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Maternal Recognition of Pregnancy in Mammals

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Abstract

Maternal recognition of pregnancy refers to the requirement for the conceptus (embryo and its associated extra-embryonic membranes) to produce a hormone that acts on the uterus and/or corpus luteum (CL) to ensure maintenance of a functional CL for production of progesterone; the hormone required for pregnancy in most mammals.

Introduction

Maternal recognition of pregnancy (MRP) is the biological process that allows a female to recognize the presence of a conceptus and remodel the endocrine, histological, and secretory function within the reproductive tract to allow attachment/implantation and further embryonic and fetal development. This process, which can be summarized as a mechanism of prevention of luteolysis, involves signaling between the embryo and the uterus leading to successful attachment/implantation. In-depth studies on MRP have been sparked by the impact of early pregnancy loss on productivity in various species such as cattle (Diskin and Morris, 2008), camelids (Tibary and Pearson, 2015), and horses (Canisso et al., 2013; Vanderwall, 2008).

Establishment of pregnancy involves interactions between two interdependent systems defined as: • Uterus, and • Conceptus (embryo and extra embryonic membranes)

- At the appropriate time, the conceptus must produce steroid hormones and /or proteins to signal its presence to the maternal system.
- This signal is necessary for corpus luteum (CL) maintenance, production of progesterone and continued endometrial development and secretory activity.
- This phenomenon was described by Short (1969) as “Maternal Recognition of Pregnancy” (MRP).

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- In most of the species, the conceptus provides a timely biochemical signal or pregnancy will terminate
- The critical series of events by which the Conceptus initially signals its presence to the dam and enables the pregnancy to continues is referred as maternal recognition of pregnancy (MRP)
- MRP must occur prior to luteolysis
- If the conceptus fails to signal its presence at exactly the correct time, the function of CL is terminated by the luteolytic action of prostaglandin F2 alpha (PGF2 alpha) from the uterus. This ensures that the female will return to estrus and mate at frequent intervals until a successful pregnancy is established.
- Uterine PGF2 alpha is produced by endometrium of cows, ewes, mares and sows and causes morphologic regression of CL and cessation of progesterone production.
- The effect of conceptus is luteostatic, since progesterone production is maintained at a level comparable to that of dioestrus during pregnancy.
- Basal secretion of luteinizing hormone (LH) from the anterior pituitary is also essential for CL maintenance and function during pregnancy.

Agents of MRP

MRP in ruminants

The MRP in ruminants IFNτ. IFNτ acts on the endometrium in a paracrine manner to prevent luteolysis, there by maintaining the CL and production of progesterone (Roberts, 1989b).

Originally, it was known as ovine trophoblast protein in sheep and bovine trophoblast protein in cattle, the name interferon Tau was given to it by International Interferon Society. There are different types of IFN and IFNτ is unique to ruminants. IFNτ is a Type I interferon with potential antiviral, anti-proliferative and some immuno modulatory biological activities. This implies that apart from being the signal for MRP, IFNτ plays other roles in early pregnancy in ruminants. These include protection of the conceptus or uterus against viral infection and modulating the maternal immune response towards tolerating the apparently foetal ‘semi allograft.

The transfer of trophoblastic vesicles in to cyclic ewes culminates into maintenance of the CL (Martaletal. 1979). Therefore, IFNτ originates from the conceptus and not the

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endometrium. In sheep, secretion of IFNτ is observed from days 10 today 21 (day 0=mating) with maximum levels between days 16 and 18. Likely by days 22–23, the synthesis of IFNτ has ceased. The size of the blastocyst is a factor that determines the amount of IFNτ produced which may necessarily not tally with the quantity of IFNτ mRNA expressed by the blastocyst. This phenomenon was observed in cow (Robinsonetal.,2006). Ovine embryos in vitro do not expand after hatching; however, they were reported to produce a small amount of IFNτ. IFNτ injection on days 11–15 post-oestrus decreased concentrations of oestrogen and progesterone receptors (PGR) in sheep endometrium on day16 when compared with serum protein-infused control ewes, whose corpora luteal were undergoing regression on days14–16 (Mirandoetal.,1993).

Interferon from the Conceptus prevents luteolysis in the cow and Ewe

Interferon tau produced from trophoblastic cells

Endometrial cells of the uterus

Inhibits the production of oxytocin receptors

Oxytocin cannot stimulate Prostaglandin synthesis.

Interferon tau also causes production of proteins from the uterine glands which migrates to uterine lumen to nourish the Conceptus

MRP in sows

In sow, the MRP signal is oestrogen. For the pregnancy to be sustained by the action of oestrogen, at least two embryos, one in each of the uterine horns are required. Otherwise, the horn with no embryos will still produce PGF2α and this will initiate embryo loss (Senger, 2005). Pig conceptus produces oestrogen on day 14 and 18 as agent of MRP. The oestrogen redirects the PGF2α synthesis towards the endometrial lumen (exocrine) rather than diffusing into the blood (endocrine) (Bazer, 2013). Therefore, PGF2α, produced by the endometrium fails to get to the ovary to cause luteolysis. In the endometrial lumen, PGF2α is metabolised

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and/or speculated to cause (local) contraction in the lumen. The latter is envisaged to aid even distribution of the embryos (being multiparous) within the available space in the uterus.

MRP in mare

In mares, the agent of MRP remains a mystery and yet to be clarified (Klein and Troedsson, 2011). Some scholars believe MRP in mare involves some glycoproteins, oestrogen and PGE2 even though these could not be substantiated (Klein and Troedsson, 2011). The study of Wilsher and Allen (2011) disproved oestrogen from being a likely agent for MRP in mares. Instead, administration of fractionated coconut or peanut oil on Day 10 post ovulation provides an effective and practical method of extending luteal life span. What is certain in this species is the need for movement of the embryo from one horn to another (McDowell et al., 1988; Sharp et al., 1989). This movement is accomplished by simple peristalsis within the endometrium and the bi-partite shape of the mare uterus seems a physiological facilitator of this movement. The simulation of embryo movement from one horn to the other using a bead or ball procrastinates luteolysis and extends CL longevity (Rivera del alamo et al., 2008). Both conceptus and endometrium synthesised PGE2 during early pregnancy (Boerboom et al., 2004). It was then proposed that PGE2 by antagonising the luteolytic effect of PGF2a is the MRP in this species. This speculation was further corroborated by the study of Ealy et al. (2010). The presence of conceptus on day 15 pregnancy blocked the induction of COX-2, that determines the synthesis of PGs. Sequel to this is reduced expression of PGF2α and abrogation of luteolysis (Boerboom et al., 2004). This evidence remains to be clarified.

Unlike ruminant, horse conceptus or the uterine flushing on days 13–15 gestation failed to show antiviral activities of interferon. Rather, the study of Herrler et al. (2000) confirmed the insulin growth factor 1 (IGF-I) binding activity and several IGF binding proteins in the pre-implanta tion equine conceptus. These are hypothesised to be essentially required to enhance embryo development and so, indirectly partake in MRP.

MRP in dogs and cats

In dogs and cats, there is dearth of information on MRP or early pregnancy factor like on other species. This may be attributed to the fact that MRP is not required for sustainance of pregnancy in these species. Whether is a conceptive or nonconceptive, CL is retained for the same period of time (about 60 days). This culminates into exhibition of pseudo-pregnancy (Senger, 2005).

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MRP in human

In human, the luteolytic agent is also PGF2a which is produced by the ovary instead of the endometrium in ruminant and pig (Aplin et al., 2008). The signal for MRP is hCG (Ross, 1978). hCG is luteotrophic and is produced by the blastocyst on days 4–5 as soon as the embryo descends from the oviduct into the endometrium.This explains the reason why detection of hCG in the serum/urine has been used as one of the earliest pregnancy diagnosis in woman (Johnson et al., 2009).

Table 1 Time of production and agents of maternal recognition of pregnancy (MRP) in mammals.

Species	Gestation length (days)	Placental takeover (days)	Agent of MRP	Day of production
Ewe	150	50	oIFNτ	9/10–21
Cow	270	180–240	bIFNτ	12–38
Sow	114	11–30	Oestradiol	11–30
Human	270	60–70	hCG	11
Mare	330	70	Proteins/oestrogen?	14–16; 15–30
Dog, cat	60	–	None	–

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