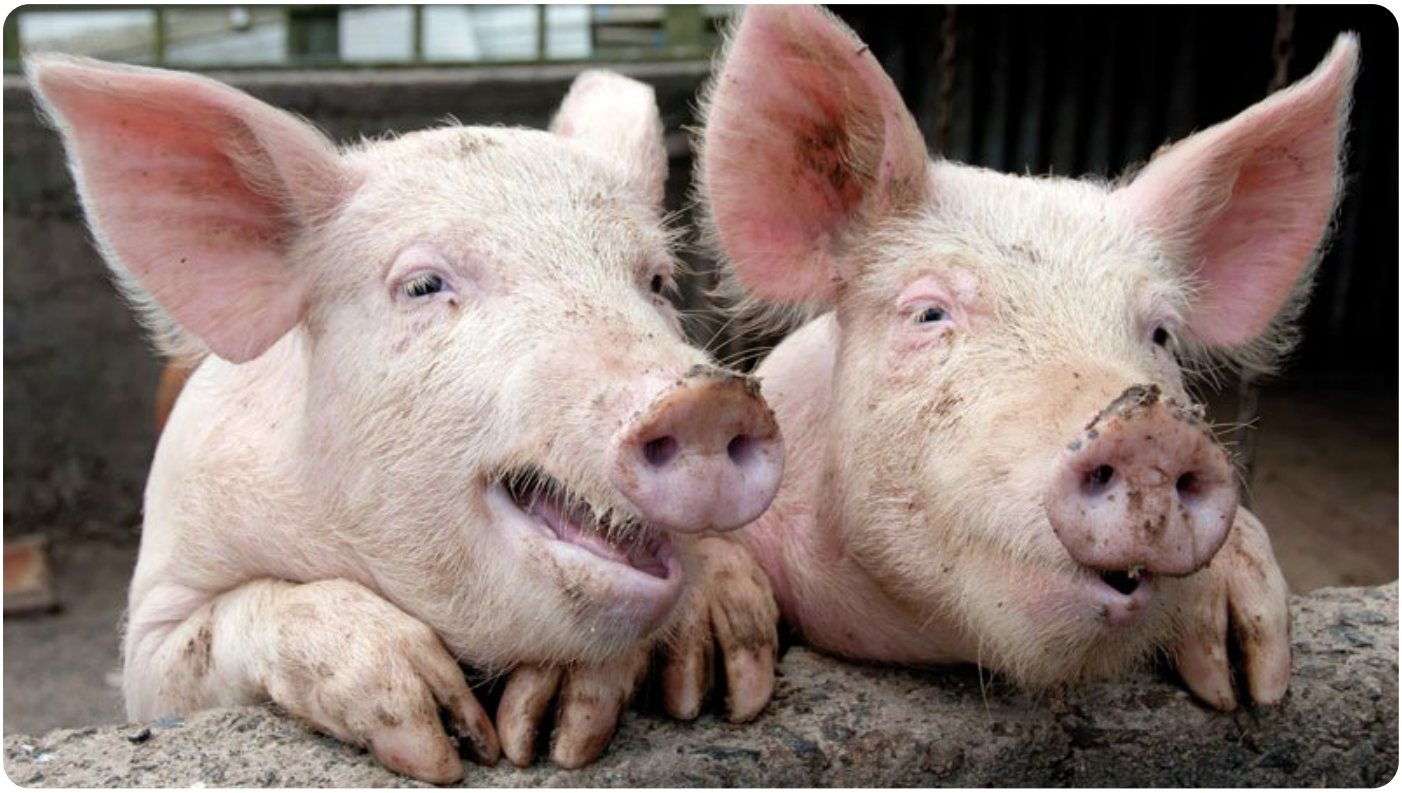
Piglets from mothers with high progesterone levels have also been shown to grow slower in the first postpartum days.

The porcine myometrial smooth muscle contains a heterogeneous distribution of prostanoid receptors.

Parameter	Cloprostenol group	Control group	Valor p
% pre-weaning mortality	5.10 ± 7.37 (*n* = 26)	6.23 ± 10.45 (*n* = 23)	0,34
ADWG lactation	0.206 ± 0.05 (*n* = 26)	0.192 ± 0.04 (*n* = 23)	0,37
Postpartum litter size	12.20 ± 3.16 (*n* = 17)	10.23 ± 3.76 (*n* = 16)	<0,01

Source: Vanderhaeghe, *et al.* (2008).

Table 4. Litter size improvement after the postpartum application of cloprostenol.



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Progesterone

Regarding high progesterone levels, the possibility of persisting resistant corpora lutea has been demonstrated in around 8% of postpartum sows (Elbers *et al.*, 1994; Lopez *et al.*, 2009). This implies that incorrect regression of the corpus luteum would maintain high progesterone concentrations, preventing endometrial regeneration and promoting subsequent infections.

Muscle contractions

$PGF_{2\alpha}$ elicits a contractile response:

- Very strong in the longitudinal muscle.
- Very slight in the circular fibers.

The magnitude of the contractions caused by sodium cloprostenol is very similar and so, by applying it postpartum, uterine involution is improved to similar levels achieved by endogenous prostaglandins (Cao *et al.*, 2002).

This process often results in the appearance of a complex where uterine infections are normally accompanied by infections of the mammary gland, known as mastitis, metritis, and agalactia (MMA) syndrome (Glock and Bilkei, 2005).

Mastitis, metritis, and agalactia syndrome

The appearance of MMA, which significantly affects sow fertility, usually implies farrowing losses (Karg and Bilkei 2002):

- Due to the pronounced agalactia.
- Because of pain due to inflammation, the sows avoid allowing the litter to suckle.

Antimicrobial treatments with antibiotics are carried out when there is a clinical process, but preventive treatment should be key to reducing the frequency of postpartum uterine infections.

Conclusions

01 The WTSI is one of the most important parameters when measuring the profitability of farms.

02 The WTFFSI indirectly determines gestation losses at the farm. Its improvement is directly related to improvement of the farm's productivity.

03 Anestruses are one of the main causes of the early removal of breeding stock.

04 The hypothalamic-pituitary-gonadal complex is influenced by various factors, meaning that a differential diagnosis of the problem must be established in order to act appropriately.

05 Prostaglandin analogs used postpartum are successful in improving uterine involution, endometrial regeneration, and reducing the occurrence of infections.

06 Persistent corpora lutea can maintain elevated P_4 levels and prevent the correct action of $PGF_{2\alpha}$.

Bibliography

- Brazer W, Geisert D y Zavy T. (1993). Fertilization, cleavage, and implementation. In reproduction in farm animals. Ed E. S. E. Hafez. Lea & Febiger. pp 188-212.
- Cao J, Shayibuzhati M, Tajima T, Kitazawa T and Taneike T. (2002). In vitro pharmacological characterization of the prostanoid receptor population in the non-pregnant porcine myometrium. Eur J Pharmacol. 442(1-2):115-123.
- Dial GD. (1984). Clinical applications of prostaglandins in swine. J Am Vet Med Assoc. 185 (12): 1523-1530.
- Elbers ARW, van Rossem H, Schukken YH, Martin SW, van Exsel ACA, Friendship RM y Tielen MJM. (1994). Return to oestrus after first insemination in sow herds (incidence, seasonality, and association with reproductivity and some blood parameters). Veterinary Quarterly 16(2), 100-109.
- EMEA. (1997). The European Agency for the evaluation of medicinal Products. Cloprostenol and R-cloprostenol summary report.
- Engblom L, Lundeheim N, Dalin AM y Andersson K. (2007). Sow removal in Swedish commercial herds. Livest Sci. 106(1):76-86.
- Glock T y Bilkei G. (2005). The effect of postparturient urogenital diseases on the lifetime reproductive performance of sows. Can Vet J 46(12), 1103-7.
- Karg H y Bilkei G. (2002). Causes of sow mortality in Hungarian indoor and outdoor pig production units. Berliner und Münchened Tierärztliche Wochenschirift 115, 366-368.
- Kimbal FA y Lauderdale JW. (1976). Comparision of luteolytic effectiveness of several prostaglandin analogs in heifers and relative binding affinity for bovine luteal prostaglandin binding sites. Prostaglandins 12, 985-995.
- Koketsu Y. (2005). Six component intervals non-productive days by breeding-female pigs on commercial farms. J. Anim. Sci., 83:1406-1412.
- Lopez JV, Ptaszynska M, Gonzalez P, Jimenez M y Martens MR. (2009). Beneficial effects on the reproductive performance of sows of administering prostaglandin analogues after farrowing.Vet Rec. 164 (26): 807-809.
- Piñeiro C, *et al.* (2008). *https://www.3tres3.com/articulos/intervalo-destete-cubricion-que-le-influye-y-como-podemos-controlarlo_2174/*
- Rodriguez-Estevez V. (2010). El anestro y la infertilidad estacional de la cerda. Grupo Asis Biomedia SL.
- Roongsitthichai A, Tummaruk P y Nutthee A. (2015). Postparturient Administration of prostaglandin F2 Alpha facilitates weaning to-service interval in primiparous sows. Vet Med.45 (2):279-282.
- Sanders M y Bilkei G. (2004). Urogenital diseases and their effect on reproductive performance in high-parity sows. Tijdschrift voor Diergeneeskunde 129, 108-112.
- Tummaruk P, Kesdangsakonwut S y Kunavongkrit A. (2009). Relationship among specific reasons for culling, reproductive data, and gross morphology of the genital tracts in gilts culled due to reproductive failure in Thailand. Theriogenology. 71(2):369-375.
- Vanderhaegaeghe C, Dewulf J, Daems A, Van soom A, De kruif A y Maes D. (2008). Influence postpartum cloprostenol treatment in sows on subsequent reproductive performance under field conditions. Reproduction in Domestic Animals 43, 484-489.