【Review】



# Reproductive Disorders in Cattle due to Nutritional Status

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## Abstract

This review presents a brief overview on nutrition and incidences of reproductive problems in cattle. Overfeeding and underfeeding are equally detrimental to normal reproductive function. The exact mechanism of nutrition on reproduction is still not clear, but it is clear that the primary target area for sensing and reacting to nutritional status is the hypothalamus. Nutrition or perhaps more specifically certain food nutrients can influence the hormonal status of animals at several levels. Generally, energy and protein are the major nutritional factors which affect reproductive process. Inadequate amount of energy develops sexual maturity in heifer cows with a low body condition score at parturition which have poor reproductive performance, possibly due to delay in onset of cyclicity. Cows overconditioned at calving will exhibit decreased appetite and develop severe negative energy balance which causes a linear decrease in the maximum diameter of successive dominant follicle, eventually resulting in anoestrus due to suppressed luteinizing hormone pulse frequency in the final oestrus cycle before anovulation. Dietary increase in protein intake can increase milk production, but can reduce fertility. It is due to the alterations in the oviduct environment or deleterious changes in the follicle. Besides these, deficiency of minerals and vitamins are also equally important from the viewpoint of infertility. However, the specific action of vitamins and minerals in reproduction needs further study. A multitude factors must be considered to understand the complex coordination of the nutrition-reproduction interface.

**Key Words: energy, hypothalamus, minerals, protein**

## 1. Introduction

The relationship between nutrition and reproduction is a topic of increasing importance among dairy producers, veterinarians, feed dealers and animal nutrition experts. It is the most important factor that affects the financial viability of cow-calf enterprises. Nutrition plays a vital role in the reproductive performances of cows as it influences fertility and may occur at several stages of the reproductive cycle, and also can affect the reproductive axis in most of the points. It gives a crucial influence to the development of postpartum reproductive function in cattle. Livestock industry and animal researchers have long been recognized the importance of proper nutrition for livestock to achieve reproductive success.

Good reproductive performance positively affects a cow's active herd life and plays an important role in dairy herd economies. Many scientists have studied about the influence of nutrition on cattle fertility. Differences in nutrition probably account for most variation in reproductive performance between herds and among animals within the herds (Wiltbank *et al*., 1964; McDowell 1972; Holness *et al*., 1978).

Over or underfeeding are equally detrimental to normal reproductive function. Underfeeding reduces milk yield, which in turn reduces the growth of calf. This reduces calf weaning weight and delays puberty, and affects in the potential life time productivity of the female calf. Therefore, fertility is a very complex process and the final outcome is the result of a close and well orchestrated interaction between hypothalamus–pituitary–ovary –uterus. The complexicity of this process indicates that any factors which interfere with the functioning of one or more of these organs involved will also influence the overall fertility outcome (Carruthers *et al*., 1978).

The effects of poor nutrition differ depending on whether the main deficiency is in energy, protein, vitamins, minerals or trace elements. Protein and energy are the nutrient components needed in the largest quantities, and directly affect body condition scores (BCS) and normal reproductive performance (Prye *et al*., 2001). Today, many people implicate deficiencies of various minerals, inadequate vitamin intake, and energy-protein imbalances as the major causes of cow infertility and poor herd performance.

There is a strong link between nutrition and fertility, where nutrient partitioning to the mammary gland in early-lactation, when dry matter intake (DMI) is reduced, resulting in negative energy balance (NEB) and many associated disorders. In the last 20 years, the advancement in genetic improvement and better management practices have led to a decline in reproductive efficiency, especially infertility, resulting in a major economic loss to the industry. Butler and Smith (1989) have shown deleterious impact of NEB on postpartum fertility. Following parturition, DMI needs to increase 4 to 6 folds in order to meet high nutrient demands for milk production (Beever *et al*., 2001). However, in high yielding cows, after post calving, cow is not able to increase DMI as fast as the increase in nutrient demands required for lactation. Therefore, the cow mobilizes body reserve of fat and protein to cope with this demand. The reduced fertility, observed in modern high yielding dairy cows, is most likely due to alterations in several consecutive steps in the reproductive process.

Vitamins and minerals also play a significant role in fertility by maintaining membrane integrity, and are involved in hormone production and maintenance of strong immune system. Of particular importance are vitamins A, D and E, macro minerals such as calcium (Ca), magnesium (Mg) and phosphorus (P), and micro minerals such as copper (Cu), selenium (Se) and zinc (Zn).

Poor nutrition, especially inadequate energy intake, can lead to extended postpartum anoestrus, causing excessive body weight loss and reduction in expression of estrus. It is becoming increasingly clear that a good reproductive management is dependent on proper attention to the optimum nutrition of the cow, whose nutrient requirements vary depending on physiological state and the specific nutrient demands to prevent metabolic disorders in the peri-parturient period (Overton and Waldron, 2004; Boland *et al*., 2001).

The underlying theme of this paper is that nutritional status is the key driver of low reproductive efficiency in cattle.

## 2. Effect of nutrition on endocrine system

The primary target area for sensing and reacting to nutritional status is the hypothalamus (Moss *et al.*, 1985). The body is regulated by two basic systems, nervous and endocrine. The endocrine or hormonal system, in general, is specifically concerned with the control of metabolic functions, rates of chemical reactions in cells, transport through cell membranes, and other functions such as growth and secretion. All of these are key components of the total lactation complex.

Hormones are chemical components comprised of steroids, peptides, proteins, and glycoprotein secreted into body fluids at one site with their actions on target tissues and organs at adjacent or other sites within the body. The tissue or organ response to the hormone is influenced by the number of receptors present on the cell membrane or within the cell and by the amount of hormone that is present. The amount of hormone presented will be under the influence of blood flow and concentration. Nutrition or perhaps more specifically certain food nutrients can influence the hormonal status of the animal at several levels.

Inadequate intake of nutrients or inadequate body reserves, needed to meet production requirements, after calving, results in suppressed reproductive performance in cattle. Pituitary and ovarian responses to endogenous or exogenous hypothalamic stimuli appear to be related to postpartum stage as well as to the severity and duration of nutrient deprivation. (Harms *et al.*, 1974)

Potential sites of action of nutrition on ovarian function include systemic effects at: (i) the hypothalamic level via gonadotrophin releasing hormone (GnRH) synthesis and release; (ii) the anterior pituitary through control of synthesis and release of follicle stimulating hormone (FSH), luteinizing hormone (LH) and growth hormone (GH); and (iii) at the ovarian level through regulation of follicle growth and steroid synthesis as shown in **Fig 1.**

Many studies in both sheep (Moenter *et al.*, 1991; Skinner *et al.*, 1995; Skinner *et al.*, 1997) and cattle (Gazal *et al.*, 1998) have established that LH is released episodically from the anterior pituitary in response to pulsatile release of GnRH from the hypothalamus. Therefore, the absence of a LH and FSH surge could be mediated at either the hypothalamus or the anterior pituitary. During spontaneous luteolysis, as progesterone concentrations decline, LH pulse frequency increases (Bergfeld *et al.*, 1996) in response to increased pulses of GnRH (Gazal *et al.*, 1998). This increase in LH pulse frequency stimulates follicular androgen production (Hansel and Convey, 1983) and hence increased oestradiol secretion from the dominant follicle. The exact mechanism whereby increasing oestradiol concentrations stimulate a gonadotrophin surge has not been fully established, but it is believed to act on specific neuronal pathways impinging on GnRH neurons within the hypothalamus, leading to an increase in the secretion of GnRH (Caraty *et al.*, 1995). Some evidence suggests that the pituitary sensitivity to GnRH pulses is decreased during under-nutrition. Tatman *et al.* (1990) found that the pituitary content of LH was lower in thin ewes while Kile *et al.* (1991) noted that under-nutrition suppressed pituitary synthesis of LH as the concentration of mRNA for both ά and β subunits of LH were less in nutritionally restricted ovariectomised ewes. However, pulsatile administration of GnRH was capable of restoring LH synthesis and secretion.

Similarly, cows fed restricted diets released more LH in response to exogenous GnRH than cows fed moderate or high diets (Rasby *et al.*, 1991) and had increased concentrations of GnRH in the stalk median eminence of the hypothalamus (Rasby *et al.*, 1992). This suggested that the greater sequestration of LH in the anterior pituitary gland and decreased LH secretion in nutritionally restricted animals is due to reduced GnRH release. Therefore, it appears that the nutritionally-induced suppression of LH may be at least in part modulated by factors affecting the GnRH pulse generator and the pituitary response to GnRH, but the mechanism responsible remain to be elucidated.

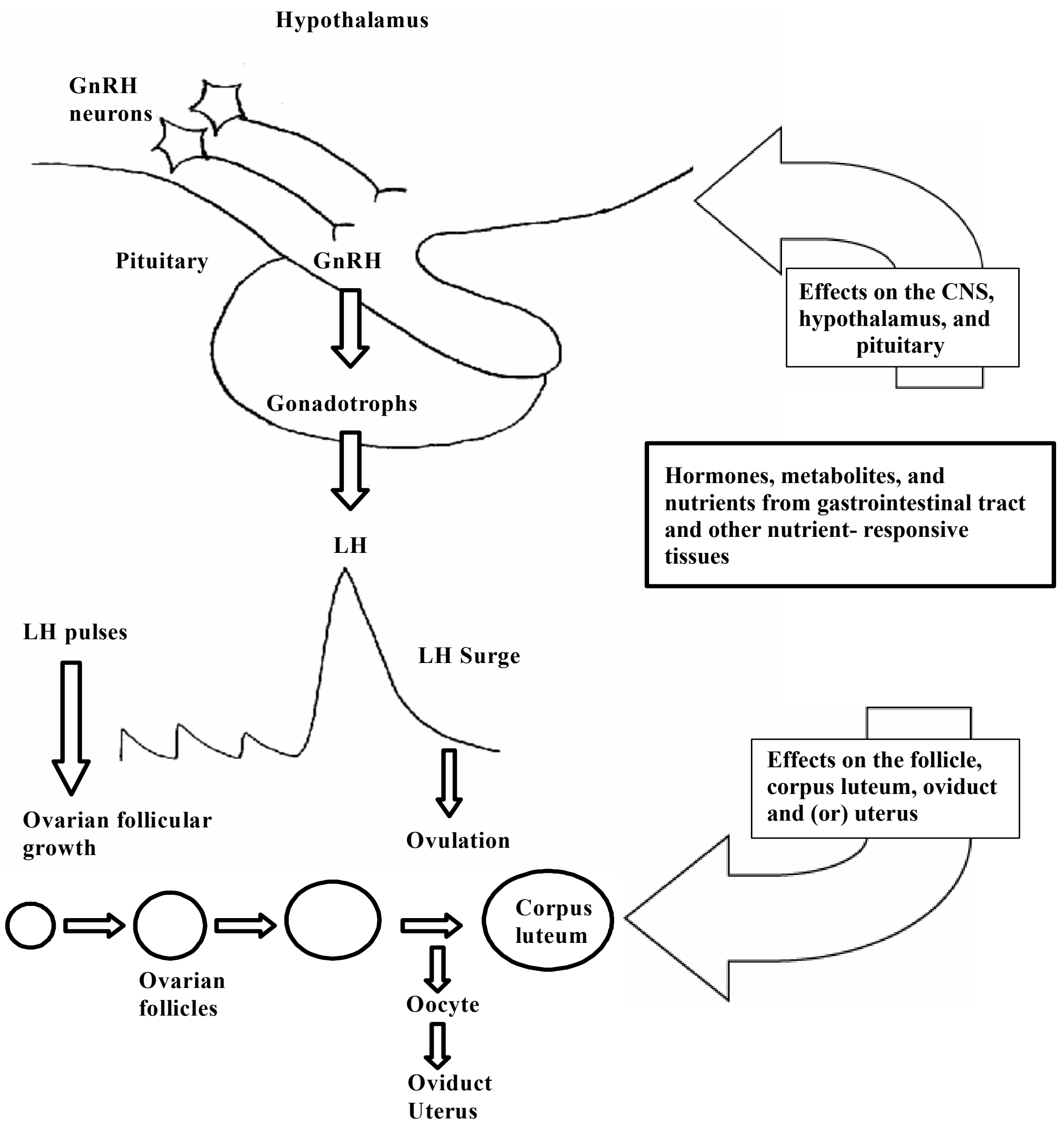


**Figure 1:** Conceptual model for the mechanisms through which nutrition affects reproduction in postpartum cows. Hormones, metabolites, and nutrients from the gastrointestinal tract and nutrient-responsive tissues affect GnRH and LH secretion through their actions on the central nervous system (CNS) and hypothalamus. These same hormones and metabolites may have direct effects on ovarian function (both follicles and corpora lutea) as well as the oocyte, oviduct, and uterus. The combined of each axis determine postpartum fertility.

Ovulation of a dominant follicle during early lactation is dependent on the re-establishment of pulsatile LH secretion conducive to preovulatory follicular growth and estradiol production (Butler, 2000). Low energy availability during NEB not only suppresses pulsatile LH secretion, but also reduces ovarian responsiveness to LH stimulation (Butler, 2000). Mackey *et al*. (1999) reported that in the case of acute nutritional deprivation, failure of ovulation was always associated with the absence of pre–ovulatory LH and FSH surges though not necessarily associated with the absence of a pro-oestrus increase oestradiol. Poor feeding during postpartum reduces luteal function and responsiveness of the ovaries to luteinising hormone (Gombe and Hansel, 1973; Martinez *et al*., 1984; Rutter and Randel, 1984; Whisnant *et al*., 1985). A decrease in the concentrations of LH and suppression in the frequency of LH pulses had been reported previously in the nutritionally induced anoestrous beef cows (Richards *et al*., 1989), heifers (Imakawa *et al*., 1986) and gilts (Armstrong and Britt, 1987), and occur as a result of reduced GnRH secretion from the hypothalamus. Evidence suggests that the pituitary sensitivity to GnRH pulses is decreased during under-nutrition. Low progesterone production during the early embryonic period has furthermore been suggested as a reason for lowered conception rates related to NEB. Adult ewes maintained on low planes of nutrition exhibited reduced ovulation rates (Haresign, 1981) a response attributed to reduced ovarian follicular development (McNeilly *et al*., 1987) rather than to an alteration of the preovulatory surge of LH. Effects on follicular development could result from disruption of pulsatile LH release.

Murphy *et al*. (1991) determined the effect of different levels of dietary intake on the pattern of follicular growth and luteal function during the oestrus cycle. Their study involved the use of beef heifers fed 0.7, 1.1 and 1.8 % of body weight as dry matter per day for 10 weeks to study the effects of dietary intake. During an oestrous cycle, commencing approximately 5 weeks after diet allocation, the maximum diameter and persistence of the dominant follicle was decreased in the restricted heifers though these heifers continued to ovulate. Similar observations have been found in subsequent studies using heifers. Under-nutrition is associated with elevated growth hormone, reduced IGF-1, an uncoupling of the link between growth hormone and insulin–like growth factor–I (IGF-I) and failure of the dominant ovarian follicle to produce enough oestradiol to generate the preovulatory LH surge. Protracted intervals to first oestrus are also associated with delays in the recovery of leptin concentrations after calving (Kadokawa *et al*., 2000) and low concentrations of leptin have been observed in cows with abnormal post-partum reproductive cycles (Mann and Blache, 2002).

## 3. Effect of energy status on fertility

Energy status is generally considered to be the major nutritional factor that influences reproductive processes, with prolonged low energy intake impairing fertility. In cattle, a strong correlation between NEB in early lactation and the resumption of ovulation postpartum is evident (Canfield *et al*., 1990). While ovulation may not occur in animals on low energy dietary intakes, follicle growth and atresia will occur. Cows fed a high energy diet after calving conceives sooner than those with a lower energy intake (Wiltbank *et al*., 1962, 1964; Dunn *et al*., 1969). Over the last several decades, large increases in milk production capability among dairy cows have been associated with declining fertility. Pregnancy rate to first service in Holstein cows have declined over the past 30 years in the U.S., Japan and Europe (Diskin *et al*., 1999). This decline has been partly attributed to severe NEB in the early postpartum period, especially in high genetic merit cows where the feed requirement for milk production is greater than the DMI capacity of the cow (Butler, 2000).

One way of viewing the relationship between nutrition and reproduction is through energy balance. When the animals' net nutrient requirement is more than the net nutrient intake, the animals will use their energy stores (glycogen, triglycerides and protein) to meet the deficit. When an animal is in this state, it is in "NEB". Shortly after parturition the increase in energy supply by feed intake is delayed compared to the increase required for milk production and a NEB develops. This NEB is characterized by a length of 6–12 weeks with a nadir usually occurring within 0–3 weeks (Jorritsma *et al*., 2003), and its magnitude varies from 0 to 25 mega joule of net energy for lactation per day (Tamminga *et al*., 1997), equivalent to the production of 0–8 kg of milk. Chronic NEB causes a linear decrease in the maximum diameter of successive dominant follicle, eventually resulting in anoestrus due to suppressed LH pulse frequency in the final oestrus cycle before anovulation. Feeding supplemental fat to beef cows during late gestation has been evaluated as a method to alleviate the negative effects of prepartum nutritional inadequacy on reproductive performance (Staples *et al*., 1998).

It is well known that cows overconditioned at calving will exhibit decreased appetite and develop more severe NEB than cows of moderate conditioning (Garnsworthy and Topps, 1982). As a result, overconditioned cows undergo increased mobilization of body fat and accumulate more triglycerols in the liver (Rukkwamsuk *et al*., 1999) that are associated with a longer interval to first ovulation and reduced fertility (Butler and Smith, 1989; Rukkwamsuk *et al*., 1999). Alterations in concentrations of growth hormone, insulin, IGF–I, glucose, and non-esterified fatty acids (NEFA) in blood are indicative of energy availability and may provide short or long term signals that mediate the effects of nutrition on LH secretion.

Dufour (1975) reported that the effects of undernutrition (energy, protein) on growing heifer resulted in increased age at puberty, subnormal conception rates, and underdeveloped udders whereas overfeeding resulted in weak oestrus symptoms, reduced conception rates, high embryonic mortality, decreased mammary gland development, and decreased milk production (Gardner *et al*., 1977).

Inadequate amount of energy delays sexual maturity in heifers (Graves and McLean, 2003). It is also reported that if energy deficient rations are fed to heifers that have begun to have normal oestrus cycles, they may stop cycling (McDonald *et al*., 1988).

Joubert (1954) indicated that level of feeding after calving has a greater effect on subsequent pregnancy than level of feeding before calving. The negative effect of an insufficient energy provision before calving will be enhanced by an energy deficiency after following parturition. It may be probably due to the liver damage which occurs in this case, and also there is an impact on fertility (Reid *et al*., 1979). The importance of energy after parturition is well known. In the first two to three weeks of lactation, energy from any source is important for the onset of ovarian activity (Butler *et al*., 1981; Terqui *et al*., 1982; Villa-Godoy *et al*., 1988) and, related to this, for uterine involution. Energy deficiency leads to acyclic, silent heat, delayed ovulations and follicular cysts. Significant correlations exist between fertility and weight loss or body condition, as indicators of NEB in the first weeks after calving and also embryonic mortality in cows with energy deficiency (Oxenreider and Wagner, 1971; Godfrey *et al.,* 1982; Rutter and Randel, 1984). The effects of energy intake on reproduction follow the pathway summarized in **Fig 2.**

Cows with greater NEB have lower peripheral concentrations of IGF-I and LH, which act synergistically to promote ovarian follicular development (Villa–Godoy *et al*., 1988). The NEB adversely affects the number and size of large ovarian follicles (Lucy *et al*., 1991; Beam and Butler, 1998), interferes with ovulation (Niekerk, 1982), and also lowers plasma progesterone concentrations (Lucky *et al*., 2000; Spicer *et al*., 1990). The combined effect of a reduction in both LH and IGF-I may compromise ovarian follicular growth and development (Lucky, 2000), which may lead to an increase incidence of inactive ovaries, ovarian cysts and non-functional corpora lutea in the postpartum cows, resulting in a prolonged interval to first ovulation after calving (Shrestha *et al*., 2004). A severe NEB is a primary cause of a delayed resumption of normal oestrous cyclicity in high-yielding dairy cows and a major limiting factor is glucose supply (Lucky, 2003). The role of nutrition for improved reproduction can be regarded as one which maximizes the production of glucose precursors; in other words, the production of propionate and gluconeogenic amino acids. There is also the need however to ensure a rumen fermentation pattern that will provide sufficient acetate for milk fat synthesis. An example of the beneficial effect on ovarian function of boosting the glucose supply is seen in the experimental approach of daily drenching of dairy cows from 7 to 42 days of lactation with 500 ml of propylene glycol (Miyoshi *et al*., 2001). Compared with controls, this treatment reduced the interval to first oestrus, eliminated the short initial luteal phase and increased conception rate. Rather

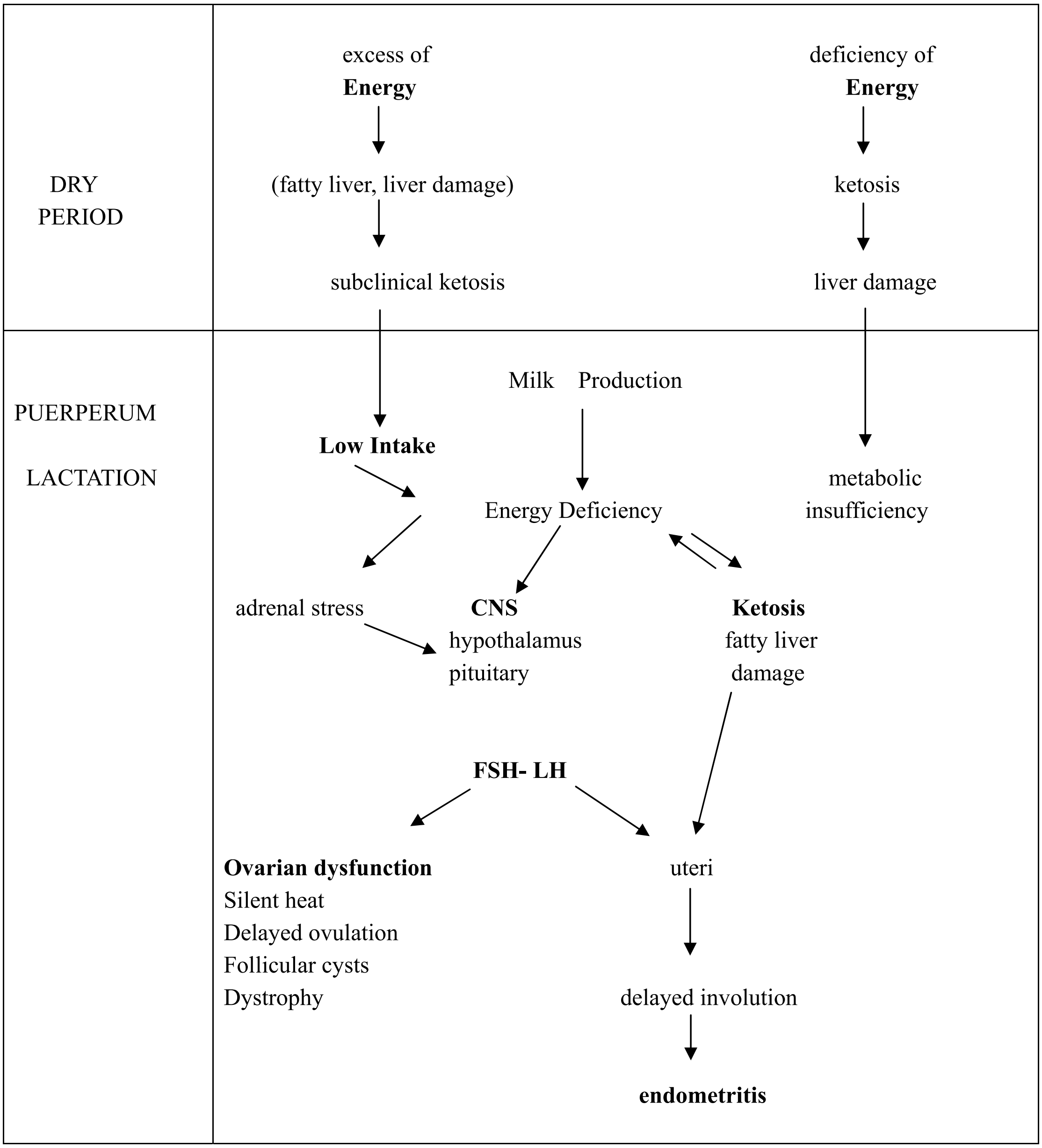


**Figure 2:** Effects of energy imbalance and acidosis ante - and post- partum on health and reproductive performance in dairy cows (Lotthammer, 1987)

than being the result of a reduction in NEB, these beneficial effects were attributed to a significant increase in plasma insulin. Some known associations between energy and reproduction are shown in **Table 1**.

**Table 1:** Some known associations between energy balance and reproduction (Scaramuzzi *et al*., 2006)

| Metabolic state | Metabolic consequences | Effects on reproduction |
|---|---|---|
| Negative energy balance | - Weight loss<br>- Fat stores depleted<br>- Muscle wasting<br>- Hypoglycemia<br>- Elevated GH<br>- Low Leptin<br>- Reduced metabolic heat<br>- Suppressed IGF system<br>- Elevated urea | - Inhibition of GnRH secretion by the hypothalamus<br>- Absence of LH pulses<br>- Inhibition of folliculogenesis<br>- Anovulation<br>- Anoestrus<br>- Delayed puberty |
| Energy balance | - Weight maintained<br>- Fat stores maintained<br>- Normal insulin<br>- Normoglycaemia<br>- Normal GH<br>- Normal Leptin<br>- Normal IGF system<br>- Normal urea | - Normal GnRH secretion by the hypothalamus<br>- Normal LH pulsatility<br>- Normal FSH concentrations<br>- Normal Oestradiol and inhibin<br>- Normal negative feedback<br>- Ovulation<br>- Oestrus<br>- Ovulation rate below natural maximum |

**3.1. The relationship between body condition score and NEB**

It is widely known that many high producing cows are often in NEB during early lactation. This is largely attributed that high yielding cows are at high nutrient mobilization state. As such, they cannot consume adequate feed to meet the nutrient requirements for high levels of milk production. The energy stores in the body tissues are more often mobilized leading to weight losses. Factors associated with the NEB have been suggested as causes of reproductive failures. One of the developed management approaches aimed at enabling farmers to track the herd progress towards meeting the desired target, is the use of BCS (Whitman, 1975). In this approach body condition is essentially the degree of body fat. Prolonged energy shortages leads to serious body weight and body condition losses which may affect reproductive efficiency.

BCS system is a method by which nutritional conditions of cattle can be conveniently monitored at a farm. It is used as a subjective estimate of the amount of subcutaneous fat on a cow (Edmonson *et al*., 1989). Cows with a low BCS at parturition have poor reproductive performance (Markusfeld *et al*., 1997), due possibly to a delay in onset of cyclicity (Butler and Smith, 1989). Furthermore, cows that lose more than 1 unit in BCS after parturition have reduced reproductive performances (Domecq *et al*., 1997). Since fat cow in the dry period have a low DMI and a shortage of energy, they use all the nutrition in the body to produce milk and suffer from a great reduction in BCS after calving. It is important to carry out regular BCS examinations in order to monitor the nutritional condition in a whole herd. Cows in which BCS was decreased by 1 or greater in 5 weeks after calving, showed the delayed first ovulation by more than 13 days, longer by 11 days in the number of days necessary for having first insemination and lower by 19% in the first insemination conception rate, in comparison with cows in which the BCS was decreased by less than 1.0. With more extensive loss of BCS, the reduction in conception rate becomes greater (Butler, 2000). Cows losing one unit or more BCS (five-point scale) during early lactation are at greatest risk for low fertility with conception rates of 17% to 38% is reported (Butler and Smith, 1989). BCS indicate the energy reserves of the body. Typically, every cow loses BCS after calving but cows calving in obese conditions or too thin can have decreased fertility later on for different reasons. Because of the strong relationship between body condition loss in early lactation and reproductive performance, BCS is a useful tool for predicting reproductive performance. Some body condition loss in early lactation is normal but excessive loss (more than one condition score between calving and joining) reduces reproductive performance and increases the risk of metabolic disease. BCS was positively associated with pregnancy rates (Burke *et al*., 1996). A relationship between fertility and BCS at the time of breeding has yet to be established. For every unit increase in BCS, a 13% unit increase in pregnancy rates was observed, which suggested that signs of behavioral oestrus were stronger and fertility was improved as BCS increased. Body condition at calving strongly influences the duration of postpartum anoestrus interval (PPI) in both dairy and beef cows. Prepartum nutritional status appears to have a greater influence on the duration of PPI than postpartum nutrition, such that beef cows calving in poor body condition have a prolonged PPI even when energy intakes during postpartum are greater than recommended (Wiltbank *et al*., 1962; Wright *et al*., 1987; Stagg *et al*., 1998). Cows with lower BCS have lower conception rates and decreased efficiency of heat detection compared with cows with a higher BCS (Moreira *et al*., 2000). Cattle should not be allowed to decline in BCS below 2.25 in order to avoid the possibility of nutritional anoestrus.

## 4. Effects of body weight on fertility

The concept of body weight at calving was first prosposed by Lamond *et al*. (1970). Buckley *et al*. (2003) reported that body weight change is an important tool for the identification of cows at risk of poor reproduction. It is generally accepted that live weight is the major factor influencing the onset of puberty and conception rates of heifers as shown in **Table 2**. Dietary restriction during the late prepartum period results in decreased weight and at calving, which lowers the number of cows and first-calf heifers that return to oestrus early in a defined breeding season (Whitman, 1975; Dziuk and Bellows, 1983; Wettemann *et al*., 2003). Dunn *et al*. (1969) indicated that animals come into estrum and conceive most readily when their body weight is rising due to an increased plane of nutrition and conversely a low pregnancy rate occurs in cattle losing weight during the breeding season. Cows will have about 70% chance of conceiving if they are gaining weight and only about 17% if they lost weight. This is emphasized in the works of Wiltbank (1977) and Haresign (1984). Ward (1968) suggested that every cow has an optimum body weight for conception, the so- called “target” or “critical” body weight. Animals weighing less than this are less able to reproduce. Wiltbank *et* al. (1964) added that breeding cows must be improving in “condition” during the mating period. Cows will probably lose weight after calving, but weight loss should be minimized through good feeding to allow them to start cycling again as soon as possible. It has been shown that heifers attain puberty at a certain body weight or body size rather than at a given age. When reared on different planes of nutrition, heifers with lower average daily weight gains were of similar weight to, but much older than their counterparts with higher daily gains at the onset of puberty (Short and Bellows, 1971). It was reported that most animals lose body weight during lactation and these cows have increased risk of poor reproductive performance (Buckley *et al*., 2003).

**Table 2:** Change in body weight as percentage of initial weight of cows and their subsequent conception rates (Richardson *et al*., 1975)

| Body weight[1] change (%) | Number of cows | Calving rate(%) | Bodyweight[2] change (%) | Number of cows | Calving rate (%) |
|---|---|---|---|---|---|
| -24 | 11 | 55 | | | |
| -20 | 13 | 46 | -20 | 4 | 25 |
| -16 | 28 | 82 | -16 | 6 | 67 |
| -12 | 32 | 82 | -12 | 11 | 64 |
| - 8 | 32 | 91 | - 8 | 29 | 69 |
| - 4 | 23 | 87 | - 4 | 36 | 78 |
| 0 to + 8 | 31 | 84 | 0 to +20 | 87 | 90 |

[1] Bodyweight change between peak weight in early pregnancy and parturition.
[2] Bodyweight change between peak weight in early pregnancy and the following mating season.

## 5. Effects of protein on fertility

Animals require protein as a source of essential amino acids and as a nitrogen source for rumen microflora. All cattle, fat or thin, need protein supplementation to consume and utilize low quality forage with any degree of effectiveness. The protein requirement of an animal is dependent on its physiological status and level of production. Ruminants are also capable of reducing protein loss by recycling urea, a product of protein metabolism that is normally excreted. Thus, some urea can be recycled to the rumen when the diet is low in nitrogen. It is also important to ensure that the diet contains the correct level of protein during the joining period. If there is too much protein in the diet the rumen bacteria are unable to convert it into microbial protein.

Feeding more dietary protein has been negatively associated with dairy cow fertility. Excess ammonia is conjugated to urea and then excreted. Thus, high urea levels are consistent with excess protein intake, possibly with concomitant energy shortage, and are likely to be associated with high levels of ammonia circulation. This results in a high level of ammonia in the rumen, which is absorbed across the rumen wall into the blood stream, where it is carried to the liver and converted into urea. Excess urea in the blood or blood urea nitrogen (BUN) can be toxic to sperm, eggs and embryos.

Increasing a cow's intake of dietary protein intake can increase its milk production, but can also reduce its fertility. It is reported that high protein resulting in high concentrations of urea nitrogen in plasma and milk (> 190 mg/L) is associated with decreased fertility in cattle (Butler *et al*., 1996; Elrod and Butler, 1993). It is due to an altered uterine environment (Elrod and Butler, 1993). The primary site of action of the effect is also unclear. Limited evidence suggests that it is localized to the reproductive system, but effects on the pituitary and hypothalamus, as well as the ovary and uterus, have all been postulated. Although a high protein intake has been postulated to have an effect on fertility for over 30 years, the evidence remains inconclusive, and the etiology and pathogenesis of the effect remain obscure. Fahey *et al*. (1998) reported that the effects of urea on embryo quality are likely to be due to alterations in the oviduct environment or deleterious changes in the follicle, rather than changes in the uterine environment. Depending upon protein quality and composition, serum concentrations of progesterone may be lowered, the uterine environment altered, and fertility decreased (Butler, 1998). Diets high in crude protein (17% to 19%) are typically fed during early lactation to both stimulate and support milk production, however, high protein diets have been associated with reduced reproductive performance (Butler, 1998; Westwood *et al*., 1998). Uterine pH was also affected in heifers fed excess rumen degradable protein (RDP) and was associated with reduced fertility (Butler, 1998). Feeding diets high in crude protein (CP) increased plasma urea concentrations which may interfere with the normal inductive actions of progesterone on the environment of the uterus and thereby cause suboptimal conditions for support of embryo development (Butler, 2000).

The CP content of the diet affects milk production and composition but studies by Laven and Drew (1999) have shown that increasing CP content of the diet reduces fertility by reducing conception rates to service, particularly in older cows, thereby prolonging days open. Some studies have shown that the degradability of protein affects fertility, but this is conflicting (Laven and Drew, 1999; Westwood *et al*., 2000). When excess protein is fed to cows, in NEB, the energetic demands of excreting this as urea may exacerabate the effects of the NEB, on reproduction, thereby decreasing fertility.

Over-feeding of protein in early lactation can exacerbate body condition loss, whilst under-feeding of protein invariably affects feed intake as well as the efficiencies of feed digestion and conversion into milk. It remains that the rumen is the key driver of feed intake and efficient feed utilization, and both can impact on overall cow performance.

It has been suggested that excess rumen degradable protein (RDP) may exacerbate NEB and its negative effect on fertility (Butler, 1998). Westwood *et al*. (2000) showed in their research that feeding more RDP deteriorated expression of oestrus at first ovulation, had a lower first service conception rate and a longer calving to conception interval. Garcia-Bojalil *et al*. (1998) observed signs of a reduced fertility with feeding excess RDP which could be eliminated by the inclusion in the diet of calcium salts of long-chain fatty acids. They also showed a negative effect of RDP on plasma progesterone, which could be restored by the inclusion of fat, resulting in an increased pregnancy rate with fat supplementation. The detrimental effect of ammonia on cleavage rates and blastocyst formation was confirmed by Sinclair *et al*. (2000), who demonstrated a reduction of the proportion of oocytes that developed after fertilization. According to Jorritsma *et al*. (2003), ammonia is most likely to play a role before ovulation, whereas the effects of urea, that has been shown to lower the pH in the uterine fluid, are exerted during cleavage and blastocyst formation of the fertilized embryo. The cause of this reduction in pH is not clear. It has been suggested that ureagenesis removes bicarbonate (Zhu *et al*., 2000) and reduces pH, at least in blood. Infusing urea in the blood lowered the uterine pH which was explained by an effect on carbonic anhydrase (Rhoads *et al*., 2004). This would suggest that excess RDP is more detrimental to fertility than excess rumen undegradable protein.

Feeding excess protein costs money and adds to environmental pollution. Therefore, if we avoid excess protein to save money and protect the environment, reproduction may be altered.

## 6. Minerals and its effect on fertility

Minerals are also important for good reproductive performance as deficiency of it is associated with decreased reproductive performances. Proper herd management should be designed to optimize the production of the highest quality product, while minimizing any adverse effects on the health and welfare of the animals. Adequate balances of major and minor trace mineral plays important roles in health as well as reproductive efficiency. The potential for minerals to play a significant role in herd fertility is indisputable. Mineral elements that are of particular importance are categorized into major [calcium (Ca), phosphorus (P), potassium (K), sodium (Na), chlorine (Cl), sulphur (S) and magnesium (Mg) and trace elements iron (Fe), iodine (I), copper (Cu), manganese (Mn), zinc (Zn), cobalt (Co) and selenium (Se)]. Minerals that affect reproduction in cattle are generally found within the trace element group, although deficiencies of Ca and P can also affect fertility. Depending on soil quality and fertilizer use, a deficiency of Na and a correlated excess of K can reduce fertility by irregular oestrus cycles, endometritis and follicular cysts (Lotthammer and Ahlswede, 1973). Grunes and Welch (1989) reported that excess intake of K resulted in Mg and Ca deficiency. Dalley *et al*. (1997) suggested that increasing K intake from 1.6 to 4.6% in rumen fistulated sheep resulted in a decline in net absorption of Mg from the entire digestive tract with a consistent reduction in plasma Mg. Schonewille *et al*. (1997) demonstrated that the increased in the dietary K concentration from 0.78 to 3.4% reduced Mg absorption from 29.8% to 22.2%. Fisher *et al*. (1994) found that the mid-lactation cows which were fed 1.6%, 3.1% or 4.6% of K in total mixed ration showed reduced plasma Mg and milk yield incase of high % of K fed cows. Goff *et al*. (1997) reported that a higher dietary K concentration in forages and diets increases probability of hypocalcemia in the peripartum period of cattle due to less absorption of ca in the small intestine. The Na:K ratio should be kept under 10:1. Of the trace minerals, Mn and Se may influence reproduction. Manganese supply is correlated with pH value of the soil because high pH values inhibit uptake from the soil. Boland *et al*. (1996) examined different forms of Cu, Zn, Mn and Se (inorganic versus organic) showing improvements in conception rates and days to first service. Ballantine *et al*. (2002) reported similar improvements from replacing inorganic sulphate salts of Cu, Mn, Zn and Co with organic forms. Manganese is needed for making steroids. Its deficiency can cause irregular heats, silent heats, poor conception, and abortions. Diets should generally contain 44 ppm Mn. Copper may affect the action of prostaglandin. Its deficiency will result in more early embryonic death. Deficiency of Cu may be caused by too much dietary molybdenum or sulfur. Diets should normally contain 12 ppm of Cu.

### 6.1. Calcium

One of the functions of Ca is to allow muscle to contract. Clearly a reduction in muscle contractility will lead to a decrease in DMI as rumen function decreases, leading to a severe NEB. As a consequence, there is an increase in fat mobilization that may result in fatty liver syndrome and ketosis. An excess of ketone bodies can further suppress appetite (Capuco *et al*., 1990), it has been shown that plasma Ca concentrations of 5 mg/dl reduce abomasal motility by 70% and the strength of the contraction by 50% (Daniel, 1983). Whilst milk fever may not actually present itself until plasma Ca reaches 4 mg/dl. Low Ca concentrations also prevent insulin production, further exacerbating this situation (Goff, 1999). Ultimately, milk yield will be reduced and fertility will suffer. Muscle tone in the uterus will also be adversely affected with cows experiencing prolonged calving and retained placenta. Uterine involution may also be impaired giving rise to fertility problems.

Hypocalcemia can be minimized by manipulating the mineral composition of the prepartum diet (feeding low Na and K diets and including acidogenic salts). It results in increased blood cortisol concentrations after calving, impairs uterine involution and is associated with increased uterine infections, and reduces fertility.

### 6.2. Phosphorus

Inactive ovaries, delayed sexual maturity and low conception rates have been reported when P intakes are low. Reproductive problems are common if P is deficient. Plasma P concentrations consistently below 4.5 mg/dL are indicative of a deficiency, but bone P is a more sensitive measure of the P status. It has long been known to influence conception rates, oestrus cycles, anoestrus, ovarian activity and overall fertility. The total dietary levels of 0.75% Ca and 0.45% P and 1.5:1 Ca:P ratio have served well for lactating cows diets over a wide range of production and feeding situations. High levels of K and Na in the ration cause the blood to be slightly alkaline that reduces the effectiveness of parathyroid hormone. Legel (1970) demonstrated in a definitive experiment that P deficiency decreased total intake which caused a lower energy supply and lower weight gain in heifers therefore, risk factor in poor fertility. High levels of P inclusion at 80 g per day have been reported to reduce the effectiveness of parathyroid hormone (PTH) (Bradley *et al*., 2000). The advice is to keep Ca:P ratio in total intake over 2:1 with marginal P supply which should be higher under stress conditions.

### 6.3. Zinc

Zinc is involved in several enzymatic reactions associated with carbohydrate metabolism, protein synthesis and nucleic acid metabolism. It is therefore essential in cells like the gonads, where active growth and division are taking place. Consequently, reproductive functions are seriously impaired by Zn deficiency, and as indicated by Underwood (1981), all phases of the reproductive process in the female from oestrus through pregnancy to lactation, may be affected.

**Table 3:** Role of micronutrients in reproduction (Smith *et al*., 2000)

| Micronutrient | Mechanism/metabolic function | Deficiency consequences |
|---|---|---|
| Vitamin A | Steroidogenesis, embryonic synchrony | Delayed puberty, low conception rate, high embryonic mortality, reduced libido |
| Vitamin E | Intra – membrane free radical detoxification | Low sperm concentration and high incidence of cytoplasmic droplets, retained foetal membrane |
| Selenium | Component of GSH – Px | Reduced sperm motility and uterine contraction, cystic ovaries, low fertility rate, retained foetal membrane |
| Copper | Enzyme component and catalyst involved in steroidogenesis, and prostaglandin sysnthesis | Low fertility, delayed/ depressed oestrus, abortion/foetal resorption |
| Zinc | Constituent of several metalloenzymes; carbohydrate and protein metabolism | Impaired spermatogenesis and development of secondary sex organs in males, reduced fertility and litter size in multiparous species |

In the trial designed to evaluate the performance of Barki ewes under field conditions in Egypt, Ali *et al*. (1998) compared two groups of mature ewes fed either a control diet containing 23–25 ppm or a test diet supplemented with an additional 100 ppm of Zn as zinc sulphate. Supplementation started 1 month before mating, and continued until lambing. The authors reported that Zn supplemented ewes consumed about 15% more feed than the controls, had a higher fertility rate, were more prolific, 89% vs. 40% and produced heavier lambs at birth, 4.0 vs. 2.9 kg and at weaning, 17.7 vs. 14.2 kg. In addition, supplementation increased serum Zn concentration, particularly during late pregnancy. These results confirmed the findings of others, who had shown the detrimental effects of a dietary Zn deficiency in farm animals on feed consumption and various phases of the reproductive cycle in the female (Masters and Fels, 1980; Underwood, 1981; Masters and Moir, 1983).

Some evidence has been provided to demonstrate the importance of micronutrients for the reproductive well being of animals as summarized in the **Table 3**.

## 7. Vitamins and its effect on reproduction

Vitamins are essential nutrients that affect economically important performance traits of dairy cows, including milk production and reproduction. The effect of vitamins on the health and productivity of livestock are often of a chronic nature and linked to suboptimal intakes of vitamins during critical periods of the production cycle. The specific action of many of the vitamins and minerals in reproduction remains unknown. Vitamins A and E play an essential role in health and reproduction.

### 7.1. Vitamin A

Vitamin A is one of the fat-soluble vitamins and is well known to regulate the development, cellular growth and differentiation, and tissue function. Its metabolites affect ovarian follicular growth, uterine environments and oocyte maturation (Schweigert and Zucker, 1988).

A deficiency of vitamin A has a direct effect on the structure and function of the pituitary gland, gonads and uterus. Livestock, particularly ruminants, consume vitamin A, mainly in its inactive form, the carotenes or provitamin A, except when it is fed as a supplement in cereal based concentrates. Provitamin A is converted into active vitamin A in the small intestine and together with preformed vitamin A supplement is stored in the liver, muscle, eggs, and milk to be used for a variety of functions, including those linked to the reproductive phenomena. Reproductive disorders observed with vitamin A deficiency in farm animals include delayed puberty, low conception rate, high embryo mortality, high perinatal mortality resulting from weak, blind offspring, and reduced libido in the male.

### 7.2. Vitamin E and Selenium

Vitamin E functions as an intra-cellular antioxidant scavenging for free reactive oxygen and lipid hydroperoxides, and converting them to non-reactive forms, thus maintaining the integrity of membrane phospholipids against oxidative damage and peroxidation (Surai, 1999). Selenium, on the other hand, functions as cofactor of the glutathione peroxidase (GSH-Px) enzyme systems responsible for regulating extra and intra-cellular hydroperoxidase (Burk and Hill, 1993). In vitamin E and selenium deficiency conditions, these free radicals accumulate and not only damage cell membranes, but also disrupt several processes linked to the synthesis of steroids (Staats *et al*., 1988), prostaglandins (Hemler and Lands, 1980), sperm motility (Alvarez and Storey, 1989), and the development of the embryo (Goto *et al*., 1992). It is not surprising therefore that negative impacts of vitamin E and selenium deficiencies have been observed on various components of the reproductive event, including ovulation rate (Harrison and Conrad, 1984), uterine motility, sperm motility and transport (Segerson and Libby, 1982), conception rate and post-partum activities (Arechiga *et al*., 1994), foetal membrane expulsion (Wichtell *et al*., 1996), embryo survival, milk production, and post natal growth (Anke *et al*., 1989). Olson (1995) summarized that over 60,000 calving, the incidence of retained fetal membrane (RFM) was about 10.3%, and that Se and vitamin E deficiencies constituted more important nutritional causes.

The incidence of RFM in Se deficient cows could be reduced by a pre-partum supplementation of either Se alone or in combination with vitamin E. The supplementation could be done by injection or via the feed, and under certain circumstances a positive response to vitamin E supplementation alone may be obtained.

## 8. Conclusions

Many past studies have more often attributed to low reproductive performance and to disturbances caused by diseases or other abnormalities. These studies have erroneously overlooked the role of nutrition that plays in reproduction. The interface between nutritional science and reproduction provides considerable potential for optimizing reproductive efficiency in cattle.

The interactions of nutrition on reproductive performance in cattle involve the most important dietary components like energy, protein, minerals, and vitamins. However further investigation is required regarding minerals and vitamins and its mechanisms in reproductive performances. Nutritional effects appear to be regulated at the ovarian and hypothalamic–pituitary levels which appear to be the main metabolic pathway affecting follicular function. Maintaining energy intake through the pre-partum period to calving and increase intake rapidly thereafter reduces NEB and the detrimental effects on coordinated ovarian and liver functions. More studies are required to confirm the effects of diets on cow's fertility.

Although it is not known whether deficiencies of nutrients limit reproduction through common or discrete mechanisms, provision of appropriate quantities of nutrient is required for optimal reproduction. Body condition, or degree of body fatness, seems to be the most reliable indicator of well–being of an animal and when coupled with changes in body weight, provides a useful method to assess reproductive potential. Cows will probably lose weight after calving, but weight loss should be minimized through good feeding to allow them to start cycling again as soon as possible. By manipulation of nutrient intake, livestock producers can strive to maintain reproductive performance. Therefore, it is important to unravel and better understand the complex interactions between nutrition and various reproductive processes, to address the increasingly serious problems of declining fertility in cattle.

In conclusion, the numerous reviews have unequivocally demonstrated that nutritional input affect reproduction, but exact mechanisms by which nutrition mediates the reproductive process remain to be elucidated. Investigators should be encouraged to develop research protocols that permit individual components of models designed to discover nutrition and reproductive interactions that can be integrated with physiological processes in a holistic manner. Scientists must be cognizant of the interactions among the nutrients and nutritional cues responsible for mediating reproduction.

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