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Wishing you a Happy New Year

Role of Progesterone in Bovine Pregnancy

Progesterone: Endocrine Architecture of Bovine Gestation

Dear Vets,

Lactation is initiated by calving, which should occur every 360–400 days to maximize lifetime milk yield in high-producing dairy animals. Pregnancy loss (PL) remains one of the major constraints to reproductive efficiency and long-term sustainability in dairy herds, exerting significant impacts on animal health, welfare and productivity.

From an economic perspective, pregnancy loss contributes to prolonged calving intervals, resulting in suboptimal milk production, additional treatment costs and increased expenses associated with insemination and potential culling. Consequently, minimizing pregnancy loss is critical for maintaining both reproductive performance and overall farm profitability.

To maintain an economically sustainable production cycle for dairy farmers and to ensure optimal reproductive performance in bovine, preventing early pregnancy loss is of critical importance. Successful establishment of pregnancy depends on several coordinated events, beginning with accurate detection of estrous, timely artificial insemination and fertilization of oocyte by sperm. Following fertilization, embryo undergoes sequential developmental stages that require a precisely regulated endocrine environment to support maternal recognition of pregnancy and sustain early gestation. During this period, progesterone plays a critical role and insufficient levels of this hormone are a major cause of early embryonic loss.

This issue of Face2Vet focuses on critical role of progesterone in bovine pregnancy. We invite you to read this issue and share your valuable experience/ thoughts by scanning below QR code or reaching us *via* email at face2vet@ intaspharma.com.

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Introduction

Bovine pregnancy is a complex and finely regulated biological process that serves as foundation for sustainable production. The success of each pregnancy determines herd reproductive efficiency, directly influencing milk yield, calf crop, genetic progress and farm profitability. As bovine typically produce only one calf per gestation, achieving and maintaining pregnancy is essential for optimal productivity in a dairy enterprise.

Despite advances in reproductive management, pregnancy loss remains a significant challenge in dairy animals. Although fertilisation rates are generally high, a considerable proportion of embryos fail to survive the earliest stages of development. Most pregnancy loss occurs during first few weeks after conception, particularly between fertilisation and maternal recognition of pregnancy, which in bovine occurs around 15-17 days after fertilization. During this period, embryo undergoes rapid developmental transitions and any disruption in conceptus growth, uterine environment or maternal embryonic communication can result in embryonic mortality. Factors such as poor oocyte quality, suboptimal uterine conditions, metabolic stress, infections and hormonal imbalances contribute substantially to early embryonic loss. Estimates suggest that nearly 40 percent of conceptions fail between 8-16 days of gestation, making early pregnancy most vulnerable phase.

Hormones play a central role in regulating reproductive events throughout pregnancy. Successful conception, implantation, placental development and maintenance of gestation rely on a coordinated interplay of endocrine signals produced by ovary, uterus and developing conceptus. Progesterone (P_4) is most critical determinant of pregnancy success in bovines. Progesterone prepares uterus for embryo arrival, stimulates endometrial secretions necessary for conceptus nourishment and establishes uterine receptivity for implantation. It also suppresses uterine contractions and modulates maternal immune system to support embryo survival. Thus, understanding the mechanisms governing pregnancy establishment, especially hormonal control mediated by progesterone is vital for improving reproductive efficiency in bovine.

Sources of Progesterone

Progesterone is synthesized primarily by corpus luteum (CL), which serves as dominant endocrine source throughout the pregnancy. After ovulation, luteinized granulosa and theca cells differentiate into large and small luteal cells that express the full steroidogenic enzyme complex—StAR, CYP11A1 and 3β-HSD allowing continuous progesterone secretion essential for uterine preparation and embryo survival. During advancing gestation, placentomes comprising fetal cotyledons and maternal caruncles gradually contribute to circulating progesterone. This occurs as trophoblast cells acquire steroidogenic capacity, although bovine corpus luteum remains functionally important until late pregnancy. Minor progesterone sources include follicular granulosa cells during preovulatory luteinization and adrenal cortex, but these contribute minimally compared to CL and placenta. Together, these coordinated sources ensure adequate progesterone levels for uterine quiescence, placental development and maintenance of pregnancy.

Pathway of Progesterone Synthesis in Luteal Cells

LH from Pituitary

↓

Increased Cholesterol Uptake

↓

StAR Protein Activation

↓

Mitochondrial Cholesterol Transport

↓

Pregnenolone Formation ($P450_{scc}$)

↓

Pregnenolone → Progesterone (3β-HSD)

↓

Progesterone Secretion into Circulation

StAR - Steroidogenic Acute Regulatory Protein, **$P450_{scc}$** - Cytochrome P450 Side-Chain Cleavage Enzyme **3β-HSD** - 3β-Hydroxysteroid Dehydrogenase

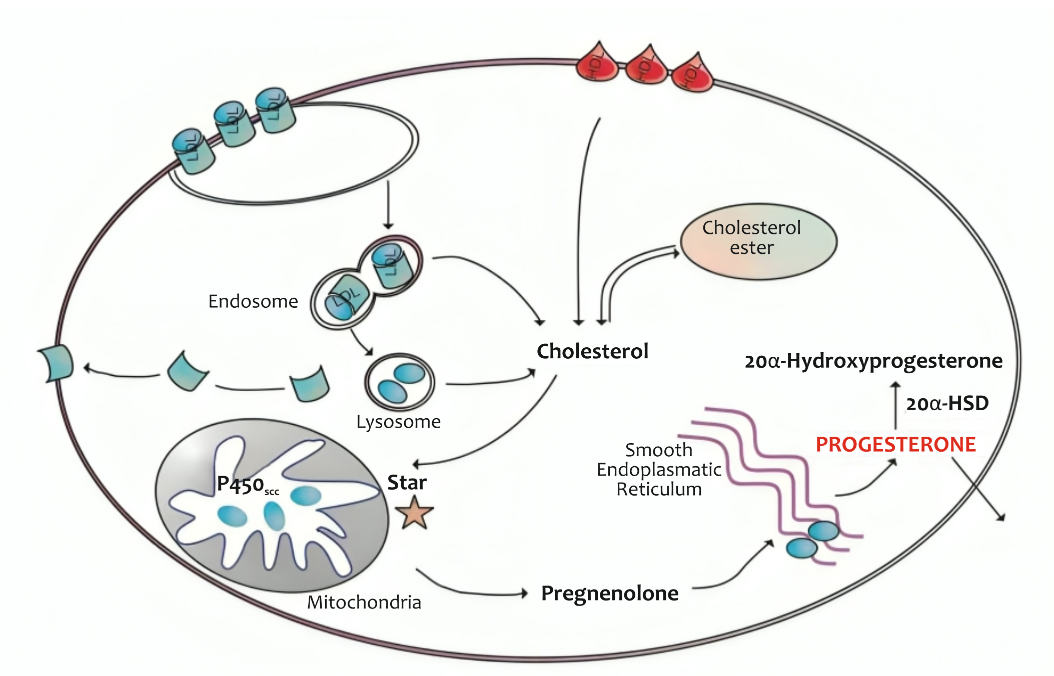

Fig. 1: Pathway of Progesterone Biosynthesis in Luteal Cell

(Source: Tomac *et al.*, 2011)

Oocyte to Offspring - Progesterone as Key Hormonal Driver

Journey from oocyte to offspring in bovine is a highly coordinated physiological process in which progesterone plays a central regulatory role. Adequate progesterone concentrations are essential for optimizing oocyte quality by supporting follicular maturation and preparing reproductive tract for successful fertilization. Following conception, progesterone drives early embryonic development by regulating uterine secretions, modulating immune tolerance and creating a conducive uterine microenvironment for embryo survival. Collectively, progesterone acts as cornerstone hormone, ensuring reproductive success from oocyte maturation to establishment and continuation of pregnancy.

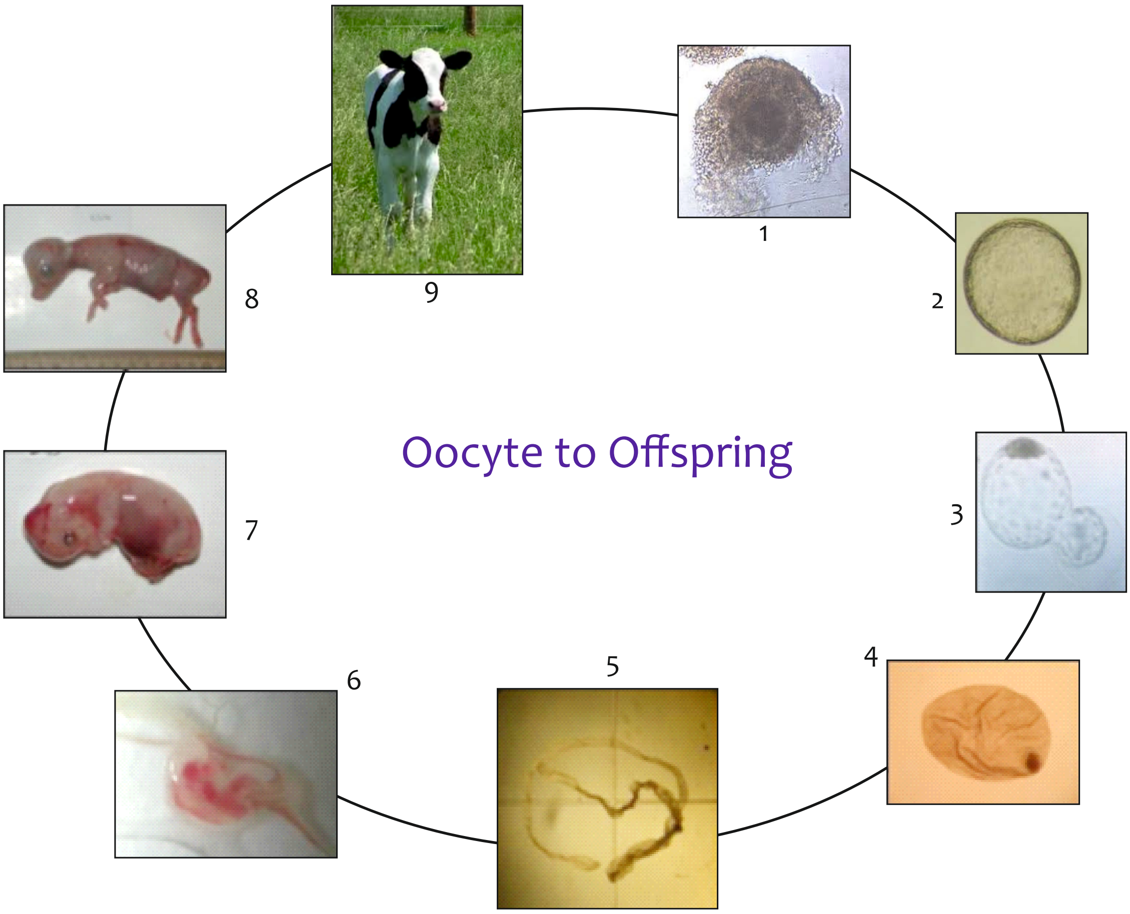

Fig. 2: Sequential Events from Oocyte to Offspring in Bovine
1. Immature cumulus-oocyte-complex, 2. Day 7 blastocyst, 3. Day 8 hatching blastocyst,
4. Day 13 ovoid conceptus, 5. Day 16 elongated conceptus, 6. Day 25, 7. Day 45, 8. Day 75, 9. Newborn
(Source: Lonergan, 2015)

Progesterone and Oocyte Quality

High progesterone concentrations during growth of ovulatory follicle are closely linked with improved oocyte quality and better pregnancy outcomes in bovines. In final phase of follicular maturation between preovulatory LH surge and ovulation, follicular fluid shifts from being estrogen dominant to progesterone dominant as granulosa cells begin luteinizing in preparation for corpus luteum formation. This hormonal shift occurs at same time oocyte resumes meiosis and completes its final maturation steps, indicating that adequate progesterone exposure during this window is crucial for optimal oocyte competence. Therefore, progesterone not only supports transition to luteal function but also plays an important role in shaping the developmental potential of oocyte in bovine.

Progesterone and Conceptus Elongation

Progesterone (P_4) is key endocrine regulator that prepares and maintains uterus in a state capable of supporting conceptus growth and elongation. After ovulation, rising progesterone stimulates extensive changes in endometrial epithelium and stroma, leading to increased secretion of histotroph. These progesterone dependent uterine secretions create optimal biochemical and molecular environment required for blastocyst expansion, transition into an ovoid stage and rapid elongation into a filamentous conceptus. Higher circulating P_4 concentrations during early

Luteal phase consistently accelerate conceptus elongation in bovine, whereas low P_4 delays trophoblast development. Importantly, progesterone acts primarily through indirect modulation of endometrium rather than direct effects on embryo, ensuring adequate nutrient supply, uterine receptivity and support for conceptus during critical pre-implantation period. Adequate level of progesterone during early pregnancy shows inconsistent benefits in improving conceptus elongation and embryonic survival. The conceptus elongation is illustrated in Fig. 3.

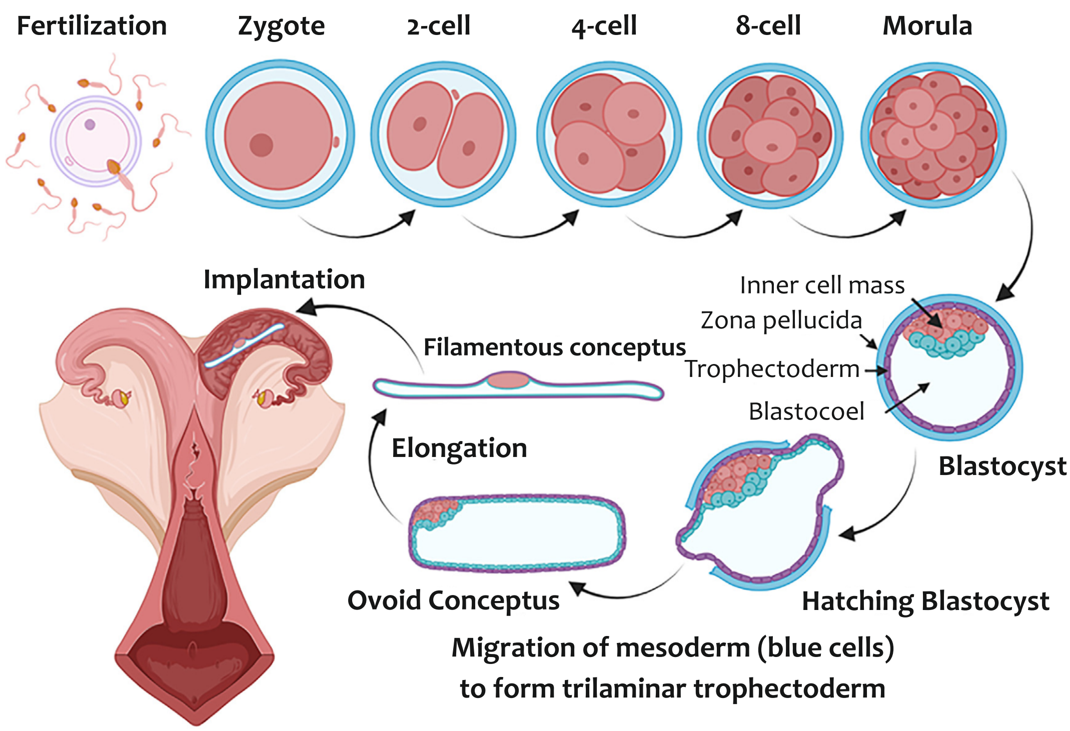

Fig. 3: Early Conceptus Development from Fertilization to Elongation
(Davenport *et al.*, 2023)

Progesterone for Maternal Regulation of Pregnancy and Maintenance of CL

Maternal recognition of pregnancy in bovine depends on timely conceptus elongation, during which embryo transitions from a spherical to a tubular and ultimately a filamentous form capable of producing interferon-tau (IFN-τ). Adequate progesterone priming of uterus is essential for this elongation process and for establishing an optimal endometrial environment. Between 15-18 days of early pregnancy, elongating bovine conceptus secretes IFN-τ, which acts on uterine endometrium by binding to type-I interferon receptors ($IFNAR_{1/2}$). This interaction activates JAK–STAT signalling pathway and induces interferon stimulated genes particularly Interferon Regulatory Factor 2 (IRF2). IRF2 suppresses uterine expression of estrogen receptor-α (ERα) and oxytocin receptor (OTR), thereby preventing oxytocin from stimulating $PGF2_{\alpha}$ release. In absence of luteolytic $PGF2_{\alpha}$ pulses, regression of corpus luteum does not occur, allowing progesterone concentrations to remain elevated and ensuring successful maternal recognition of pregnancy. The mechanisms by which progesterone contributes to maternal recognition of pregnancy and supports corpus luteum (CL) maintenance in bovine is depicted in Fig. 4 and Fig. 5.

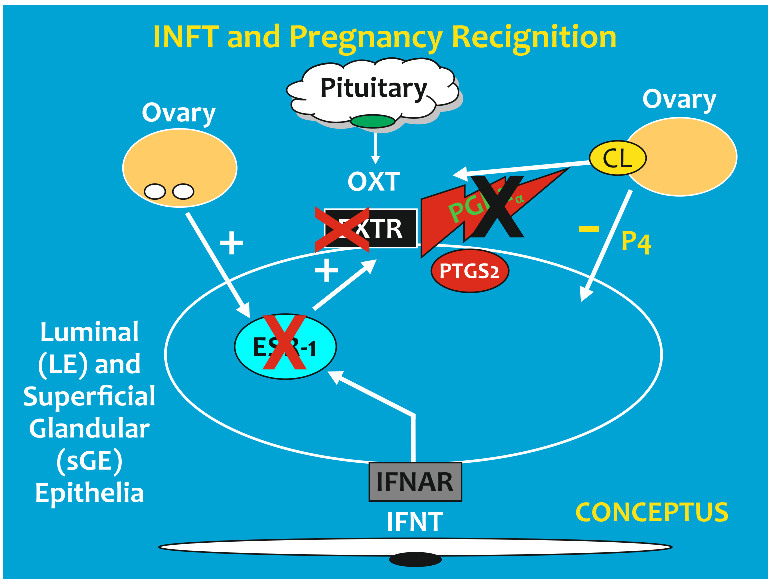

Fig. 4: Interferon and Pregnancy Recognition
(Source: Bazer, 2013)

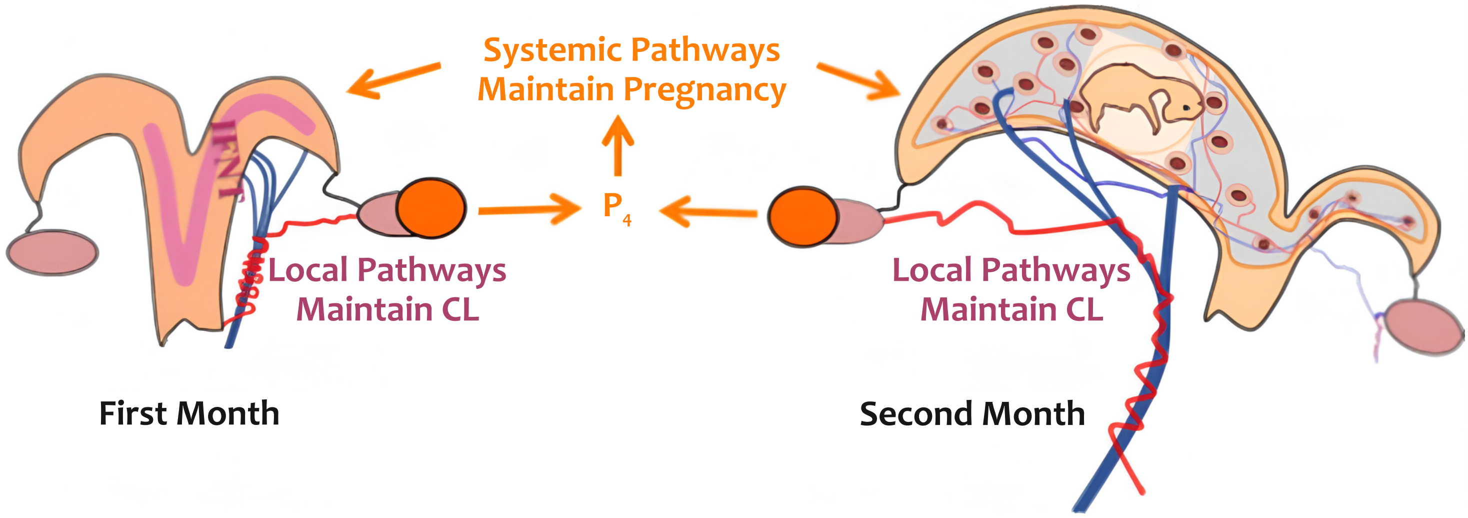

Fig. 5: Progesterone Pathways Supporting Early Pregnancy
(Source: Wiltbank *et al.*, 2018)

Pathway of Maternal Recognition of Pregnancy

Conceptus (Day 15–18)

↓

Elongating trophoblast secretes IFN-τ

↓

IFN-τ acts on uterine lining (Endometrium)

↓

Binds with type-I interferon receptors ($IFNAR_{1/2}$)

↓

Activates JAK–STAT signalling

↓

Induces interferon-stimulated genes (ISGs)→ Especially IRF_2

↓

IRF2 blocks uterine expression of Estrogen and Oxytocin receptor

↓

Without Estrogen and Oxytocin cannot trigger $PGF2_{\alpha}$ pulses

↓

No $PGF2_{\alpha}$ luteolytic pulses from uterus

↓

Maintenance of corpus luteum (CL)

↓

Progesterone dominated uterine environment

↓

Embryo survival - Pregnancy establishment (Maternal recognition)

Progesterone Induces Uterine Adaptations Supporting Early Pregnancy

Suppression of Uterine Contractility

Progesterone exerts a potent relaxant effect on bovine uterus primarily by reducing expression of oxytocin receptors (OXTR) in endometrial epithelium and inhibiting prostaglandin $F2_\alpha$ ($PGF2_\alpha$) synthesis pathway. This results in suppression of pulsatile myometrial contractions and a marked reduction in luteolytic $PGF2_\alpha$ release from uterus. A quiescent uterine environment is essential during peri-implantation period to prevent mechanical disruption or displacement of fragile elongating conceptus. Inadequate progesterone particularly during 4–7 days after ovulation, leads to heightened uterine activity, increased uterine tone and a greater risk of early embryonic loss. Thus, progesterone establishes biomechanical stability required for conceptus elongation and eventual adhesion of conceptus to uterine epithelium.

Progesterone for Endometrial Differentiation and Uterine Secretory Functions

Progesterone is principal driver of endometrial differentiation during early luteal phase, initiating proliferation and hypertrophy of luminal epithelium (LE), glandular epithelium (GE) and stromal compartments. Under progesterone stimulation, endometrial glands markedly increase their secretory activity, producing the nutrient-rich uterine luminal fluid known as histotroph. This histotroph contains essential substances including glucose, amino acids, lipids, ions, cytokines, uterine milk proteins, insulin-like growth factors and various locally regulated proteins required for conceptus survival. Bovine embryo particularly during elongation phase (days 12–17) relies entirely on histotroph for energy metabolism, membrane biosynthesis, trophectoderm expansion and initiation of IFN-τ secretion. Therefore, magnitude and timing of progesterone exposure directly influence histotroph composition, conceptus growth and overall success of pregnancy.

Immunomodulatory Effect of Progesterone

Progesterone plays a pivotal immunoregulatory role in maintaining uterine tolerance during early pregnancy by suppressing pro-inflammatory cytokines such as TNF-α and IFN-γ, while promoting anti-inflammatory signalling pathways that protect semi-allogeneic embryo from immune-mediated rejection. It modulates activity of key uterine immune cell populations, including regulatory T cells and uterine natural killer (NK) cells, shifting them toward a pregnancy supportive phenotype. Progesterone also stimulates production of progesterone induced blocking factor (PIBF), which attenuates NK-cell cytotoxicity within uterine microenvironment. Collectively, these coordinated actions establish a controlled, low-inflammation uterine milieu that stabilizes conceptus development, reduces the risk of early embryonic loss and promotes successful establishment of pregnancy in bovines.

Supportive Role in Placentation

Progesterone serves as a chief modulator of placentation by promoting trophoblast proliferation, migration and differentiation, which drive placentome formation and establish an effective fetal maternal interface. It regulates key genes involved in placental morphogenesis and nutrient transport while sustaining uterine glandular secretions that nourish conceptus until placenta becomes fully functional. As gestation progresses, progesterone maintains uterine quiescence and supports vascular remodelling by enhancing angiogenic factors and growth mediators necessary for placental and fetal expansion.

Progesterone threshold required to maintain pregnancy in Bovine

A minimum plasma progesterone concentration of about 2 ng/ml is required to support early embryonic development and uterine receptivity during early pregnancy. Progesterone levels are typically maintained between 3-8 ng/ml throughout mid (2-4 months) and late pregnancy (5-9 months) to maintain uterine quiescence and support fetal growth. As parturition approaches, progesterone levels decline progressively, falling to <1 ng/ml in days preceding calving. This reduction is critical for the initiation of parturition (Terblanche and Labuschagne, 1981).

Importance of Progesterone in Prevention of Pregnancy Loss

Loss of pregnancy/abortion in dairy animals can occur at multiple stages of gestation and due to various etiologies. The first critical period occurs during first week after breeding and is associated with fertilization failure and early embryonic death, resulting in substantial pregnancy losses. In general, 20–50% of high-producing lactating dairy animals experience pregnancy loss during first week of gestation. The second pivotal period, extending from 8 to 27 days, encompasses embryo elongation and classical maternal recognition of pregnancy phase, with pregnancy losses averaging approximately 30%, although considerable variation exists among farms (25–41%). Failures or delays in trophoblast elongation and embryonic development during this period may result in pregnancy loss, possibly due to suboptimal uterine histotroph. The third pivotal period occurs during second month of pregnancy (28–60 days), with reported losses of approximately 12%. The fourth period, during third month of pregnancy, is characterized by substantially lower pregnancy losses (~2%) compared with earlier stages. The second month of gestation (28–60 days) represents a particularly critical window for pregnancy maintenance in dairy animals, during which transition from choriovitelline to chorioallantoic placentation and establishment of functional placentomes take place. Deficiencies in placental development, vascularization or embryonic growth during this period are major contributors to pregnancy loss, especially when accompanied by metabolic, infectious or uterine disorders. Evidence indicates that reduced circulating progesterone concentrations and compromised corpus luteum function significantly increased risk of fetal loss, whereas presence of an accessory corpus luteum markedly improves pregnancy survival. During this stage, progesterone is essential for maintaining uterine quiescence, supporting placental vascularization and regulating endometrial secretions required for sustained fetal nourishment. Adequate progesterone concentrations also suppress luteolytic prostaglandin release, thereby ensuring continued corpus luteum function and stable hormonal support for developing fetus. Administration of exogenous progesterone preparations **(Inj. Progesyn)** at second month of pregnancy may help prevent pregnancy loss (habitual abortion) in dairy animals.

Approaches for Optimizing Progesterone Levels to Support Pregnancy

Exogenous Progesterone Supplementation

Exogenous progesterone (P_4) supplementation is a widely adopted strategy to increases circulating progesterone concentrations during pregnancy in bovine. According to evidence from multiple studies, exogenous progesterone supplementation is effective for pregnancy maintenance in animals with a history of repeat breeding, early embryonic loss, low luteal progesterone levels, or under conditions of high metabolic stress. Supplementation of exogenous progesterone (**Inj. Progesyn** @ 250 mg (3 ml) *via* IM route) carried out between 3 to 7 days after artificial insemination has been shown to be beneficial, as it supports adequate circulating progesterone concentrations and improves early pregnancy establishment. In contrast, progesterone administration before 3-day post-insemination may be detrimental, as it can disrupt normal luteal development and induce premature luteolysis, while supplementation initiated after 7-day post-insemination generally shows no additional benefit (Do Couto *et al.*, 2024).

Induction of Accessory Corpus Luteum

Although dairy animals typically develop a single corpus luteum (CL) after ovulation, several hormone-based interventions can induce the formation of an accessory CL, thereby enhancing circulating progesterone (P_4) concentrations. Administration of gonadotropin-releasing hormone (GnRH) or GnRH agonists at specific intervals after artificial insemination (AI) reliably promotes accessory CL formation. Injection of Buserelin **(Gynarich)** at a dose of 10–20 µg *via* IM, IV, or SC routes between 5 to7 days post-AI facilitates the formation of an accessory corpus luteum from first follicular wave, whereas Inj. Buserelin **(Gynarich)** administration between 11 to 14 days post-AI induces accessory CL formation from second follicular wave. The resulting elevation in plasma progesterone concentrations, along with a concomitant reduction in estradiol secretion, creates a more favorable endocrine environment for early embryonic development. Importantly, animals that develop an accessory CL are reported to be approximately 0.32 times less likely to experience pregnancy loss compared with animals possessing only a single CL.

Nutritional Supplements

Various nutritional interventions play a critical role in maintenance of pregnancy in bovine by supporting corpus luteum (CL) function and endometrial receptivity. Omega fatty acids enhance luteal health by modulating arachidonic acid metabolism and reducing prostaglandin F2α synthesis, thereby shifting eicosanoid production toward less luteolytic and less inflammatory prostaglandins, which promotes luteal cell survival, improves luteal vascularization, prolongs corpus luteum lifespan and sustains progesterone secretion during the critical period of maternal recognition of pregnancy. Amino acids contributing to pregnancy establishment by enhancing endometrial cell proliferation, protein synthesis and secretion of uterine histotroph that supports early embryonic development prior to placentation. Multivitamins and selected herbs further complement these effects by optimizing luteal steroidogenesis, reducing oxidative stress and modulating uterine inflammatory responses. In this context, supplementation of **Progimax bolus** @ 1–2 bolus daily for 10 days post–artificial insemination supports CL health and strengthens the endometrium, thereby facilitating embryo and fetal development and improving pregnancy maintenance in bovines.

Conclusion

Progesterone is central endocrine regulator, governing successful establishment and maintenance of pregnancy in bovines, influencing oocyte competence, conceptus elongation, uterine receptivity, immunomodulation, placentation and maternal recognition of pregnancy. Strategic interventions including exogenous progesterone supplementation, induction of accessory corpus luteum and targeted support of luteal and endometrial function, can enhance circulating progesterone concentrations and optimize uterine environment for embryo survival. Implementing these evidence-based approaches provides a practical framework for improving fertility outcomes and sustaining reproductive efficiency in dairy animals.

References

Bazer, F. W. **(2013)**. Pregnancy recognition signaling mechanisms in ruminants and pigs. *J. Anim. Sci. Biotechnol.*, ***4***: 23.

Brooks, K., Burns, G., and Spencer, T. E. **(2014)**. Conceptus elongation in ruminants: roles of progesterone, prostaglandin, interferon tau and cortisol. *J. Anim. Sci. Biotechnol.*, ***5***: 53.

Davenport, K. M., Ortega, M. S., Johnson, G. A., Seo, H., and Spencer, T. E. **(2023)**. *Review: implantation and placentation in ruminants. Animal* **17**: 100796.

do Couto, S. R. B., Silenciato, L. N., Okada, M. D. S. D., e Silva, O. R., Ferreira, J. E., and de Mello, M. R. B. **(2024)**. Use of Progesterone as a Strategy to Improve Reproductive Efficiency in Cattle.

Lonergan, P. **(2011)**. Influence of progesterone on oocyte quality and embryo development in cows. *Theriogenology*, **76**: 1594-1601.

Lonergan, P. **(2015)**. New insights into the function of progesterone in early pregnancy. *Anim. Front*, **5**: 12-17.

Lonergan, P. **(2023)**. The importance of progesterone in pregnancy establishment in cattle. *Livestock*, ***28***: 271-276.

Lonergan, P., and Sánchez, J. M. **(2020)**. Symposium review: Progesterone effects on early embryo development in cattle. *J. Dairy. Sci.*, ***103***: 8698-8707.

Lonergan, P., Forde, N., and Spencer, T. **(2015)**. Role of progesterone in embryo development in cattle. *Reprod. Fertil. Dev.*, ***28***: 66-74.

Lonergan, P., O'hara, L., and Forde, N. **(2018)**. Role of diestrus progesterone on endometrial function and conceptus development in cattle. *Anim. Reprod. , (AR)*, ***10***: 223-227.

Mann, G. E., and Lamming, G. E. **(1999)**. The influence of progesterone during early pregnancy in cattle. *Reprod. Domest. Anim.*, ***34***.

Tomac, J., Cekinović, Đ., and Arapović, J. **(2011)**. Biology of the corpus luteum. *Period. Biol.*, ***113***: 43-49.

Terblanche, HM and Labuschagne, J. M. **(1981)**. Plasma progesterone in cattle. II. Levels during the oestrous cycle, pregnancy and parturition. *Journal of the South African Veterinary Association*, **52**:187-189.

Wiltbank, M. C., Mezera, M. A., Toledo, M. Z., Drum, J. N., Baez, G. M., García-Guerra, A., and Sartori, R. **(2018)**. Physiological mechanisms involved in maintaining the corpus luteum during the first two months of pregnancy. *Anim. Reprod.*, ***15***: 805.

Wiltbank, M. C., Baez, G. M., Garcia-Guerra, A., Toledo, M. Z., Monteiro, P. L., Melo, L. F., and Sartori, R. **(2016)**. Pivotal periods for pregnancy loss during the first trimester of gestation in lactating dairy cows. *Theriogenology*, ***86***: 239-253.

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