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Retention of fetal membranes in cattle a review

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Abstract
Failure in expulsion of fetal membranes within 24 hr. is known as Retained placenta or retained foetal membranes, is. In dairy cattle and buffalo it is common in occurrence after parturition in and is a major cause of financial loss to farmers. RFM results in inflammation, fever, weight loss, reduced milk production, and extended calving intervals. some common negative sequelaes of RFM are like delayed uterine involution, increased services per conception, lower pregnancy rates, metritis, ketosis, mastitis, negative effect in a future pregnancy, tetanus (present in soil). The condition RFM in dairy cattle is a serious reproductive illness. Both reproductive and productive efficiency of dairy cows is compromised, which results in a significant financial loss for the dairy industry. RFM's precise aetiology is still not well understood. Loop hole in knowledge of the mechanisms underlying cotyledon dehiscence, foetal membrane evacuation, and placental maturation. However, management may be improved, and new remedial and preventative techniques can be introduced to assist lower the occurrence of RFM and, in turn, help reducing the losses related to RFM.

Keywords: Fetal membranes, cattle, RFM

Introduction
RFM is condition which have multiple reason of occurrence although it can be treated but sometimes can lead to adverse health effects leading to negative effect on reproductive performance. Fetal membranes also known as “placenta” is a crucial organ play important role in nutrients and oxygen prenatal transfer to the foetus from the dam normally it drops shortly after delivery. Failure in expulsion of fetal membranes within 24 hr is known as Retention of fetal membranes, or retained placenta, is. After parturition. One of the most common complications is retained placenta conditions occurring in cattle, buffaloes and less common in other farm animals following parturition. In cow 8-12 hrs. (Is normal placenta expulsion time) after this it is considered as retained placenta. While in mare retention is considered if not fall within 3 hr.

Synonyms
- Retained placenta
- Retention of the after birth

following pulling of microorganisms into the uterus, retention causes a number of issues, including uterine fever, swelling, loss of weight, and a decrease in milk production, and prolonged calving intervals, which could lead to an open cow during the calving process in following year and if the infection is so aggravated than it can lead to animal death. It is major cause of economic loss to farmers.

Etiology: Inflammatory alterations, placental immaturity, hormonal imbalances, neutropenia, a lack of polymorph migration to the site of attachment, and immunological inadequacies could all contribute to the placenta's inability to detach from the endometrium. Lack of cotyledon proteolysis is yet another fetal membranes retention concept (Sharpe *et al.*, 1990) [44] and (Eiler and Hopkins, 1992) [20].

Incidence
RFM incidence in Friesian cows has been estimated to be around 3.6% from the United Kingdom and 24.9% from Egypt (Esslemont and Kossaibati, 1996) [24]. According to Gaafar *et al*. (2010) [30], Zebu cows and their crossbreeds account for 26%, 16%, and 13% of all cattle in India. During the summer following the delivery of a male foetus and higher milk production

In prior Seasons, an increase in instances is associated with increasing parity (El-Malky *et al*., 2010) [22]. Further the incidence rates of abortions, stillbirths, and twin calves increased by 25.9, 16.4, and 43.8%, respectively. (Ahmad *et al.*, 1999) [84].more commonly found in dairy cattle and buffalo than the beef cattle and buffalo. The incidence varies between 4.0 to 14.0% in Murrah buffaloes (Gupta *et al.*, 1999; Ahmed *et al.*, 2009; Khan *et al.*, 2009) [85, 87, 46]. A comparatively lower incidence (1.5%) is seen in ewes (Fthenakis *et al.*, 2000) [51] and goat (Purohit *et al.*, 2006) [88].

Sequelae and Economic Significance

The dairy industry suffers a considerable economic drain as a result of decreased milk production brought by RFM's. (Dubuc *et al.*, 2011; Kumari *et al.*, 2015) [18, 48].

increased days open, resumption of ovarian activity, delayed uterine involution, and a decrease in the pregnancy rate McDougall (2001) [54], increased culling of impacted animals Beagley *et al.* (2010) [4], increase in services per conception number Holt *et al.* (1989) [39] Reduction in the rate of conception and rise in the metritis incidence Gaafar *et al.* (2010) [30] are the significant negative consequences of RFM.

The first service time increases by 2-3 days in RFM affected cows and conception rate reduced by a factor of 4 – 10, thereby compared to normal ones calving to conception period prolong 6-12 days (Fourichon *et al.*, 2000) [28].

Morphologically there are three types of retained placentas

1. Abortion and premature birth with immature placentomes

The membranes are expelled normally when abortion occur before day 120 of gestation and beyond this period retention is likely due to immature placentomes. In these condition placentomes are lacking preparatory changes produced by high estrogens at parturition. Maturity occurs approximately 2-5 days before the end of gestation length.

2. Hyperemia

Trauma may cause chorionic villi to swell, which may prevent separation at the cotyledon caruncle junction. (Laven *et al.*, 1996) [66] And Grunert (1986) [33]. Bovine placenta detachment normaly involves cotyledon villi resembling fingers detachment from the caruncle crypts. Larger edematous villi may therefore be more difficult to separate from the crypts. In addition, due to trauma increase in mast cells activity leads to high heparin release at uterus injury site can cause.(Gross *et al*., 1985) [31] collagenases inhibited by Heparin (Au YP *et al.*, 1992) [3] as well as delay uterine involution.; as a result, these factors may contribute to RFM. (Eiler H *et al.*, 2007) [20].

3. Small portions of necrotic epithelium between the cryptal walls and the chorionic villi

On basis of severity

- **Primary retention of placenta:** The RFM that develops when the separation of cotyledons from the maternal caruncles does not happen this condition is called primary retention of placenta.
- **Secondary retention of placenta:** The RFM that develops because it is difficult to mechanically expelling already seprated foetal membranes (e.g., uterine atony), is called secondary retention of placenta.

Predisposing factors

Abortion leads to increase in incidence (especially with brucellosis or mycotic abortion),

Dystocia, twin pregnancies, Stillbirth, Hypocalcemia, extreme environmental temperature, advancing age of the cows, premature birth or induction of parturition, Placentitis, nutritional disturbances Induced parturition Shortened gestation, Nutritional deficiency such as vitamin A, vitamin E, selenium, carotin, Immunosuppression, RFM might be caused by uterine infections during gestation. Hormonal imbalances, such as low levels of oxytocin, can cause uterine inertia. The retention of foetal membranes may result from high levels of cortisol and the hormone progesterone in late gestation. Lack of activity and living in close confinement make retained placenta more likely, Fetotomy.

Etiology

- Uterine inertia
- Abortion
- Multiple births
- Still-birth, Advanced age of cow Caesarean delivery
- Dystocia
- Low calf weight and Short gestation period
- Summer calving
- Sex of calf (male)
- Hormonal imbalance
- Induced delivery (PGF2u, Dexamethasone)
- Vit. A deficiency
- Vit. E deficiency
- Excess iron
- Infection (eg. Brucella, moulds, Vibrio spp. etc.)
- Placentas

Physiology of Placental Maturation and Separation

Collapseing of blood vessels of fetal placenta and the villi, which are present on the cotyledons surface, shrink when the foetus is born. Strongly uterus contraction seen continues to for 48 hours after the expulsion of the fetus and become less vigorously thereafter, to prevent hemorrhages this contractions are necessary and also an aid in the fetal membranes expulsion. In addition to performing the above mentioned function, these peristaltic and contraction waves also lower the volume of blood flowing through the endometrium. The endometrium's blood supply is reduced, which leads to caruncular crypts dilatation or relaxation, as it is a key factor in the separation of the cotyledon villi and the caruncle crypts.

RFM is mostly caused by the foetal cotyledons' villi failing to separate from the caruncle's crypts. The caruncles change from oval shape to round and shrink in size, and the crypts enlarge as a result of the uterine wall contracting and the decreased blood supply. Additionally, the villi get smaller and shrink. The cotyledons of the developing foetus separate from the endometrial caruncles in this manner.

The retention of the foetal membranes is also a result of the deficiency in caruncle-cotyledon collagen breakdown. Collagen (adhesive factor) is typically broken down by the cotyledons' own collagenase enzyme, allowing the cotyledons and caruncles to separate.

Role of different factors in Placental Maturation and Separation

Role of Hormone

Foetal induction of cortisol activates the indicators beginning

the foetal transportation process, which will lead to initiation of the progesterone conversion into estrogen. Different enzymes derived from placenta (Flint *et al.*, 1979) [27]. The myometrium's oxytocin receptor sensitivity increases in response to rising oestrogen levels, which also causes PGF2 concentration to rise (Fuchs *et al.*, 1999) [29]. Prostaglandin synthase 2 (PTGS2) production of endometrial PGF2 increases with the decrease in progesterone levels and increase in levels of estrogen (Streyl *et al.*, 2012) [75]. With the release of PGF2, the progesterone cycle ends around the time of delivery, causing myometrial contractions (Shenavai *et al.*, 2012) [72]. The PTGS2 expression has been thought to begin from the foetal side first, followed than by the dam side, during the final stages of pregnancy (approaching calving), supporting the belief that parturition begins from foetal side (Arosh *et al.*, 2004) [2]. Expanded prostaglandin fixation thus prompts downfall of corpus luteum (CL) (Janszen *et al.*, 1993) [40]. The rising level of progesterone decline as CL lysis, relaxin hormone also increases (Musah *et al.*, 1987) [60]. Collagenases release start when relaxin levels rise and progesterone levels fall. The relaxation of the cervix, the loosening of the pelvic tendons, and the breakdown of collagen fibres are all caused by relaxin. (Engelen *et al.*, 2009) [24]. Further, A block on the myometrial withdrawal and collagenase occurs due to high level of progesterone during the pregnancy.

Movement and decrease in progesterone close to parturition time important for the removal of membranes of placental (Maj and Kenkofer 1997) [53]. In cattle during growth the Estrone-3-sulfate is the significant placental estrogen, (Hoffmann and Schuler 2002) [38], the majority of which is 17-estradiol near the gestation end. The cotyledons' trophoblastic cells create the hormones oestrogen and progesterone, which then act on the appropriate receptors in the caruncular cells. (Schuler *et al.*, 2002) [71]. This local signaling cause placentome softening, vagina, cervix, and related tissues by evolving course of action/ direction of collagen strands and favoring their intake of water (Taverne and Noakes, 2009) [24]. Thus, it is obvious that the routes assisting in the normal separation and deliver of the placenta are linked to and dependent upon one another, and they typically begin at the actual moment of foetal delivery. Additionally, serotonin is important for regulating bovine placental adhesion. High amounts of foetal and placental serotonin are used throughout pregnancy to promote placental connection by promoting proliferation of placental cell Eiler, (2001) [26], and matrix metalloproteinase (MMP) activity inhibition (Eiler and Hopkins, 1993) [22]. Before parturition, the Monoamine oxidase enzyme system matures, metabolises serotonin, and then lowers its levels. This promotes detachment of placental and parturition. (Fecteau and Eiler, 2001) [26].

Maternal Immune Responses Role

The functioning of the dam's immune system responses initiated against the foetal membranes and altered hormonal conditions utilised to assist enzymatic breakdown of foetal and maternal attachment points play a vital part in placenta detachment. An increase in leukocyte chemotaxis and action is a characteristic of routine placental excision in cattle (Kimura *et al.*, 2002) [47]. Identification of the foetal MHC-I molecule by the immunological system of the dam also assisted in parturition and separation of placenta (Davies *et al.*, 2004) [12]. As these particles are absent in the first trimester of pregnancy, but foetal trophoblast cells express them throughout the last trimester (Davies *et al.*, 2004) [12] and may play a direct role in the onset of the inflammatory response that was previously employed to break down the junctions between the maternal and foetal placenta portions (Davies *et al.*, 2004) [12]. Following ordinary parturition placental maintenance was recently connected with MHC-I similitude between dam also, it developing foetus (Benedictus *et al.*, 2012) [5]. Maternal and foetal macrophages from MHC-harmonious pregnancies discoloured significantly with antibodies against TNF vs. macrophages from inharmonious pregnancies as the pregnancy approached term (Davies *et al.*, 2004) [12]. Separated DNA, evidence of apoptosis, is seen in the exterior cell layer of blastocysts before parturition and in endometrial epithelial cells in MHC-incompatible cesarean-segment testing, but in healthy pregnancies it is not seen (Davies *et al.*, 2004) [12]. An increase in MHC-I presented patrimonial antigens along with expanding level of estrogen initiate placentae development. Increased prostaglandin levels, oxytocin production, and release all contribute to the uterine muscles' ability to contract automatically or intrinsically which is crucial for calving.

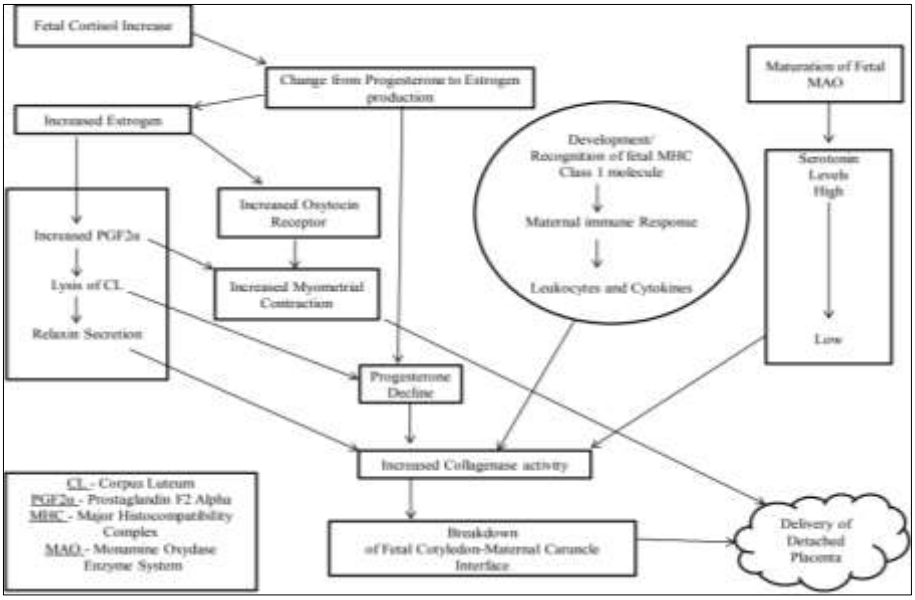

Fig 1: Physiological processes leading to fetal membrane separation in cattle

Role of Mechanical Forces

Mechanical removal of fetal layer happens via contraction in 3 stages of labour (Laven and Peters 1996) [49]. Uterine musculature contractions take Active to date, very little has contributed to placental evacuation or separation. However, it is thought that myometrial contractions at the foetal side of the placentome (cotyledonary villi) modify the pressure, generating alternate hyperemic and ischemia conditions and ultimately resulting to the detechment or release of the membranes (McNaughton and Murray 2009) [55]. After the foetus is delivered, the placenta's blood supply decreases, which causes the villi to shrink. In the course of parturition, the cotyledonary villi break down due to the burst of the umbilical cord, reducing the actual area of contact and accelerating foetal membrane dehiscence. Through contractile and involuting alterations to the uterus, placentomes are deformed in a way that makes possible the typical and effortless passage of membranes of foetal (Borel *et al.*, 2006) [8]. The present conviction is that unconstrained myometrial compression is significant for the last section of membranes, although RFM does not require main myometrial dysfunction to exist. (Grunert 1986) [33].

RFM Causes and Risk Factors

Abortion (Muller and Owens1974) [59] induction of parturition (Terblanche *et al.*, 1976) [77] shortening of gestational length (Joosten *et al.*, 1987) [41] twinning (Muller and Owens,1974) [59] dystocia (Rajala and Grohn 1998) [69], fetotomy (Wehrend *et al.*, 2002) [81], Cesarean section (Joosten *et al.*, 1987) [41], carotene, vitamin E and selenium deficiencies (Julien and Conrad 1976) [42] Bovine viral diarrhea virus like infectious agents (Niskanen *et al.*,1995) [63] Major risk factors for RFM are Brucella, Campylobacter organisms and immunosuppression (Laven and Peters 1996) [66]. Process involved behind both multi hormonal changes and biochemical brought by above indicated risk factors are not completely understood. In normal placental separation and delivery, these events are believed to be necessary, suggestive of that any type of intervention with one or more situations may result in fetal membrane retention.

Role of Immune Suppression

It is desirable for maternal immunological responses to the developing foetus for successful maintenance of pregnancy suppression. To this day Uncertainty exists regarding the role of immunosuppression in the foetal membranes retention. (Peter and Bosu 1987) [68]. during pregnancy the involvement of immunosuppressio in the immune response Suppression is necessary to prevent decline of the feto-placental unit, any lapse in this defence mechanism through disruption of the immunoprotective systems' normal shut-down process can cause RFM in animals Kimura *et al.*, (2002) [47] and Pathak *et al.*, (2015) [48] reported that leukocytes changes functioning from the normal (Neutrophils) compared to cows that did not retain the foetal membranes in terms of their motion or migration to the area of the action when a signal from the placentomes. There is proof that immune reactive acid phosphatase is present in substantial amounts in cow placentomes that have already evacuated their placentas compared to those whose placentas have been retained (Miyoshi *et al.*, 2002) [58]. Further, cytokine concentrations were different in cows that had RFM VS cows which normally delivered. RFM incidence and a clear correlation have been reported between 7 mRNA levels of IL-1B, IL-6, IL-8, and TNFα genes at the placental and uterine level Boro *et al.*, (2014) [9] cows with RFM, in peripheral blood pro-inflammatory cytokine (IL1b, IL6, IL8 and TNFα) reported to be low levels when compared to the levels similar found 2 to 3 weeks before to parturition (Kimura *et al.*, 2002,Boby *et al.*, 2013 and Boro *et al.*, 2015) [47, 6, 89]. Levels of IL-10 have been reported to significantly difference in cows affected with RFM vs. cows not affected (Boby *et al.*, 2013) [6]. protein 7b related to Ras, on the other hand, it is been found to be present in small amounts in the portion of maternal retained placentae and functions as a negative regulator of Toll-like receptor 9 signalling, preventing the cytokines production which support inflammation (through IL-6 and TNF-) in macrophages (Kankofer *et al.*, 2015) [44]. Findings are consistent with the widely held theory that retained foetal membranes may result from altered neutrophil and macrophage function.

Role of Antioxidant

RFM is worsened during pregnancy by the placenta's decreased antioxidant activity (Gupta *et al.*, 2005) [35]. wischral *et al.*, (2001) [82] found that a lower placental superoxide dismutase and plasma estrogen concentration before parturition was a common finding in dairy cows resulted in RFM. It is really thought that the placenta's compromised antioxidant ability and decreased oestrogen production are what cause placental retention, which in turn causes a reduction in PGF2 release and a gradual collection of arachidonic and linoleic acid reserves inside placental tissue. Supplementation of Vitamine E in cows used to diminish the frequency of RFM, but the advantages of nutrient E supplementation decider the amount of nutrient E that was essentially existing prior to supplementation of the same (Leblanc *et al.*, 2002) [50]. As Vitamin E and selenium Supplementation has been accounted for to further improvement in antioxidant potential, at feto-maternal interface boosts leukocyte activity and chemotaxis, aiding the natural separation and foetal membranes expulsion. (Bourne *et al.*, 2007) [10].

Role of Enzyme

RFM is largely caused by changes in enzyme activity, as can be seen from the placentomes of held versus unheld placentas, where there are varying protease activities (Eiler and Fecteau 2007) [20]. Less activity of cotyledon collagenase and type III collagen persistence are present in RFM-affected cows. In addition to this, RFM-affected cows exhibited decreased lattice metalloproteinase-9 (MMP-9) activity and lacked various forms of grid metalloproteinase-2 (MMP-2) enzyme (Maj and Kankofer 1997) [53]. MMP-2 and MMP-9 have a significant part in sepration of cotyledon-caruncle connections furthermore, consequently in discharge/division of fetal layers (Eiler and Hopkins 1992) [21]. Still now, the specific point/spot of discharge of collagenases and different proteases in the cow is secret, in spite of the fact that it is trusted that Leukocytes, cotyledon or caruncular epithelium may be the conceivable source (Eiler and Hopkins 1992) [21]. Break in the usual hormonal changes that used to happen inside the uterine climate stop epithelial cell protease discharge and further immunosuppression may think twice about protease movement. In this way, compromising protease activity lead to occurrence of RFM.

Role of Hormone

Dexamethasone administration, either with or without induction of prostaglandin work is viewed as a usual risk factor for the RFM development in dairy cattle, although the exact mechanism is unknown (Gross *et al.*, 1985) [31]. Glucocorticoids can prevent secretion of collagenase, which is responsible for breaking down the collagen bonds between foetal and maternal taps of the placenta (Guerin *et al.*, 2004) [34]. Additionally, dexamethasone uses to retrict cotyledonary cell PGF2 α combination (Izhar *et al.*, 1992) [90]. So that the chances of RFM are diminished.

With the utilization of PGF2 α and dexamethasone, yet this combination doesn't counter its complete event (Gross *et al.*, 1986) [32]. When using relaxin together with dexamethasone or cloprostenol risk of RFM is reduced (Musah *et al.*, 1987) [60], perhaps on the grounds that relaxin support collagenase subsequently slow down dexamethasone activity.

Calcium Role

RFM and diminished circling calcium level are accepted to be related with each other (Curtis *et al.*, 1983) [11]. Melendez *et al*. (2004) [56] has detailed that RFM impacted dairy cows particularly had calcium levels lower in plasma contrasted with those that had not encountered RFM after they were taken care of anionic eating regimens. For action of collagenase there is requirement of calcium, yet in RFM impacted cows the level of blood calcium are up to check from where it can't forestall the collagenase action (Gross *et al.*,1985) [31]. Melendez *et al.*, (2003) [57] has concluded that anionic eating regimens supplementation with in relation to energy and oral calcium demonstrated no more gainful in diminishing RFM and related affected. Hypocalcemia inclines cows to dystocia Au *et al.*, (1992) [3] what's more, loss of uterine tone, subsequently meddling with final step of placental division/relaxing, yet till now the immediate role which calcium used to play in placental detachment isn't completely known

Role of Calving Related Problem

Risk factors (dystocia, fetotomy, and cesarean segment) for RFM use to force injury to the uterus. Edema of chorionic villi uses to happen because of injury that in turn disables detachment of cotyledon-caruncle interface (Laven what's more and Peters 1996) [66]. The caruncle is where the finger-like cotyledonary villi used to separate during the typical separation process in the bovine placenta. However, large/oversized finger-like processes (villi) are difficult to differentiate from the maternal crypts. At the site of the lesion caused by the uterine trauma, mast cells generate heparin (Gross *et al.*, 1985) [31]. Heparin in turn represses collagenases (Au *et al.*, 1992), and furthermore defers involution of uterus, in this way contribute to occurrence of RFM (Eiler and Fecteau 2007) [20]. (Dystocia) Difficult birth and affront to uterine muscle structure additionally cause reduction in removal/contracting force of same, this can impair membrane function partition/ejection and lead to auxiliary maintenance

Nonsteroidal Anti-Inflammatory Drugs (NSAIDS) Role

NSAIDS for example flunixin meglumine given to cows after cesarean section, found to have higher occurrence of RFM thought about to cows which are non-treated which is accepted to be interceded by method of decrease in prostaglandin union (Waelchli *et al.*,1999) [80].

Prevention and Treatment Strategies

Goals of treatment is to maintenance of fetal layers is to help early separation and dehiscence of the layers to lessen the odds of metritis occurrence, increment chances of cyclicity early resumption, decline related milk misfortunes, diminish reproductive shortcoming, and reduction costs brought about due to veterinarian visits

Managemental Aspect

Because non-infectious reasons of placental retention are multifactorial and difficult to diagnose, additional attention has to be directed to preventative rather than therapeutic approaches plans. The genetic component should be taken into account while choosing animals so that the likelihood of developing RFM is as low as possible (Ahmed and Zaabal, 2009) [87]. To prevent dystocia, breed of suitable birth weight bulls must be selected (Skidmore and Loskutoff, 1999) [73].

Nutrition

For decreasing possibilities of fetal layer maintenance supplementation with nutrients and mineral blend during prepartum period is viewed as a prophylactic advance. Gupta *et al.*, (2005) [35] have observed that supplementation before 21 days of parturition with cancer prevention agents, for example, 1100 IU of nutrient E (DL - tocopherol acetic acid derivation) and single intramuscular injection with Se 30 mg (sodium selenite) diminishes rate of RFM in cows.

Clinical signs

- On bases of degree of infection:
- Noninfectious or low-grade infection:
- Placenta hanging out.
- No foetid smell from the placenta.
- Normal appetite.
- Normal pulse and temperature.
- Milk yield normal.
- Placenta colour is normal, moist and glistening.
- Severe infection and/or prolonged duration:
- Anorexia
- High fever
- High pulse rate
- Reduced milk yield
- Straining
- Foetid smell from placenta
- Discolored and dry placenta

Manual Removal

Procedure of placenta manual removal

Give anesthesia epiduraly (5-7 ml lignocaine).

Using right hand hanging placenta should be grasped and twist like a rope so that the placenta can be more easily handled

Insert the left hand inside the uterus while it's lubricated. The placenta and uterus should be separated by the hand.

Cotyledon and its caruncle should be Individualy Grasped between the thumb and fingers and the two structures (cotyledon and caruncle) it should be gently detached by rolling, pushing and squeezing motion, by using the other hand (right hand) aid to traction is done.

The cotyledons from the caruncles should be Remove or separate the cervical area the closest come first, followed by the non-gravid horn and finally the gravid horn. The hanging placenta should be kept under strain during this procedure.

The ovarian end or cranial end of the gravid horn may occasionally be out of reach from the hand, especially in large and exotic breeds of cow or when the placenta is removed earlier, however, in rare occasions, traction on the placenta brings the apex of the horn closer, allowing for the removal of cotyledons from this area.

Since they serve as infection foci, it is highly desired to eliminate all of the foetal membranes and avoid leaving any behind in the uterus.

Tying a weight on the placenta a layman's practices is not suggested as the weight will causes the cow to strain which will causes incomplete breaking and premature sepration of placenta, leaving some part still inside the uterus. Uterine horn invagination also uterus prolapse may occur due to tying of this weight.

If cow is suffering from fever, manual removal of the RFM is not advised since uterine injury raises the risk of septicemia and perimetritis.

Placenta removal physically is still usually practiced technique with no gainful impact on proliferation or milk yield (Drillich *et al.,* 2006) [17]. No advantageous impacts on regenerative execution were accounted for cows when were exposed to manual expulsion and foundational anti-microbial treatment when analyzed without treatment (Drillich *et al.*, 2007) [16]. The result of approaches to these treatment is that intrauterine therapy results in a significant loss in terms of cost, additional time for veterinarian treatments, and the usage of antibiotics.

Further, per-vaginal evacuation of fetal layers used to affect regenerative viability of creature as it expands the odds of auxiliary disease (Bolinder *et al.,* 1988) [7]. Affirmation acquired from present writing abstain one from managing fetal membranes physically (Peters and Laven 1996) [66]. Positively, manual evacuation of placenta, more injury to endometrium in this case, also phagocytic action is diminished (Vandeplassche *et al.*, 1982) [79] also, which thusly support bacterial intrusion and contamination (Peters and Laven 1996) [66]. With execution of absolute attention to detail still placenta complete evacuation is extremely challenging, while with expulsion of dead/corrupted segments bacterial contamination can be set up (Paisley *et al.,* 1986) [65] or post pregnancy metritis can arrangement easily

Antiseptic

It has been demonstrated that chlorhexidine and diluted iodine can be used to treat and prevent RFM. Generally speaking, their efficacy has yet to be demonstrated. Such mixes, particularly iodine solutions, should be used with extreme caution since they have been shown to be quite upsetting to the endometrium.

Antimicrobial

Conflicting results have been reported, with the antimicrobials therapy usage for the treatment of RFM (Peters and Laven 1996) [66]. The goal of using antimicrobials in RFM affected dairy cows is to decrease or free animals from metritis and its negative outcome on animal fertility

Intra Uterine Infusion

Antimicrobial intrauterine infusion or boluses use have no significant effects on reducing the metritis risk or enhancing fertility subsequent (Peters and Laven 1996) [66]. Cows that were having rectal temperature raised, when treated to intrauterine anti-microbial treatment did not shown anykind of improvement in postpartum fever. The impact of chlortetracycline intra uterine in the RFM and clinical metritis treatment as far as useful and regenerative execution. However, the desired effects of treatment were only observed in animals with clinical metritis, and in terms of milk production there was no difference between treated and untreated animals seen or conceptual execution. These findings highlight the fact that intrauterine anti-microbials can be effective in metritis managment, but there is less chances that their use will hasten membrane discharge or separation and reduce the likelihood of metritis in cows carrying RFM. Although intrauterine anti-microbials are intended to inhibit uterine bacterial growth, they also stop the necrotizing processes that really support the separation or dehiscence of the foetal layer. (Roberts 1986) [70] Treatment with Intrauterine antibiotic medications in cows repress grid metalloproteinase (Kaitu'u *et al.,* 2005) [43], and typical placental dehiscence/detachment processes is thus prevented.

Numerous preparations for intrauterine use are available in the market. These are Cleanex, Povidone iodine bolus, Furea, Lixen IU, Steclin, C-/lox-TZ etc. Any of the above should be continued in suspension form for 3 to 5 days i.e., with help of a catheter prepared solution is infused in the uterus.

Ecbolic

Prostaglandins and oxytocin till date are as often as possible utilized chemicals for RFM treatment. Cases of RFM related to uterine atony are serenely treated with these hormones. As intrinsic contractions of uterus is support by them that assume a significant part in separation process. Hormone oxytocin is an intense utero dynamic chemical of decision in the quick post pregnancy dairy creature. Day by day treatment with dose of 20 IU of oxytocin for three to multiple times have been utilized for held fetal membrane (Youngquist and Threlfall 2007) [20]. Stocker and Waelchli (1993) [74] have shown that following a caesarean section, over 80% of cows receiving PGF2 treatment learned how to completely pass their foetal membranes within 12 hours as opposed to untreated cows. (58.5%)

Indigenous preparations

For the removal of a retained placenta, for instance, there are many indigenous remedies available on the market. Uterotone liquid, Involon, Uterifit etc. Any of the following should be utilised for the manual removal of the placenta when the usual expulsion fails following this treatment, as well as for the expulsion of the retained placenta. Dosage: 100 ml every day for three days after a loading dosage of 200 ml on the first day. The dose should be doubled for animals having weight above 400 kg. After removing placenta manualy, one of these preparations is indicated because these help in cleaning of uterus by increasing the tone of uterus, i.e. helps in removal of placental remnants, pus and debris of tissue. These preparations also helps in uterine horns involution timely.

Collagenase Treatment

To treat RFM a new approach is the collagenase injection into the umbilical arteries.

Compare to traditional treatments it is a superior approach may be because it specifically directed at solving problem of the lack of proteolysis of cotyledon.

Since Clostridium histolyticum's bacterial collagenase can break down a variety of collagen forms, it is utilised.

Technique

Firstly By placing one hand within the vagina, search the umbilical cord in RFM (identified by two firm arteries and two pencil-sized veins that separate from the fingers when touched).

After locating the cord, introduce second hand also into the vagina and retracte the cord by using alternating hands in the vagina.

Once the umbilical cord is in the vulva, using Kelly's forceps the arteries are clamped.

Inject collagenase solution (2lakh units + 40 mg. calcium chloride + 40 mg sodium bicarbonate + 1 litre saline) rapidly.

If antibiotic is required, oxytetracycline (100 mg. total dose) can be added to 1 litre of collagenase solution.

Comments

In 85% of affected cows Collagenase treatment is effective within 36 hours of tretment.

There are no side-effect of treatment as it is safe.

It is thought that the collagenase treatment technique is more effective than the traditional therapies since it is specifically undertaken to assist or favour proteolysis of cotyledon from its associated maternal caruncle (Eiler and Hopkins 1993) [22]. If RFM is not treated, it undergo autolysis but there are extremely limited possibilities that it will be expelled within a week or longer after calving (Paisley *et al.*, 1986) [65]. In a number of species Collagenase therapy application has found useful for retained fetal membranes treatment (Haffner 1998) [37]. Early foetal membrane release is a result of collagenase therapy (Eiler and Hopkins 1993) [22]. no evidence of production losses Till date has been reported in collagenase treated cases of RFM vs. untreated cows

Ozone Therapy

Other than the previously suggested customary methodologies, recently new treatments staying away from utilization of anti-toxins are currently in practice. Ozone therapy is one of the methods that have recently been practised. Ozone has been shown to be a reliable sanitizer that also works to kill pathogenic parasites and their spores also (Travagli *et al.*, 2009) [78]. Ohtsuka *et al.*, (2006) [64] found that the ozone actuates lymphocytes or on the other hand monocytes, ther by upholds discharge of cytokines such as (IFN) α, β, γ, cancer putrefaction factor (TNF-α), interleukins (IL) 1, 2, 4, 6, 8 and 10, granulopoietins (GM-CSF)

Furthermore, changing development factor β (TGF β) from these cell types. Ozone helps in tissue recovery, favors granulation and epithelialization and furthermore further develops the neighborhood uterine digestion. Treatment with ozone, bacterial resistance chances are almost nil, milk and meat withdrawal periods, as they used to be the main burdens with conventional anti-infection medicines (Drillich *et al.*, 2001) [15]. Regenerative performance is impacted in cows with RFM the has been assessed by Djuicer *et al.* (2012) [91] following the use of two arrangements of ozone gas. In comparison to the control group, it has been observed that the deliberate holding up period, the calving to origination period, the overall pregnancy rate, and administrations per origination were refined applications of gas arrangements into the uterine body.

Immunomodulators

mares which are infertile chronically, having been found that the E Coli lipopolysaccharide alongside with oxytocin produces the results which were desired, as it decreases the incident of uterine infection and inflammation, ultimately aids in enhancing their reproductive efficiency. Leukocytes and endometrial epithelial cells have been observed to respond strongly to LPS, which promotes the release of a variety of inflammatory mediators and immune-regulatory cytokines. Nadja *et al.* (2007) [62] have found that infusion of of intrauterine E coli LPS in mares there is no adverse effect, resulting in supporting its use in RFM expulsion cases. Within six hours of infusion, cattle and mares pulls out or attract polymorphonucleocytes to the uterus. When recombinant human interleukin 8 (rhIL-8) intra uterine infusion is done (Zerbe *et al.*, 2003) [84].

Miscellaneous

The veterinary practices practiced by many societies have left a remarkable effect towards the veterinary treatment Lin *et al.* (2003) [52], being economic efficiency and good effects (Mwale *et al.*, 2005) [61]. There is a widespread notion between farmers that the dairy animal experienceing difficulty in birth and weakness at the time of advanced pregnancy could be the responsible factor behind the occurrence of RFM. The mixture of oil and milk is used because it act as source of energy in such cases. However, camel milk is preferred as it have high content of mineral s. It is believed uterine contraction are supported by the common salt, so because of this reason farmers for smooth expulsion of fetal membranes use to massage it on animal's back (Dilshad *et al.*, 2008) [13]. Further, turmeric powder and Jaggery mixed with water or Garlic also provided to animals with the idea that it is energising and has a cleaning effect and thereby helping in expulsion of fetal membrane.

RFM Common Negative Sequelae

- Delayed uterine involution
- Metritis
- Ketosis
- Mastitis
- Abortion in a subsequent pregnancy
- Increased services per conception
- Decreased pregnancy rates
- Tetanus (present in soil)

Conclusion

RFM is one of the important dairy animal reproductive problem. Being responsible for high financial loss occurring to the dairy industry by compromises both the reproductive and productive efficiency of dairy animals. The etiology exactly behind RFM till date is not fully understood. Improper understanding of the maturation of placenta mechanism, cotyledon dehiscence and expulsion fetal membranes are still there. But, management may be improved, and the new remedies and preventative techniques can be introduced to assist lower the occurrence of RFM and, in turn, help mitigate the losses connected to RFM.

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