Retained fetal membrances in Dairy Cows – Significance & Correlations

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Summary

Retained Fetal Membranes (RFM) are a frequent condition in dairy cows. It may be expected in around 7% of multiparous cows after calving, but the incidence may be significantly higher in individual herds. The cost inferred by RFM is largely due to a loss of milk production and impaired reproduction and can be assumed to be around $300 per case but may be varying by farm. The risk factors, the causes and the pathogenesis are complex and only partly understood. RFM is linked to most metabolic diseases, but also to infectious disease and various individual risk factors. RFM predisposes for other disease. It is unclear what treatment options there are and whether treatment is beneficial in the first place. Prevention is mostly achieved by nutrition involving antioxidants, monensin and principles of preventing hypocalcaemia. A prediction of RFM is difficult.

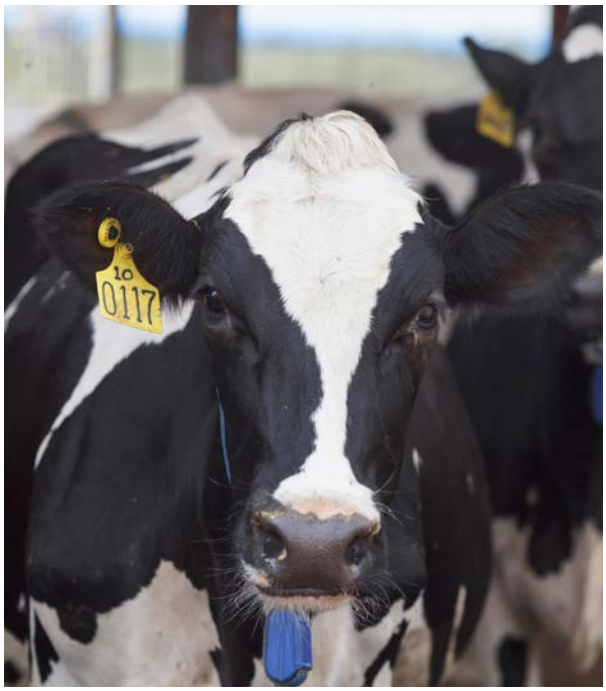
Retained Fetal Membranes in Cattle – What is the definition and how common is it?

Retained Fetal Membranes (RFM), also referred to as "Retained Placenta" (RP) describes the delay or absence of expulsion of fetal membranes (the placenta) post-partum. This phenomenon is described in most mammals and has a high significance in cattle. Usually, the placenta should be expelled within 6 hours after calving (Smith 2002; van Werven *et al*. 1992), there are however, various definitions on when fetal membranes become "retained" – The literature gives definitions between 8 hours up to 48 hours (Beagley JC *et al*. 2010). The retention is not necessarily associated with clinical symptoms such as elevated temperature, but eventually a temperature of >39.5°C may show in 80% of cases (Drillich *et al*. 2006).

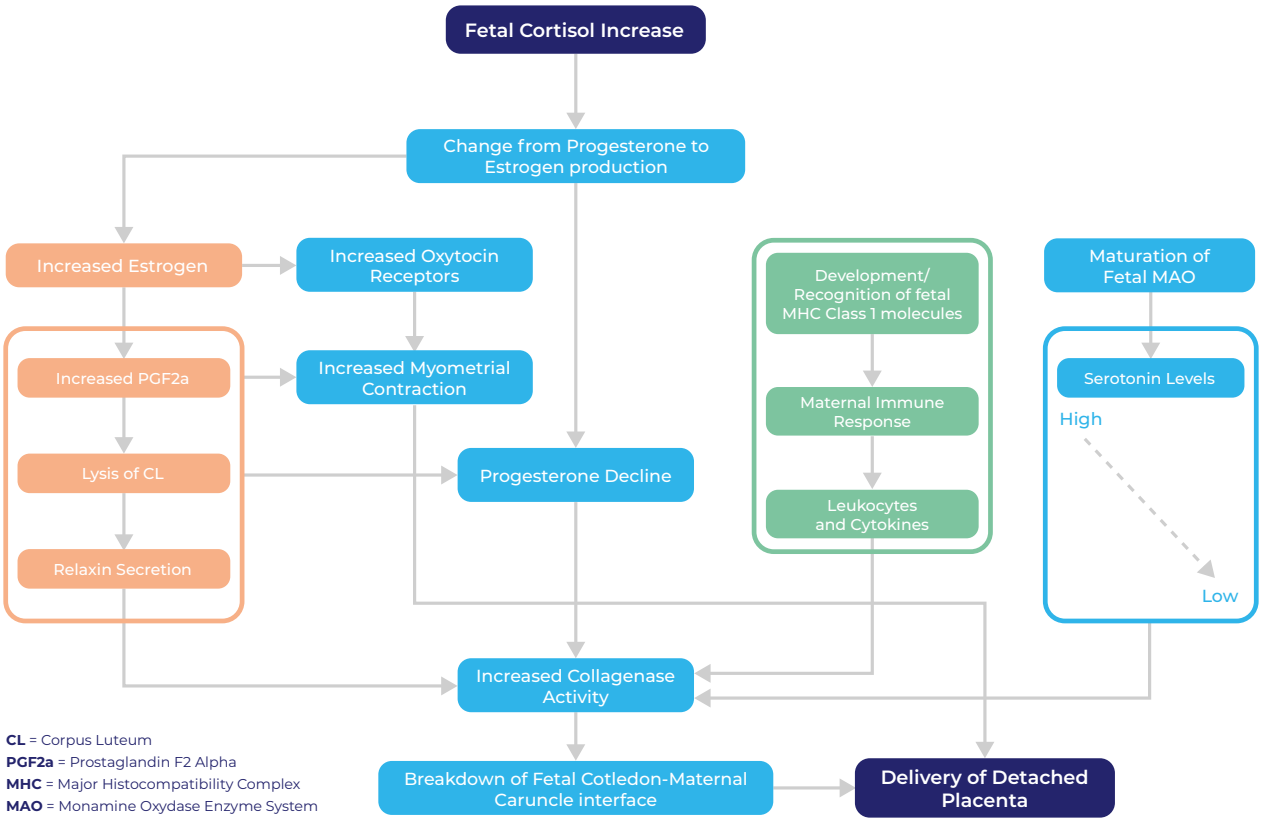
Between 1995 and 2001, a stable incidence of 7.8% was reported for RFM in the North American Animal Health Monitoring System (Goff 2006). In a 1987 retrospective analysis of 160.000 calvings from the Netherlands, an incidence of 6.6% was found, however with increasing tendency (Joosten *et al*. 1987). It seems safe to assume that there are large variations between herds and production systems, uncertainties in recording compliance and hence an incidence between 3% and 12% may be expected (Smith 2002).

Why do RFM occur?

The detachment and expulsion of the placenta is the result of a complex interaction in hormonal and immunological changes. The physiologic process may be best understood as an inflammatory process expelling the tissue that is, after all, foreign to the maternal organism and therefore triggers a rejection. This rejection has been suppressed during pregnancy. Hence, the pathogenesis of RFM certainly is multifactorial and still not completely understood (Attupuram *et al*. 2016). The development of RFM involves immunological, nutritional, hormonal and biomechanical factors.



Beagley (2010) gives an overview of the various processes associated with normal placental detachment and expulsion:



A concise overview of factors attributing to RFM is given by (Mordak *et al*. 2015):

- Prior and during calving, the maternal organism goes through a series of various hormonal and metabolic fluctuations.
- The known pathomechanisms of Negative Energy Balance (NEB), mineral imbalances (e.g., hypocalcaemia and vitamin shortages (mainly αTocopherol, leading to oxidative stress) predispose to decreased detachment and expulsion of fetal membranes.
- Before and during calving, plasma cortisol levels are rising, leading to an immunosuppression that may block the detachment process of the placenta, which is largely the result of an inflammatory process.
- Adrenalin, which is present during calving leads to hypotony or atony of the uterus, hampering the expulsion of the placenta. This effect may be increased by dystocia or other abnormalities around calving.

Of these factors, the immunological component appears to be decisive as it combines the various aspects. In this respect, RFM may be understood as visible sequel of a prolonged pregnancy-associated immunosuppression. Downregulation of the immune system is normal to preserve pregnancy, however in cases of RFM the switch towards rejection against the placenta may not happen or is delayed; in animals with RFM, chemotaxis and phagocytosis are reduced and hence the necessary detachment of the placenta does not occur (Heuwieser und Grunert 1987) (Kimura *et al*. 2002). Oxidative stress certainly is a triggering factor in this process (Kankofer 2002).

What are the consequences of RFM?

The consequences of RFM have been reviewed repeatedly. In the individual, the consequences are (Beagley JC *et al*. 2010):

- Increased time to first service after calving
- Increased number of services to conception
- Increased days open
- Decreased pregnancy rate

Moreover, RFM is linked to other disease such as

- Mastitis
- Metritis / Endometritis
- Ketosis

In a meta-analysis (Fourichon *et al*. 2000) showed that cows with RFM took on average three days longer to the first insemination, had a conception rate in first insemination that was up to 10% lower compared to cows without the condition and the days open increased by 10 days. The cost of RFM are however difficult to assess as the cost inferred by days open will vary from farm to farm and are dependant on the management system. In a detailed analysis using a Monte-Carlo-Simulation, (Liang *et al*. 2017) estimated the cost of one case of fetal membranes being $ 150 for first lactation animals, and $ 313 for multiparous cows with milk loss and increased days open being the biggest contributors. Using a deterministic computer-based spreadsheet-(Gohary und LeBlanc 2018) analysis, (Gohary und LeBlanc 2018) calculated the cost for a case of RFM being $386 on average, with $287 deriving from milk production loss, $ from reproductive losses, $ due to an increased risk for secondary disease and $1 due to culling.

Although the losses may be computed for groups of animals and herds rather animals easily, deriving mainly from costs in milk production and fertility, in the individual, this may be more difficult due to huge individual variation in production, fertility and actual severity of the disease (Laven und Peters 1996).

What are the risk factors for RFM?

Due to the complex and multifactorial nature of RFM, the risk factors are diverse and include metabolic, infectious, immunological and nutritional components.

- **Metabolism:** The correlation of RFM with hyperketonemia, excess lipid mobilization is generally recognized (Qu *et al*. 2014; van Werven *et al*. 1992; Beagley JC *et al*. 2010) (van Werven *et al*. 1992). Hyperketonemia negatively affects chemotaxis and phagocytosis of neutrophile granulocytes and hence blocks the detachment of the placenta. Same applies to hypocalcaemia (Milk Fever), which is also regularly linked to RFM (Roche 2006).
- **Infectious disease:** A number of infectious diseases, viral, bacteriological, mycotic and parasitic are reported to increase the odds for animals developing RFM. Well known examples are BVD or Q-Fever. These are listed and reviewed elsewhere (Smith 2002)
- **Immunological:** The decrease of immunocompetence around parturition has been described (Kimura *et al*. 2002)
- **Nutritional:** The role of oxidative stress in the pathogenesis of RFM is repeatedly stressed (Mordak *et al*. 2015; Qu *et al*. 2014; Goff 2006). The role of Body Condition as a risk factor is valued differently: Both high and low BCS are named as risk factors for RFM (Qu *et al*. 2014; Roche 2006) (van Werven *et al*. 1992). Also, hypocalcaemia is regularly associated with occurrence of the condition (Roche 2006; Melendez *et al*. 2006).
- **Management factors:** RFM is reported to regularly occur after induced parturition (Bolinder *et al*. 1988; Beagley JC *et al*. 2010). Traditionally the risk of RFM is thought to increase with lactation number, gestation length and birth weight of the calf (Joosten *et al*. 1987) as well as dystocia, caesarean section and twinning (Beagley JC *et al*. 2010).

In short, there hardly is a uniform description of risk factors predisposing cows for RFM. Assessing or quantifying all risk factors appears difficult, if impossible, due to limited statistic power in retrospective studies; most are not able to mirror the complexity of the condition anyway (LeBlanc 2008). This moreover makes accurate prediction using standard techniques difficult (Qu *et al*. 2014).

What to do with RFM?

The literature on treatment options regarding RFM is diverse and not equivocal. While the general consensus is that a manual removal seems to be useless if not detrimental (Beagley JC *et al*. 2010), the use of antibiotics, systemically or locally is values differently. Some studies show positive effects of antibiotic treatment (Goshen und Shpigel 2006) while others show no advantage regarding milk production or fertility (Drillich *et al*. 2006, 2006, 2006; Drillich *et al*. 2007). The injection of collagenase into the umbilical cord post-partum is reported to fasten the detachment of the placenta (Eiler und Hopkins 1993), but there is little information on the actual usage of this method. The use of hormones like PGF2a or Oxytocin to increase uterine tonus is a traditional approach, but this method does not show significant results if clinically tested (Garcia *et al*. 1992; Beagley JC *et al*. 2010). In short it must be stated that “The therapy of retained fetal membranes is a controversial subject” (Biner *et al*. 2015).

Can RFM be prevented or predicted?

The complex nature of RFM has been repeatedly stressed in this review. Prevention of RFM will be the result of a good transition management and balanced nutrition in that period, but it appears difficult to specifically aim for it. However, some nutritional strategies have been reported to reduce the incidence of RFM.

- **Monensin.** In a large study involving 2000 cows, the intraruminal administration of monensin over 95 days via a bolus was shown to reduce the incidence of RFM significantly (Melendez *et al*. 2006)
- **Selenium / α-Tocopherol.** The supplementation of transition cow diets with these antioxidants has repeatedly been connected with a significant reduction of RFM cases in dairy herds. (Goff 2006) (Allison und Laven 2000)
- **Calcium.** The prevention of milk fever, for example by feeding anionic salts, is also reducing the incidence of RFM (Roche 2006; Melendez *et al*. 2004).

The prediction of RFM using traditional clinical or paraclinical methods is difficult. Complex models using NEFA, haptoglobin, mineral status and leukocyte function may be used to quantify individual cows' risk for showing RFM (Chebel 2021; Pohl *et al*. 2015).

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