



Transition-period Metabolic Disorders in Bovines: Pathophysiology, Diagnosis and Integrated Management Strategies

Lokesh Khandelwal¹, P. L. Gore¹, Kham Suan Tonsing¹, Roohani Sharma¹, Saroj Rai²,
Muthu Karunakaran³ and Mohan Mondal¹ 

¹Dept. of Animal Physiology, ICAR- National Dairy Research Institute (ERS), A-12 Block, Kalyani, West Bengal (741 235), India

²Dept. of Livestock Production & Management, ICAR- National Dairy Research Institute (ERS), A-12 Block, Kalyani, West Bengal (741 235), India

³Dept. of Bioenergetics and Environmental Science, ICAR-National Institute of Animal Nutrition & Physiology, Audugudi, Bengaluru, Karnataka (560 030), India



Corresponding ✉ drmondal@gmail.com

 0000-0002-3477-611X

ABSTRACT

This review synthesized current knowledge on major conditions including fatty liver, ketosis, milk fever, and hypomagnesaemia, with emphasis on their underlying mechanisms, risk factors, and management strategies. Metabolic diseases were recognized as major constraints to productivity, health, and welfare in dairy cattle, particularly during the transition period. These disorders primarily arise from negative energy balance and mineral imbalances associated with physiological, nutritional, and environmental stress. The pathophysiology of these disorders involved complex interactions among metabolic, endocrine, and immune systems, which resulted in reduced milk production, impaired fertility, and increased susceptibility to infectious and metabolic diseases. Subclinical forms were found to be more prevalent than clinical cases and contributed substantially to economic losses due to their often undetected nature and long-term effects on performance. Advances in diagnostic approaches, including metabolic profiling and precision livestock farming technologies, improved early detection, monitoring, and decision-making at the herd level. Biomarkers such as non-esterified fatty acids, β -hydroxybutyrate, calcium, and magnesium were widely used for identifying both subclinical and clinical conditions and for assessing metabolic status. Nutritional strategies, including controlled-energy diets, dietary cation-anion difference manipulation, and targeted supplementation of minerals and vitamins, were identified as key preventive measures. Integrated herd-level management approaches that combined nutrition, health monitoring, housing, and environmental management were shown to be essential for mitigating disease risk and improving overall herd performance. Overall, improving metabolic health was considered critical for enhancing productivity, animal welfare, and sustainability in modern dairy production systems.

KEYWORDS: Transition period, ketosis, pathophysiology, biomarkers, diagnosis, management

Citation (VANCOUVER): Khandelwal et al., Transition-period Metabolic Disorders in Bovines: Pathophysiology, Diagnosis and Integrated Management Strategies. *International Journal of Bio-resource and Stress Management*, 2026; 17(10), 01-13. [HTTPS://DOI.ORG/10.23910/1.2026.7096](https://doi.org/10.23910/1.2026.7096).

Copyright: © 2026 Khandelwal et al. This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License, that permits unrestricted use, distribution and reproduction in any medium after the author(s) and source are credited.

Data Availability Statement: Legal restrictions are imposed on the public sharing of raw data. However, author have full right to transfer or share the data in raw form upon request subject to either meeting the conditions of the original consents and the original research study. Further, access of data needs to meet whether the user complies with the ethical and legal obligations as data controllers to allow for secondary use of the data outside of the original study.

Conflict of interests: The author has declared that no conflict of interest exists.

1. INTRODUCTION

The transition period of dairy cattle, spanning approximately three weeks before to three weeks after parturition, is widely recognized as the most critical phase for the development of metabolic disorders (Ingvarsen, 2006; Mezzetti et al., 2021). During this stage, cows undergo profound physiological and metabolic adjustments associated with the onset of lactation, including rapid shifts in endocrine status, increased nutrient partitioning toward milk production, and initiation of colostrum synthesis. Concurrently, dry matter intake declines during late gestation, resulting in a mismatch between nutrient supply and demand. This imbalance leads to negative energy balance (NEB), which is a primary underlying factor in most transition-related metabolic diseases (Tamminga, 2006; Mulligan and Doherty, 2008; Mondal and Prakash, 2004) (Figure 1). These metabolic adaptations are endocrine regulated and promote energy mobilization. Increased lipolysis elevates circulating non-esterified fatty acids (NEFA), which are taken up by the liver and converted into ketone bodies such as β -hydroxybutyrate (BHBA). When hepatic capacity is exceeded, triglycerides accumulate, predisposing cows to fatty liver and ketosis. At the same time, calcium homeostasis is challenged due to increased demand for milk synthesis, increasing the risk of hypocalcemia. The prevalence of metabolic disorders

in dairy herds is substantial. Subclinical ketosis affects approximately 15–40% of cows in early lactation, while clinical ketosis occurs in 2–15% of animals (Ospina et al., 2010; Duffield et al., 2009). Fatty liver is also highly prevalent, with subclinical forms reported in up to 50% of high-producing cows shortly after calving (Bobe et al., 2004). Similarly, milk fever affects 5–10% of multiparous cows, whereas subclinical hypocalcemia occurs in 30–60% of cows depending on management and parity (Reinhardt et al., 2011; Venjakob et al., 2017). Although less frequent, hypomagnesemia can lead to severe clinical outcomes including sudden death, particularly in grazing systems (Martens et al., 2018; Stewart, 2022). The economic consequences of these disorders are considerable. Ketosis alone is estimated to cost between \$200 and \$400 per affected cow annually due to reduced milk yield, treatment costs, reproductive inefficiency, and increased culling rates (Cainzos et al., 2022). Fatty liver, often subclinical, contributes to long-term reductions in productivity and fertility (Bobe et al., 2004; Zhang et al., 2023). In addition, milk fever predisposes cows to secondary disorders such as retained placenta, displaced abomasum, and mastitis, further amplifying economic losses (Curtis et al., 1983; Goff, 2008). Beyond economic implications, metabolic diseases significantly compromise animal welfare. Affected cows experience systemic metabolic stress, immune dysfunction, and increased susceptibility to infectious diseases such as mastitis and metritis (Hammon et al., 2006; Sordillo and Mavangira, 2014). These welfare concerns are increasingly important in modern livestock production systems, where consumer expectations emphasize ethical and sustainable practices. The development of metabolic disorders is multifactorial, involving interactions among nutrition, endocrine regulation, immune responses, and management practices (Ingvarsen, 2006; Gross, 2024). Factors such as body condition score at calving, dietary composition, housing conditions, and calving-related stress influence disease susceptibility (Mammi et al., 2021; Magro et al., 2024). Recent advances in precision livestock farming have further enhanced the ability to monitor feeding behavior, rumination, and metabolic indicators in real time, enabling earlier detection and intervention (Liu et al., 2023). The major metabolic disorders affecting transition dairy cows are summarized in Table 1, while key risk factors influencing their occurrence are outlined in Table 2. Therefore, a comprehensive understanding of the pathophysiology, diagnosis, and management of metabolic diseases in bovines is essential for improving productivity, animal welfare, and sustainability. This review aimed to integrate current knowledge on major transition-period metabolic disorders and to highlight practical strategies for their prevention and control in modern livestock systems.

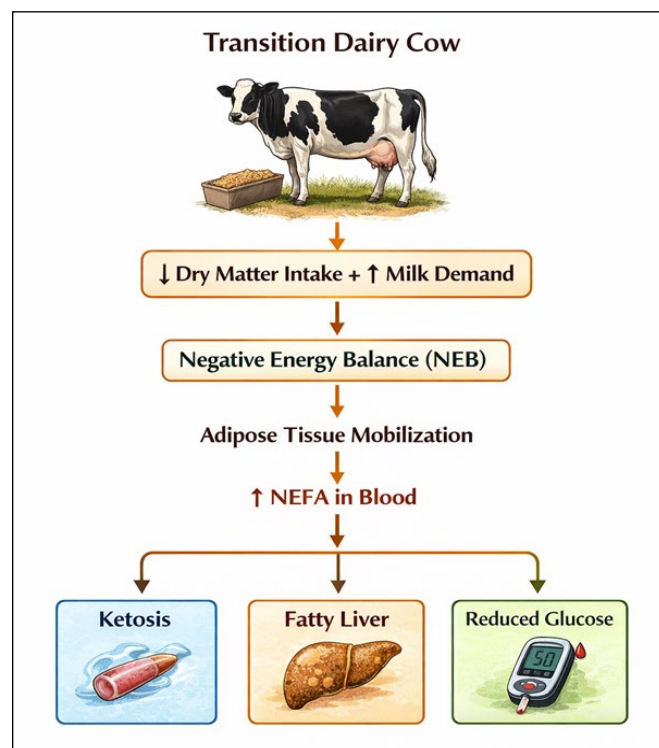


Figure 1: Schematic representation of negative energy balance (NEB) and its role in the development of major metabolic disorders in transition dairy cows

Table 1: Major metabolic disorders in dairy cows during the transition period: causes, clinical features and prevalence.

Disorder	Primary cause	Key metabolite changes	Clinical signs	Prevalence
Fatty liver	Excess NEFA mobilization	↑ NEFA, ↑ TG	Reduced appetite, low milk	Up to 50% (subclinical)
Ketosis	Negative energy balance	↑ BHBA	Anorexia, reduced milk	15–40%
Milk fever	Calcium imbalance	↓ Ca	Recumbency, weakness	5–10%
Hypomagnesemia	Low Mg intake	↓ Mg	Tetany, sudden death	Variable

NEFA: Non-esterified fatty acids; BHBA: β-hydroxybutyrate

Table 2: Key risk factors associated with transition-period metabolic disorders in dairy cows.

Factor	Effect
High BCS	↑ Fat mobilization
Low feed intake	↑ NEB
High DCAD diet	↓ Ca mobilization
High K pasture	↓ Mg absorption
Multiparity	↑ disease susceptibility

2. FAT COW SYNDROME (FCS)

2.1. Etiology and risk factors

Fat cow syndrome, or fatty liver disease, arises primarily from excessive energy intake during the dry period, leading to over-conditioning (Rukkwamsuk et al., 1999). Over-conditioned cows (body condition score [BCS] > 3.75) exhibit excessive adipose tissue mobilization postpartum, releasing large amounts of nonesterified fatty acids (NEFAs) into circulation (Gillund et al., 2001). The liver is the central site for NEFA uptake and metabolism, but its capacity to oxidize fatty acids completely is limited (Herdt, 2000). Consequently, NEFAs are re-esterified into triglycerides, accumulating in hepatocytes.

Additional risk factors include parity, with multiparous cows more susceptible, as well as nutritional imbalances, abrupt diet changes, and concurrent periparturient diseases such as ketosis and hypocalcemia (Constable et al., 2016). Genetic predispositions related to metabolic flexibility and insulin sensitivity may also play roles (De Koster and Opsomer, 2013).

2.2. Pathophysiology

The pathophysiology of FCS revolves around the inability of the liver to cope with excessive NEFA influx. Normally, fatty acids are oxidized for energy or exported as very low-density lipoproteins (VLDLs). In cows, however, VLDL synthesis and export are inefficient compared to monogastrics (Bohe et al., 2004). Consequently, triglycerides accumulate within hepatocytes, leading to hepatic lipidosis. This condition reduces gluconeogenic capacity, exacerbates hypoglycemia,

and predisposes cows to ketosis (Djokovic et al., 2009; Gross et al., 2013).

Advanced stages involve not only lipid accumulation but also hepatocellular damage, inflammation, and fibrosis (Zhang et al., 2023). Insulin resistance, which is common in over-conditioned cows, intensifies lipolysis, creating a self-perpetuating cycle of fat mobilization and hepatic overload (De Koster and Opsomer, 2013). Furthermore, altered cytokine expression and oxidative stress may contribute to liver dysfunction and systemic inflammation (Sordillo and Mavangira, 2014).

2.3 Clinical and subclinical presentations

Clinical cases of FCS are relatively uncommon but severe. Signs include anorexia, rapid body weight loss, reduced milk production, weakness, and increased susceptibility to infections (Constable et al., 2016). Subclinical fatty liver is far more widespread and insidious, impairing reproductive performance, immune function, and milk yield without overt clinical signs (Busato et al., 2002; Nowak et al., 2006).

Subclinical forms are particularly concerning because they often go unnoticed, yet they interact synergistically with other metabolic disorders, increasing the risk of ketosis, displaced abomasum, and retained placenta (Curtis et al., 1983; Drackley et al., 2005).

2.4. Diagnosis

Diagnosis of FCS relies on a combination of history, clinical evaluation, and laboratory findings. Common indicators include elevated NEFA and beta-hydroxybutyrate (BHBA) levels in blood (Ospina et al., 2010; Mondal and Baruah, 2015). Hepatic biopsy remains the gold standard, enabling direct quantification of triglyceride content (Bohe et al., 2004).

Non-invasive methods such as ultrasonography are gaining traction, allowing visualization of hepatic echogenicity (Constable et al., 2016). Biochemical markers including liver enzymes (AST, GGT), bilirubin, and cholesterol are also used to assess hepatic function (Djokovic et al., 2009; Gerspach and Ruetten, 2016). The commonly used diagnostic thresholds for metabolic disorders are presented in Table 3.

Table 3: Diagnostic thresholds and biomarkers for detection of metabolic disorders in dairy cows

Parameter	Threshold	Interpretation
BHBA	≥ 1.2 mmol l ⁻¹	Subclinical ketosis
BHBA	> 3.0 mmol l ⁻¹	Clinical ketosis
NEFA (prepartum)	> 0.3 mmol l ⁻¹	High risk
Calcium	< 2.0 mmol l ⁻¹	Subclinical hypocalcemia
Magnesium	< 0.8 mmol l ⁻¹	Hypomagnesemia

2.5. Treatment

Treatment strategies focus on restoring energy balance and supporting liver metabolism. Common interventions include intravenous glucose infusion to alleviate hypoglycemia and insulin therapy, sometimes combined with glucose, to promote peripheral glucose uptake and suppress lipolysis (Djokovic et al., 2009). Lipotropic agents such as choline, methionine, and niacin are also used to enhance hepatic fat metabolism (Zom et al., 2011). In addition, propylene glycol drenching provides gluconeogenic precursors that help improve energy status (Capel et al., 2021). More recently, oleic acid infusion has been reported to reduce lipolysis and improve insulin sensitivity (Abou-Rjeileh et al., 2023). Supportive therapies may include antioxidants such as selenium and vitamin E to counteract oxidative stress (Khan et al., 2022). However, treatment outcomes are often modest, highlighting the importance of prevention.

2.6. Prevention

Prevention is primarily based on nutritional and managerial strategies. Body condition management is critical, as ensuring cows calve at a body condition score (BCS) of 2.5–3.5 reduces the risk of excessive fat mobilization (Rukkamsuk et al., 1999). Controlled energy diets during the dry period help prevent over-conditioning and associated metabolic disturbances (Herd, 2000). The use of feed additives such as rumen-protected choline and monensin has been shown to improve hepatic lipid metabolism and reduce the risk of fatty liver (Plaizier et al., 2000; Zom et al., 2011). In addition, adequate micronutrient supplementation, including selenium, vitamin E, and B-vitamins, supports metabolic resilience and immune function (Singh et al., 2024). Precision monitoring approaches further enhance prevention by enabling early detection of at-risk animals through assessment of NEFA and BHBA levels, rumination activity, or automated metabolic sensors (Magro et al., 2024; Liu et al., 2023). By adopting integrated preventive strategies, farmers can minimize the incidence of fatty cow syndrome and its associated economic and health losses.

3. KETOSIS

3.1. Etiology and pathogenesis

Ketosis is one of the most prevalent metabolic disorders in dairy cattle, particularly in the first weeks of lactation when energy requirements exceed dietary intake (Gross, 2024). As milk production commences, cows enter a state of negative energy balance (NEB), which drives mobilization of adipose tissue. This results in elevated plasma concentrations of nonesterified fatty acids (NEFAs) (Ospina et al., 2010; Melendez et al., 2009; Mondal and Prakash, 2004).

Within the liver, non-esterified fatty acids (NEFAs) undergo three principal metabolic fates, including complete oxidation to carbon dioxide and ATP, partial oxidation to ketone bodies such as acetoacetate, β -hydroxybutyrate (BHBA), and acetone, and re-esterification into triglycerides with subsequent storage within hepatocytes, thereby contributing to the development of fatty liver (Bobe et al., 2004; Zhang et al., 2023).

Excessive ketone body formation leads to clinical ketosis, while lower but sustained elevations cause subclinical ketosis (SCK). Importantly, cows are inefficient in exporting triglycerides as very low-density lipoproteins (VLDLs), further predisposing them to hepatic lipidosis and perpetuating ketonemia (Herd, 2000; Gross et al., 2013).

Endocrine adaptations exacerbate this metabolic stress. Decreased insulin and elevated growth hormone promote lipolysis, while reduced glucose availability limits lactose synthesis, thereby impairing milk production (Steen et al., 1997; Herd, 2000). Ketone bodies also suppress appetite, worsening the NEB and creating a vicious cycle (Gulinski, 2021).

3.2. Clinical and subclinical forms

Clinical ketosis typically manifests between days 5–60 of lactation and is characterized by anorexia, selective appetite (particularly refusal of concentrates), decreased milk yield, weight loss, and a sweet odor of acetone on the breath or milk (Constable et al., 2016). Neurological signs such as ataxia, abnormal licking, or aggression occur in “nervous ketosis.”

Subclinical ketosis (SCK) is far more prevalent, often affecting 15–40% of cows (Duffield et al., 2009; Ospina et al., 2010). Although asymptomatic, SCK is strongly associated with secondary disorders including displaced abomasum, metritis, mastitis, and reduced fertility (Duffield et al., 2009; Curtis et al., 1983). SCK is economically more significant than clinical ketosis because of its silent but widespread impact on productivity (Cainzos et al., 2022).

3.3. Diagnosis

Diagnosis relies on detecting elevated ketone bodies or non-esterified fatty acids (NEFAs) in blood, milk, or urine. Blood β -hydroxybutyrate (BHBA) is considered the gold standard,

with thresholds of ≥ 1.2 – 1.4 mmol l⁻¹ indicating subclinical ketosis and >3.0 mmol l⁻¹ indicating clinical ketosis (Ospina et al., 2010; Serrenho et al., 2022). NEFA concentrations exceeding 0.3–0.4 mmol l⁻¹ during the prepartum period and >0.6 mmol l⁻¹ postpartum are predictive of increased disease risk (Melendez et al., 2009; Ster et al., 2012). Milk ketone testing methods, such as Ketotest®, provide rapid on-farm screening, with milk BHBA levels showing strong correlation with blood concentrations (Enjalbert et al., 2001; Faruk et al., 2020). Urine-based tests, including Rothera's test and dipsticks, detect acetoacetate and acetone but are generally less sensitive and can be influenced by hydration status.

Technological advances, including machine learning algorithms and automated cow-side sensors, are improving prediction and detection of ketosis based on milk composition, rumination, and behavior (Satofa and Bauer, 2021; Magro et al., 2024).

3.4. Economic impact

The financial consequences of ketosis are multifactorial. Cainzos et al. (2022) reported direct costs from veterinary treatments and indirect costs from decreased milk yield, impaired reproduction, and higher culling rates. Duffield et al. (2009) demonstrated that cows with hyperketonemia produced 1.5–3 kg less milk per day during early lactation, with prolonged consequences throughout lactation. Reproductive losses include extended days open, increased services per conception, and greater risk of early culling (Ospina et al., 2010; Gillund et al., 2001).

3.5. Prevention and control

Prevention strategies focus on nutritional and managerial adjustments during the transition period:

3.5.1. Nutritional strategies

Preventive strategies include maintaining optimal body condition score (BCS) of 2.75–3.5 at calving to reduce the risk of excessive fat mobilization (Busato et al., 2002). Providing controlled-energy diets during the dry period is essential to prevent over-conditioning and associated metabolic disturbances (Herd, 2000). The inclusion of propylene glycol as a glucogenic precursor is recommended for cows at risk to support energy balance (Capel et al., 2021). Additionally, supplementation with rumen-protected choline and niacin has been shown to improve hepatic lipid metabolism and reduce the incidence of metabolic disorders (Zom et al., 2011).

3.5.2. Additives

Monensin improves energy metabolism and reduces ketosis incidence (Plaizier et al., 2000).

3.5.3. Metabolic monitoring

Routine testing for NEFA and BHBA during the transition

period facilitates early identification of high-risk cows (Ospina et al., 2010; Cascone et al., 2022).

3.5.4. Management practices

Avoid overcrowding, provide adequate bunk space, and minimize social stress during transition (Ingvarsen, 2006; Mammi et al., 2021).

4. MILK FEVER (PARTURIENT PARESIS)

4.1. Etiology and pathophysiology

Milk fever, or periparturient hypocalcemia, is a disorder of calcium homeostasis occurring around calving, when the sudden onset of lactation causes a rapid decline in blood calcium (Goff and Horst, 1997; DeGaris and Lean, 2008). The initiation of colostrum synthesis requires 2–3 g of calcium liter⁻¹, far exceeding the amount normally available in extracellular fluids (Horst et al., 1997). If homeostatic mechanisms namely parathyroid hormone (PTH) release, renal reabsorption, and mobilization of skeletal calcium fail to compensate quickly, hypocalcaemia ensues (Goff, 2008).

High dietary cation-anion difference (DCAD) diets prepartum blunt PTH responsiveness by causing metabolic alkalosis, reducing calcium mobilization (Horst et al., 1997; Goff, 2008). Older cows are more susceptible due to reduced efficiency of calcium mobilization from bone.

4.2. Clinical and subclinical forms

Clinical milk fever is characterized by progressive neuromuscular weakness. Cows exhibit muscle tremors, ataxia, recumbency, and in severe cases, coma and death (Constable et al., 2016). Case fatality rates may reach 5–10% without treatment.

Subclinical hypocalcemia, defined as blood calcium <2.0 mmol l⁻¹ without clinical signs, is more widespread and economically damaging (Reinhardt et al., 2011). It has been linked with increased risk of displaced abomasum, retained placenta, ketosis, mastitis, and reduced reproductive performance (Caixeta et al., 2017; Wilhelm et al., 2017).

4.3. Diagnosis

Diagnosis is based on clinical presentation and measurement of serum calcium. Clinical hypocalcemia is typically <1.4 mmol l⁻¹, while subclinical cases range from 1.4–2.0 mmol l⁻¹ (Reinhardt et al., 2011).

4.4. Prevention

Effective prevention revolves around nutritional management during the dry period:

4.4.1. DCAD manipulation

Feeding low-DCAD diets (anionic salts) induces mild metabolic acidosis, enhancing PTH sensitivity and calcium mobilization (Horst et al., 1997; Goff and Koszewski, 2018).

Urine pH monitoring is used to confirm dietary effectiveness (Fehlberg et al., 2022).

4.4.2. *Controlled calcium intake*

Feeding low-calcium diets prepartum stimulates endogenous calcium mobilization (Goff and Horst, 1997; Oetzel, 2000).

4.4.3. *Vitamin D supplementation*

Enhances intestinal calcium absorption (Poindexter et al., 2023; Hodnik et al., 2020).

4.4.4. *Oral calcium boluses*

Widely used at calving to reduce hypocalcemia risk (Melendez et al., 2021; Miltenburg et al., 2016).

4.5. *Treatment*

Treatment of clinical milk fever involves intravenous calcium borogluconate, often followed by oral supplementation to maintain calcium levels (Braun et al., 2012). Rapid response is typical, with recumbent cows standing within hours if treated promptly.

5. HYPOMAGNESEMIA (GRASS TETANY)

5.1. *Etiology and risk factors*

Hypomagnesemia arises when magnesium intake or absorption is insufficient to meet metabolic demands. Because magnesium is not mobilized effectively from body stores, daily dietary supply is essential (Martens et al., 2018). Risk is highest in early lactation cows grazing lush, rapidly growing pastures low in magnesium but high in potassium and nitrogen, which antagonize magnesium absorption (Stewart, 2022; Doncel et al., 2021).

Other risk factors include cold, wet weather that reduces pasture magnesium content, older cows, and concurrent hypocalcemia (Martens and Stumpff, 2019).

5.2. *Pathophysiology*

Magnesium is critical for neuromuscular function, enzyme activation, and calcium homeostasis (Martens et al., 2018). Deficiency reduces acetylcholine release at neuromuscular junctions, causing muscle spasms and tetany. Additionally, hypomagnesemia impairs PTH secretion and action, exacerbating hypocalcemia (Goff, 1999).

5.3. *Clinical signs*

Clinical hypomagnesemia (“grass tetany”) manifests as hyperexcitability, muscle tremors, convulsions, and sudden death. Often, cows are found dead in pasture, highlighting the acute nature of the disease (Stewart, 2022). Subclinical hypomagnesemia, although less dramatic, impairs milk yield, reproduction, and immune function (Melendez et al., 2023).

5.4. *Diagnosis*

Diagnosis involves measuring serum magnesium (<0.8 mmol

l⁻¹ in clinical cases). However, postmortem confirmation is often required because of the sudden nature of death (Donovan et al., 2004).

5.5. *Prevention and treatment*

5.5.1. *Prevention*

Prevention strategies focus on ensuring adequate magnesium status through supplementation via mineral mixes, water, or feed (Urdaz et al., 2003). Dietary cation–anion difference (DCAD) manipulation is also important to avoid high potassium forages that can impair magnesium absorption (Rérat et al., 2009). Additionally, maintaining sufficient magnesium intake during both pre- and postpartum periods is essential for preventing hypomagnesemia and supporting metabolic stability (Martens and Stumpff, 2019).

5.5.2. *Treatment*

Treatment involves the immediate administration of intravenous calcium–magnesium solutions, followed by oral magnesium supplementation to stabilize magnesium levels and prevent recurrence (Goff, 1999).

6. INTERRELATIONSHIPS AMONG METABOLIC DISORDERS

Metabolic diseases in cattle rarely occur in isolation. Instead, they are interlinked through common etiological pathways such as negative energy balance (NEB), mineral imbalances, and endocrine dysregulation (Ingvarsen, 2006; Mondal and Prakash, 2003). Understanding these interconnections is crucial for comprehensive herd management. The interconnected pathways highlight the complex interactions among metabolic disorders during the transition period (Figure 2).

6.1. *Ketosis and fat cow syndrome*

Fat cow syndrome (FCS) and ketosis are intimately linked. Over-conditioned cows mobilize excessive adipose tissue postpartum, elevating nonesterified fatty acids (NEFAs) that overwhelm hepatic capacity (Rukkwamsuk et al., 1999; Bobe et al., 2004). This not only leads to fatty liver but also drives increased ketogenesis, predisposing cows to ketosis (Herdt, 2000; Gross et al., 2013). Conversely, persistent ketosis exacerbates hepatic triglyceride accumulation, creating a vicious cycle (Zhang et al., 2023).

6.2. *Hypocalcemia and ketosis*

Subclinical hypocalcemia reduces feed intake, thereby intensifying NEB and increasing susceptibility to ketosis (Goff and Horst, 1997; Caixeta et al., 2017). Calcium also plays a role in insulin secretion and muscle contractility; impaired calcium homeostasis disrupts energy metabolism and increases risk of displaced abomasum, which itself is strongly associated with ketosis (Curtis et al., 1983; Wilhelm et al., 2017).

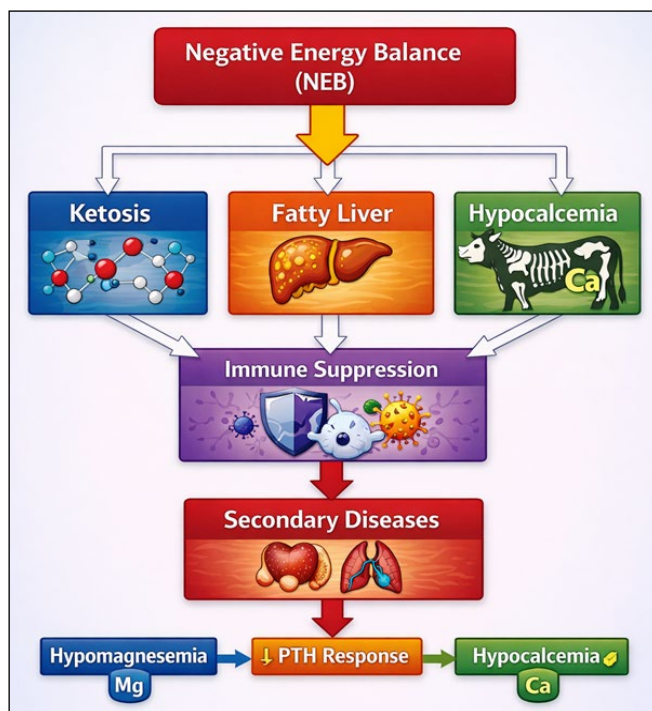


Figure 2: Interrelationships among major metabolic disorders in dairy cows, highlighting shared pathways including negative energy balance, immune suppression, and endocrine dysregulation

6.3. Hypomagnesemia and hypocalcemia

Magnesium is essential for parathyroid hormone (PTH) release and action; thus, hypomagnesemia impairs calcium homeostasis and increases the risk of hypocalcemia (Martens et al., 2018; Goff, 1999). This explains why hypomagnesemia often occurs concurrently with milk fever, particularly in cows grazing lush pastures high in potassium (Doncel et al., 2021).

6.4. Combined immunosuppression

All four major metabolic disorders—FCS, ketosis, milk fever, and hypomagnesemia—are associated with immunosuppression. Elevated NEFAs and ketones impair neutrophil function (Hammon et al., 2006; Ster et al., 2012). Hypocalcemia compromises smooth muscle contraction, delaying uterine involution and predisposing to metritis (Curtis et al., 1983; Abuelo, 2025). Hypomagnesemia influences stress responses and immune signaling (Martens and Stumpff, 2019). Collectively, these effects increase secondary diseases such as mastitis and metritis (Sordillo et al., 2009; Arfuso et al., 2023).

7. PREVENTION AND MANAGEMENT STRATEGIES

7.1. Nutritional approaches

Nutrition during the dry and transition periods is the

cornerstone of prevention (Ingvarsen, 2006; Mulligan and Doherty, 2008). An integrated approach combining nutritional, management, monitoring, and precision livestock farming strategies is essential for effective control (Figure 3). The major preventive and management strategies for controlling metabolic disorders are summarized in Table 4.

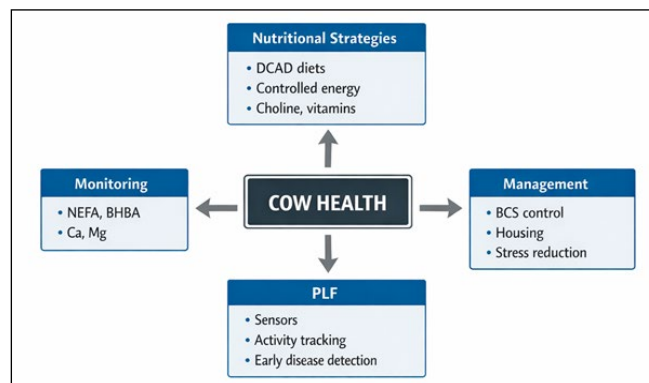


Figure 3: Integrated nutritional, management, monitoring, and precision livestock farming (PLF) strategies for prevention and control of metabolic disorders in dairy cows

Table 4: Nutritional and management strategies for prevention and control of metabolic disorders in dairy cows.

Strategy	Target Disorder	Mechanism
DCAD diet	Milk fever	Improves Ca mobilization
Propylene glycol	Ketosis	Provides glucose precursor
Choline	Fatty liver	Enhances lipid metabolism
Mg supplementation	Hypomagnesemia	Improves Mg availability
PLF monitoring	All	Early detection

7.1.1. Energy balance

Controlled-energy diets prevent over-conditioning and excessive fat mobilization (Rukkwamsuk et al., 1999; Herdt, 2000). Inclusion of glucogenic precursors such as propylene glycol improves energy status (Capel et al., 2021).

7.1.2. Protein Management

Adequate but not excessive rumen degradable protein avoids exacerbating NEB and promotes optimal fertility (Tamminga, 2006).

7.1.3. Mineral supplementation

Mineral supplementation plays a critical role in preventing metabolic disorders in dairy cattle. Dietary cation–anion difference (DCAD) diets are widely used for calcium management and prevention of hypocalcemia (Horst

et al., 1997; Goff and Koszewski, 2018). Magnesium supplementation is essential for preventing grass tetany and maintaining neuromuscular function (Urdaz et al., 2003; Martens and Stumpff, 2019). In addition, supplementation with selenium and vitamin E helps mitigate oxidative stress and enhances immune resilience in transition cows (Khan et al., 2022).

7.1.4. Vitamin management

Vitamin D supplementation supports calcium metabolism, while B-vitamins such as niacin and choline improve hepatic lipid handling (Poindexter et al., 2023; Singh et al., 2024).

7.2. Monitoring and early detection

Routine monitoring of biomarkers such as NEFAs, BHBA, calcium, and magnesium during the transition period enables early detection (LeBlanc, 2010; Ospina et al., 2010). Emerging technologies include precision sensors measuring rumination, feeding time, and milk components (Magro et al., 2024; Liu et al., 2023). Machine learning models further enhance predictive capacity for subclinical diseases (Satola and Bauer, 2021).

7.3. Therapeutic interventions

While prevention is paramount, treatment protocols are vital:

7.3.1. Ketosis

Oral drenching with propylene glycol, intravenous glucose, insulin, and butaphosphan-cyanocobalamin combinations (Capel et al., 2021).

7.3.2. Fatty liver

Lipotropic agents (choline, methionine), antioxidants, and oleic acid infusion to improve insulin sensitivity (Zom et al., 2011; Abou-Rjeileh et al., 2023).

7.3.3. Milk fever

Intravenous calcium borogluconate followed by oral supplementation (Braun et al., 2012; Oetzel, 2017).

7.3.4. Hypomagnesemia

IV calcium-magnesium solutions followed by oral magnesium salts (Goff, 1999).

7.4. Herd-level strategies

Herd-level strategies play a crucial role in preventing metabolic disorders in transition dairy cows. Transition cow management checklists (Overton, 2014) enable farmers to systematically evaluate housing, nutrition, and monitoring practices to ensure optimal herd health. Preventive supplementation protocols, including oral calcium boluses, magnesium licks, and propylene glycol for high-risk cows, have been shown to reduce the incidence of metabolic disorders (Melendez et al., 2021; Bhanugopan and Lievaart, 2014). In addition, cow comfort and housing management

are essential, as reducing overcrowding, ensuring adequate bunk space, and minimizing heat stress significantly influence feed intake and metabolic stability (Calderon and Cook, 2011).

8. ECONOMIC SIGNIFICANCE

The economic burden of metabolic disorders is multi-dimensional, encompassing treatment costs, production losses, reproductive inefficiency, and premature culling (Cainzos et al., 2022). The economic impacts associated with major metabolic disorders in dairy cattle are summarized in Table 5.

Table 5: Economic impact of major metabolic disorders in dairy cattle production systems.

Disorder	Impact
Ketosis	↓ Milk yield, fertility
Fatty liver	Hidden losses
Milk fever	Secondary diseases
Hypomagnesemia	Sudden death

8.1. Ketosis

Estimated at \$200–400 per cow annually, primarily due to decreased milk yield (1.5–3 kg day⁻¹) and impaired fertility (Duffield et al., 2009).

8.2. Fat cow syndrome

Indirect costs from reduced conception rates, longer calving intervals, and increased susceptibility to secondary diseases (Bobe et al., 2004; Zhang et al., 2023).

8.3. Milk fever

Increases risk of displaced abomasum, retained placenta, and mastitis, multiplying indirect costs (Curtis et al., 1983; DeGaris and Lean, 2008).

8.4. Hypomagnesemia

Although less common, sudden deaths in high-producing or pasture-grazed cows create catastrophic losses, particularly in seasonal calving herds (Doncel et al., 2021; Stewart, 2022).

At the herd level, integrated metabolic disease prevention has been shown to improve profitability significantly by reducing culling and improving reproductive efficiency (Cainzos et al., 2022; Lean et al., 2013).

9. FUTURE PERSPECTIVES

Future approaches to managing metabolic diseases in bovines will rely on integration of nutrition, genetics, and technology. Temporal variations in metabolic and endocrine parameters may further influence transition dynamics (Mondal et al., 2005).

9.1. Precision livestock farming (PLF)

Real-time sensors and wearable devices to monitor feeding behavior, rumination, and biochemical markers (Liu et al., 2023).

9.2. Machine learning and AI

Prediction of subclinical disease risk based on multi-parameter data streams (Satofa and Bauer, 2021).

9.3. Nutritional innovations

Use of nutraceuticals, omega-3 fatty acids, and targeted antioxidants to enhance metabolic resilience (Khan et al., 2022).

9.4. Genetic selection

Breeding for cows with improved metabolic flexibility, resilience to NEB, and reduced susceptibility to hypocalcemia or ketosis (Buonaiuto et al., 2023).

9.5. Molecular insights

Transcriptomics and metabolomics to identify biomarkers for early detection of fatty liver and ketosis.

9.6. Sustainability focus

Integrated metabolic health improves not only animal welfare but also reduces resource wastage, aligning with global sustainability goals.

10. CONCLUSION

Metabolic diseases in bovines, including fat cow syndrome, ketosis, milk fever, and hypomagnesemia, remained major challenges in dairy and beef production systems, driven primarily by transition-period stresses such as negative energy balance and mineral imbalances. Subclinical forms were more prevalent and economically damaging than clinical cases. Advances in nutrition, monitoring, and preventive strategies improved management; however, integrated herd-level approaches were essential. Future directions emphasized precision livestock farming and genetic strategies to enhance productivity, animal welfare, and sustainability.

11. ACKNOWLEDGMENT

This work was supported by ICAR-National Dairy Research Institute through a IRC approved project (F-41).

12. REFERENCES

Abou-Rjeileh, U., Neto, J.D., Chirivi, M., O'Boyle, N., Salcedo, D., Prom, C., 2023. Oleic acid abomasal infusion limits lipolysis and improves insulin sensitivity in adipose tissue from periparturient dairy cows. *Journal of Dairy Science* 106(8), 4306–4323. DOI: <https://doi.org/10.3168/jds.2022-22402>.

Abuelo, A., 2025. Hypocalcemia in dairy cattle. In: Simões, J., (Ed.), *Encyclopedia of Livestock Medicine for Large Animal and Poultry Production*. Springer Nature Switzerland, 1–7. DOI: https://doi.org/10.1007/978-3-031-52133-1_48-1.

Arfuso, F., Minuti, A., Liotta, L., Giannetto, C., Trevisi, E., Piccione, G., 2023. Stress and inflammatory response of cows and their calves during peripartum and early neonatal period. *Theriogenology* 196, 157–166. DOI: <https://doi.org/10.1016/j.theriogenology.2022.11.019>

Bhanugopan, M., Lievaart, J.J., 2014. Survey on the occurrence of milk fever in dairy cows and the current preventive strategies adopted by farmers in New South Wales, Australia. *Australian Veterinary Journal* 92(6), 200–205. DOI: <https://doi.org/10.1111/avj.12183>.

Bobe, G., Young, J.W., Beitz, D.C., 2004. Invited review: Pathology, etiology, prevention, and treatment of fatty liver in dairy cows. *Journal of Dairy Science* 87(10), 3105–3124. DOI: [https://doi.org/10.3168/jds.S0022-0302\(04\)73446-3](https://doi.org/10.3168/jds.S0022-0302(04)73446-3).

Braun, U., Blatter, M., Buchi, R., Hassig, M., 2012. Treatment of cows with milk fever using intravenous and oral calcium and phosphorus. *Schweizer Archiv für Tierheilkunde* 154(7), 381–388. DOI: <https://doi.org/10.1024/0036-7281/a000368>.

Buonaiuto, G., Lopez-Villalobos, N., Costa, A., Niero, G., Degano, L., Mammi, L.M.E., 2023. Stayability in simmental cattle as affected by muscularity and body condition score between calvings. *Frontiers in Veterinary Science* 10, 1141286. DOI: <https://doi.org/10.3389/fvets.2023.1141286>.

Busato, A., Faissle, D., Kupfer, U., Blum, J.W., 2002. Body condition scores in dairy cows: Associations with metabolic and endocrine changes in healthy dairy cows. *Journal of Veterinary Medicine A* 49(9), 455–460. DOI: <https://doi.org/10.1046/j.1439-0442.2002.00476.x>.

Cainzos, J.M., Andreu-Vazquez, C., Guadagnini, M., Rijpert-Duvivier, A., Duffield, T., 2022. A systematic review of the cost of ketosis in dairy cattle. *Journal of Dairy Science* 105(7), 6175–6195. DOI: <https://doi.org/10.3168/jds.2021-21539>.

Caixeta, L.S., Ospina, P.A., Capel, M.B., Nydam, D.V., 2017. Association between subclinical hypocalcemia in the first 3 days of lactation and reproductive performance of dairy cows. *Theriogenology* 94, 1–7. DOI: <https://doi.org/10.1016/j.theriogenology.2017.01.039>.

Calderon, D.F., Cook, N.B., 2011. The effect of lameness on the resting behavior and metabolic status of dairy cattle during the transition period in a freestall-housed dairy herd. *Journal of Dairy Science* 94(6), 2883–2894. DOI: <https://doi.org/10.3168/jds.2010-3855>.

- Capel, M.B., Bach, K.D., Mann, S., McArt, J.A.A., 2021. A randomized controlled trial to evaluate propylene glycol alone or in combination with dextrose as a treatment for hyperketonemia in dairy cows. *Journal of Dairy Science* 104(2), 2185–2194. DOI: <https://doi.org/10.3168/jds.2020-19111>.
- Cascone, G., Licitra, F., Stamilla, A., Amore, S., Dipasquale, M., Salonia, R., 2022. Subclinical ketosis in dairy herds: Impact of early diagnosis and treatment. *Frontiers in Veterinary Science* 9, 895468. DOI: <https://doi.org/10.3389/fvets.2022.895468>.
- Constable, P., Hinchcliff, K., Done, H.S., Grünberg, W., 2016. *Veterinary medicine: A textbook of the diseases of cattle, horses, sheep, pigs and goats* (11th Edn.). Saunders, New York. Available from: https://www.researchgate.net/publication/311774533_Veterinary_Medicine_A_textbook_of_the_diseases_of_cattle_horses_sheep_pigs_and_goats.
- Curtis, C.R., Erb, H.N., Sniffen, C.J., Smith, R.D., Powers, P.A., Smith, M.C., 1983. Association of parturient hypocalcemia with eight periparturient disorders in Holstein cows. *Journal of the American Veterinary Medical Association* 183(5), 559–561. DOI: <https://doi.org/10.2460/javma.1983.183.05.559>.
- De Koster, J.D., Opsomer, G., 2013. Insulin resistance in dairy cows. *Veterinary Clinics of North America: Food Animal Practice* 29(2), 299–322. DOI: <https://doi.org/10.1016/j.cvfa.2013.04.002>.
- DeGaris, P.J., Lean, I.J., 2008. Milk fever in dairy cows: A review of pathophysiology and control principles. *Veterinary Journal* 176(1), 58–69. DOI: <https://doi.org/10.1016/j.tvjl.2007.12.029>.
- Djokovic, R., Samanc, H., Ilic, Z., Kurcubic, V., 2009. Blood glucose, insulin and inorganic phosphorus in healthy and ketotic dairy cows after intravenous infusion of glucose solution. *Acta Veterinaria Brno* 78(3), 449–453. DOI: <https://doi.org/10.2754/avb200978030449>.
- Doncel, B., Puentes Santisteban, J.D., Caffarena, D., Riet-Correa, F., 2021. Hypomagnesemia in beef cattle. *Pesquisa Veterinária Brasileira* 41, e06826. DOI: <https://doi.org/10.1590/1678-5150-pvb-6826>.
- Donovan, G.A., Steenholdt, C., McGehee, K., Lundquist, R., 2004. Hypomagnesemia among cows in a confinement-housed dairy herd. *Journal of the American Veterinary Medical Association* 224(1), 96–99. DOI: <https://doi.org/10.2460/javma.2004.224.96>.
- Drackley, J.K., Dann, H.M., Douglas, N., Guretzky, N.A.J., Litherland, N.B., Underwood, J., 2005. Physiological and pathological adaptations in dairy cows that may increase susceptibility to periparturient diseases and disorders. *Italian Journal of Animal Science* 4(4), 323–344. DOI: <https://doi.org/10.4081/ijas.2005.323>.
- Duffield, T.F., Lissemore, K.D., McBride, B.W., Leslie, K.E., 2009. Impact of hyperketonemia in early lactation dairy cows on health and production. *Journal of Dairy Science* 92(2), 571–580. DOI: <https://doi.org/10.3168/jds.2008-1507>.
- Enjalbert, F., Nicot, M.C., Bayourthe, C., Moncoulon, R., 2001. Ketone bodies in milk and blood of dairy cows: Relationship between concentrations and utilization for detection of subclinical ketosis. *Journal of Dairy Science* 84(3), 583–589. DOI: [https://doi.org/10.3168/jds.S0022-0302\(01\)74511-0](https://doi.org/10.3168/jds.S0022-0302(01)74511-0).
- Faruk, M.S., Park, B.O., Ha, S., Lee, S.S., Mamuad, L.L., Cho, Y., 2020. Comparative study on different field tests of ketosis using blood, milk, and urine in dairy cattle. *Veterinary Medicine* 65(4), 199–206. DOI: <https://doi.org/10.17221/69/2019-vetmed>.
- Fehlberg, L.K., Pineda, A., Cardoso, F.C., 2022. Validation of 2 urine pH measuring techniques in a prepartum negative DCAD diet and the relationship with production performance. *JDS Communications* 3(1), 13–18. DOI: <https://doi.org/10.3168/jdsc.2021-0130>.
- Gerspach, C., Ruetten, M., 2016. Investigation of coagulation and serum biochemistry profiles in dairy cattle with different degrees of fatty liver. *Schweizer Archiv für Tierheilkunde* 12, 811–818. DOI: <https://doi.org/10.17236/sat00096>.
- Gillund, P., Reksen, O., Grohn, Y.T., Karlberg, K., 2001. Body condition related to ketosis and reproductive performance in Norwegian dairy cows. *Journal of Dairy Science* 84(6), 1390–1396. DOI: [https://doi.org/10.3168/jds.S0022-0302\(01\)70170-1](https://doi.org/10.3168/jds.S0022-0302(01)70170-1).
- Goff, J.P., 1999. Treatment of calcium, phosphorus, and magnesium balance disorders. *Veterinary Clinics of North America: Food Animal Practice* 15(3), 619–639. DOI: [https://doi.org/10.1016/S0749-0720\(15\)30167-5](https://doi.org/10.1016/S0749-0720(15)30167-5).
- Goff, J.P., 2008. The monitoring, prevention, and treatment of milk fever and subclinical hypocalcemia in dairy cows. *Veterinary Journal* 176(1), 50–57. DOI: <https://doi.org/10.1016/j.tvjl.2007.12.020>.
- Goff, J.P., Horst, R.L., 1997. Physiological changes at parturition and their relationship to metabolic disorders. *Journal of Dairy Science* 80(7), 1260–1268. DOI: [https://doi.org/10.3168/jds.S0022-0302\(97\)76055-7](https://doi.org/10.3168/jds.S0022-0302(97)76055-7).
- Goff, J.P., Koszewski, N.J., 2018. Comparison of 0.46% calcium diets with and without added anions with a 0.7% calcium anionic diet as a means to reduce periparturient hypocalcemia. *Journal of Dairy Science* 101(6), 5033–5045. DOI: <https://doi.org/10.3168/jds.2017-13832>.

- Gross, J.J., 2024. Ketosis in dairy cows. In: Gross, J.J., (Ed.), Production diseases in farm animals: pathophysiology, prophylaxis and health management. Springer International Publishing, pp. 115–133. DOI: https://doi.org/10.1007/978-3-031-51788-4_6.
- Gross, J.J., Schwarz, F.J., Eder, K., van Dorland, H.A., Bruckmaier, R.M., 2013. Liver fat content and lipid metabolism in dairy cows during early lactation and during a mid-lactation feed restriction. *Journal of Dairy Science* 96(8), 5008–5017. DOI: <https://doi.org/10.3168/jds.2012-6245>.
- Gulinski, P., 2021. Ketone bodies-causes and effects of their increased presence in cows' body fluids: A review. *Veterinary World* 14(6), 1492–1503. DOI: <https://doi.org/10.14202/vetworld.2021.1492-1503>.
- Hammon, D.S., Evjen, I.M., Dhiman, T.R., Goff, J.P., Walters, J.L., 2006. Neutrophil function and energy status in Holstein cows with uterine health disorders. *Veterinary Immunology and Immunopathology* 113(1–2), 21–29. DOI: <https://doi.org/10.1016/j.vetimm.2006.03.022>.
- Herd, T.H., 2000. Ruminant adaptation to negative energy balance: Influences on the etiology of ketosis and fatty liver. *Veterinary Clinics of North America: Food Animal Practice* 16(2), 215–230. DOI: [https://doi.org/10.1016/S0749-0720\(15\)30102-X](https://doi.org/10.1016/S0749-0720(15)30102-X).
- Hodnik, J.J., Jezek, J., Staric, J., 2020. A review of vitamin D and its importance to the health of dairy cattle. *Journal of Dairy Research* 87(1), 84–87. DOI: <https://doi.org/10.1017/S0022029920000424>.
- Horst, R.L., Goff, J.P., Reinhardt, T.A., Buxton, D.R., 1997. Strategies for preventing milk fever in dairy cattle. *Journal of Dairy Science* 80(7), 1269–1280. DOI: [https://doi.org/10.3168/jds.S0022-0302\(97\)76056-9](https://doi.org/10.3168/jds.S0022-0302(97)76056-9).
- Ingvartsen, K.L., 2006. Feeding- and management-related diseases in the transition cow: Physiological adaptations around calving and strategies to reduce feeding-related diseases. *Animal Feed Science and Technology* 126(3–4), 175–213. DOI: <https://doi.org/10.1016/j.anifeedsci.2005.08.003>.
- Khan, M.Z., Ma, Y., Xiao, J., Chen, T., Ma, J., Liu, S., 2022. Role of Selenium and Vitamins E and B9 in the alleviation of bovine mastitis during the periparturient period. *Antioxidants* 11(4), 657. DOI: <https://doi.org/10.3390/antiox11040657>.
- Lean, I.J., Van Saun, R., DeGaris, P.J., 2013. Mineral and antioxidant management of transition dairy cows. *Veterinary Clinics of North America: Food Animal Practice* 29(2), 367–386. DOI: <https://doi.org/10.1016/j.cvfa.2013.03.004>.
- LeBlanc, S., 2010. Monitoring metabolic health of dairy cattle in the transition period. *Journal of Reproduction and Development* 56(Suppl), S29–S35. DOI: <https://doi.org/10.1262/jrd.1056S29>.
- Liu, N., Qi, J., An, X., Wang, Y., 2023. A review on information technologies applicable to precision dairy farming: Focus on behavior, health monitoring, and precise feeding of dairy cows. *Agriculture* 13(8), 1858. DOI: <https://doi.org/10.3390/agriculture13101858>.
- Magro, S., Costa, A., Cavallini, D., Chiarin, E., De Marchi, M., 2024. Phenotypic variation of dairy cows' hematic metabolites and feasibility of non-invasive monitoring of the metabolic status in the transition period. *Frontiers in Veterinary Science* 11, 1437352. DOI: <https://doi.org/10.3389/fvets.2024.1437352>.
- Mammi, L.M.E., Cavallini, D., Fustini, M., Fusaro, I., Giammarco, M., Formigoni, A., 2021. Calving difficulty influences rumination time and inflammatory profile in Holstein dairy cows. *Journal of Dairy Science* 104(1), 750–761. DOI: <https://doi.org/10.3168/jds.2020-18867>.
- Martens, H., Stumpff, F., 2019. Assessment of magnesium intake according to requirement in dairy cows. *Journal of Animal Physiology and Animal Nutrition* 103(4), 1023–1029. DOI: <https://doi.org/10.1111/jpn.13106>.
- Martens, H., Leonhard-Marek, S., Röntgen, M., Stumpff, F., 2018. Magnesium homeostasis in cattle: Absorption and excretion. *Nutrition Research Reviews* 31(1), 114–130. DOI: <https://doi.org/10.1017/S0954422417000257>.
- Melendez, P., Lopez, F., Lama, J., Leon, B., Pinedo, P., 2023. Plasma ionized calcium and magnesium concentrations and prevalence of subclinical hypocalcemia and hypomagnesemia in post-partum grazing Holstein cows from southern Chile. *Veterinary Animal Science* 19, 100277. DOI: <https://doi.org/10.1016/j.vas.2022.100277>.
- Melendez, P., Marin, M.P., Robles, J., Rios, C., Duchens, M., Archbald, L., 2009. Relationship between serum nonesterified fatty acids at calving and the incidence of periparturient diseases in Holstein dairy cows. *Theriogenology* 72(6), 826–833. DOI: <https://doi.org/10.1016/j.theriogenology.2009.06.001>.
- Melendez, P., Roeschmann, C., Arevalo, A., Moller, J., 2021. The effect of oral calcium boluses at parturition on blood metabolites and milk yield in grazing Holstein cattle. *Livestock Science* 248, 104510. DOI: <https://doi.org/10.1016/j.livsci.2021.104510>.
- Mezzetti, M., Cattaneo, L., Passamonti, M. M., Lopreiato, V., Minuti, A., Trevisi, E., 2021. The transition period updated: A review of the new insights into the adaptation of dairy cows to the new lactation. *Dairy* 2(4), 617–636. DOI: <https://doi.org/10.3390/dairy2040048>.

- Miltenburg, C.L., Duffield, T.F., Bienzle, D., Scholtz, E.L., LeBlanc, S.J., 2016. Randomized clinical trial of a calcium supplement for improvement of health in dairy cows in early lactation. *Journal of Dairy Science* 99(8), 6550–6562. DOI: <https://doi.org/10.3168/jds.2016-10961>.
- Mondal, M., Baruah, K.K., 2015. Development of a rapid microtiterplate-based colorimetric method for estimation of non-esterified fatty acids in bovine plasma. *Research & Reviews: Journal of Veterinary Science and Technology* 4(3), 29–34. DOI: <https://doi.org/10.37591/rrjovst.v4i3.572>. <https://sciencejournals.stmjournals.in/index.php/RRJoVST/article/view/572>.
- Mondal, M., Prakash, B.S., 2003. Changes in plasma growth hormone, luteinizing hormone and progesterone and blood metabolites following long-term exogenous somatotiberin administration in growing buffaloes (*Bubalus bubalis*). *Journal of Animal and Veterinary Advances* 2, 259–270. DOI: <https://doi.org/10.3923/javaa.2003.259.270>. <https://makhillpublications.co/view-single-article?doi=javaa.2003.259.270>.
- Mondal, M., Prakash, B.S., 2004. Changes in plasma non-esterified fatty acids, glucose and α -amino nitrogen and their relationship with body weight and plasma growth hormone in growing buffaloes (*Bubalus bubalis*). *Journal of Animal Physiology and Animal Nutrition* 88, 223–228. DOI: <https://doi.org/10.1111/j.1439-0396.2004.00476.x>.
- Mondal, M., Rajkhowa, C., Prakash, B.S., 2005. Diurnal changes in blood metabolites and their relation to plasma growth hormone and time of feeding in mithun heifers (*Bos frontalis*). *Chronobiology International* 22, 807–816. DOI: <https://doi.org/10.1080/07420520500263359>.
- Mulligan, F.J., Doherty, M.L., 2008. Production diseases of the transition cow. *Veterinary Journal* 176(1), 3–9. DOI: <https://doi.org/10.1016/j.tvjl.2007.12.018>.
- Nowak, W., Jaśkowski, J., Wylegała, S., 2006. Effects of nutrition in the transition period on the fertility of milking cows. *Medycyna Weterynaryjna* 62, 632–636. Available from: <https://www.cabidigitallibrary.org/doi/full/10.5555/20063108550>.
- Oetzel, G.R., 2000. Management of dry cows for the prevention of milk fever and other mineral disorders. *Veterinary Clinics of North America: Food Animal Practice* 16(2), 369–386. DOI: [https://doi.org/10.1016/S0749-0720\(15\)30110-9](https://doi.org/10.1016/S0749-0720(15)30110-9).
- Oetzel, G.R., 2017. Fresh cow metabolic diseases. In: *American Association of Bovine Practitioners Conference Proceedings*, p. 3282. DOI: <https://doi.org/10.21423/aabppro20173282>.
- Ospina, P.A., Nydam, D.V., Stokol, T., Overton, T.R., 2010. Evaluation of nonesterified fatty acids and beta-hydroxybutyrate in transition dairy cattle in the northeastern United States: Critical thresholds for prediction of clinical diseases. *Journal of Dairy Science* 93(2), 546–554. DOI: <https://doi.org/10.3168/jds.2009-2277>.
- Overton, M., 2014. Transition cow management checklist. In: *Proceedings of the Dairy Cattle Welfare Council*. Available from: https://www.researchgate.net/publication/242230554_Transition_Cow_Management_Checklist.
- Plaizier, J.C., Martin, A., Duffield, T., Bagg, R., Dick, P., McBride, B.W., 2000. Effect of a prepartum administration of monensin in a controlled-release capsule on apparent digestibilities and nitrogen utilization in transition dairy cows. *Journal of Dairy Science* 83(12), 2918–2925. DOI: [https://doi.org/10.3168/jds.S0022-0302\(00\)75192-7](https://doi.org/10.3168/jds.S0022-0302(00)75192-7).
- Poindexter, M.B., Zimpel, R., Vieira-Neto, A., Husnain, A., Silva, A.C.M., Faccenda, A., 2023. Effect of prepartum source and amount of vitamin D supplementation on lactation performance of dairy cows. *Journal of Dairy Science* 106(2), 974–989. DOI: <https://doi.org/10.3168/jds.2022-22388>.
- Reinhardt, T.A., Lippolis, J.D., McCluskey, B.J., Goff, J.P., Horst, R.L., 2011. Prevalence of subclinical hypocalcemia in dairy herds. *Veterinary Journal* 188(1), 122–124. DOI: <https://doi.org/10.1016/j.tvjl.2010.03.025>.
- Rérat, M., Philipp, A., Hess, H.D., Liesegang, A., 2009. Effect of different potassium levels in hay on acid-base status and mineral balance in periparturient dairy cows. *Journal of Dairy Science* 92(12), 6123–6133. DOI: <https://doi.org/10.3168/jds.2009-2449>.
- Rukkwamsuk, T., Kruip, T.A.M., Wensing, T., 1999. Relationship between overfeeding and overconditioning in the dry period and the problems of high producing dairy cows during the postparturient period. *Veterinary Quarterly* 21(2), 71–7. DOI: <https://doi.org/10.1080/01652176.1999.9694997>.
- Satoła, A., Bauer, E.A., 2021. Predicting subclinical ketosis in dairy cows using machine learning techniques. *Animals* 11(7), 2131. DOI: <https://doi.org/10.3390/ani11072131>.
- Serrenho, R.C., Williamson, M., Berke, O., LeBlanc, S.J., DeVries, T.J., McBride, B.W., 2022. An investigation of blood, milk, and urine test patterns for the diagnosis of ketosis in dairy cows in early lactation. *Journal of Dairy Science* 105(9), 7719–7727. DOI: <https://doi.org/10.3168/jds.2021-21590>.
- Singh, A.K., Kerketta, S., Kumari, P., Mahesh, M.S., Rajak, S.K., Kumar, R., 2024. Recent developments in

- B-vitamin nutrition of dairy cattle. In: Mahesh, M.S., Yata, V. K. (Eds.), *Feed additives and supplements for ruminants*. Springer Nature Singapore, 399–421. DOI: https://doi.org/10.1007/978-981-97-0794-2_17.
- Sordillo, L.M., Mavangira, V., 2014. The nexus between nutrient metabolism, oxidative stress and inflammation in transition cows. *Animal Production Science* 54(10), 1204–1214. DOI: <https://doi.org/10.1071/AN14503>.
- Sordillo, L.M., Contreras, G.A., Aitken, S.L., 2009. Metabolic factors affecting the inflammatory response of periparturient dairy cows. *Animal Health Research Reviews* 10(1), 53–63. DOI: <https://doi.org/10.1017/S1466252309990016>.
- Steen, A., Gronstol, H., Torjesen, P.A., 1997. Glucose and insulin responses to glucagon injection in dairy cows with ketosis and fatty liver. *Journal of Veterinary Medicine Series A* 44(10), 521–530. DOI: <https://doi.org/10.1111/j.1439-0442.1997.tb01138.x>.
- Ster, C., Loiselle, M.C., Lacasse, P., 2012. Effect of postcalving serum nonesterified fatty acids concentration on the functionality of bovine immune cells. *Journal of Dairy Science* 95(2), 708–717. DOI: <https://doi.org/10.3168/jds.2011-4695>.
- Stewart, A.J., 2022. Hypomagnesemic tetany in cattle and sheep. In: *MSD Veterinary Manual*. Retrieved on: August 2022. Available from: <https://www.msddvetmanual.com/metabolic-disorders/disorders-of-magnesium-metabolism/hypomagnesemic-tetany-in-cattle-and-sheep>.
- Tamminga, S., 2006. The effect of the supply of rumen degradable protein and metabolisable protein on negative energy balance and fertility in dairy cows. *Animal Reproduction Science* 96(3–4), 227–239. DOI: <https://doi.org/10.1016/j.anireprosci.2006.08.003>.
- Urdaz, J.H., Santos, J.E.P., Jardon, P., Overton, M.W., 2003. Importance of appropriate amounts of magnesium in rations for dairy cows. *Journal of the American Veterinary Medical Association* 222(11), 1518–1523. DOI: <https://doi.org/10.2460/javma.2003.222.1518>.
- Venjakob, P.L., Borchardt, S., Heuwieser, W., 2017. Hypocalcemia-cow-level prevalence and preventive strategies in German dairy herds. *Journal of Dairy Science* 100(12), 9258–9266. DOI: <https://doi.org/10.3168/jds.2016-12494>.
- Wilhelm, A.L., Maquivar, M.G., Bas, S., Brick, T.A., Weiss, W.P., Bothe, H., 2017. Effect of serum calcium status at calving on survival, health, and performance of post-partum Holstein cows and calves under certified organic management. *Journal of Dairy Science* 100(4), 3059–3067. DOI: <https://doi.org/10.3168/jds.2016-11743>.
- Zhang, C., Shao, Q., Liu, M., Wang, X., Loo, J.J., Jiang, Q., 2023. Liver fibrosis is a common pathological change in the liver of dairy cows with fatty liver. *Journal of Dairy Science* 106(5), 2700–2715. DOI: <https://doi.org/10.3168/jds.2022-22021>.
- Zom, R.L.G., van Baal, J., Goselink, R.M.A., Bakker, J.A., de Veth, M.J., van Vuuren, A.M., 2011. Effect of rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle. *Journal of Dairy Science* 94(8), 4016–4027. DOI: <https://doi.org/10.3168/jds.2011-4233>.