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A Review on Protein Metabolism Disorder in Livestock-Analytical Approach

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Abstract:

Now a day's metabolic disorder is major cause of conern in high yielding livestock and poultry. Metabolic profiling tests, which are using specific parameters known to be responsive to dietary intake, can be used to complement dietary evaluation of current feeding programme adequacy or a response to a feeding programme change. Due to high productivity and environmental concern metabolic disorder are very common in lactating dairy animals and other livestock, so analytical approach with accurate diagnosis is very important for quick diagnosis and as per diagnosis treatment of livestock with leads to better health and productivity from livestock.

Introduction:

Metabolic profile test is the detection of low molecular weight metabolites and their intermediates from biofluids or tissues. It is used widely in many fields, such as pharmacology, toxicology, and diagnostics, and its use and technological development have increased rapidly (Zhang *et al.*, 2012). Metabolite changes that are observed in diseased individuals as a primary indicator have been an important part of clinical practice.

Many diseases are often discovered in an advanced stage because of the lack of specific symptoms and the diagnostic difficulties. The more advanced stage of diseases, the more invasive diagnostic and treatment interventions needed. An early molecular diagnosis is therefore of vital importance in order to increase the survival rate. A good diagnostic method should have the characteristics of high sensitivity, specificity, and functionality and meets the requirements of high throughput, portability, and low cost for subsequent clinical application (Nicholson *et al.*, 1999).

Routine Usage of Metabolic Profile Tests:

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Ration evaluation is the cornerstone of herd nutritional assessment, but can be fraught with uncertainty and difficulty in obtaining true measure of dry matter or nutrient intake. Metabolic profile tests are routinely used in dairy cattle farms to identify nutrition and management challenges; for example, to assess the nutritional status of healthy cows performing at an acceptable level in an attempt to identify and thereby recognise any nutritional problems before they emerge as a production or health related issue in the herd. Metabolic profiling tests, which are using specific parameters known to be responsive to dietary intake, can be used to complement dietary evaluation of current feeding programme adequacy or a response to a feeding programme change. Also, they help to identify or eliminate potential nutritional issues in cows or herds with poor performance records, high incidence of transition problems, low milk production, poor pregnancy rates, etc. In addition, these tests can be used to assess animals which are clinically healthy, but are not meeting milk production potential or reproductive efficiency (Anonymous, 2017; 2018b). Also metabolic profile tests as a screening tool can be used to assess prevalence of various subclinical metabolic diseases: ketosis, hypocalcaemia, hypomagnesaemia, subacuteruminal acidosis (SARA) and etc., in the absence of obvious clinical disease problems (Anonymous, 2017; 2018b).

Clinical or sub clinical metabolic disease problems in dairy herds can be corroborated with metabolic profile testing. Metabolic profile testing of a herd to finding the prevalence of SARA, sub-clinical ketosis (SCK), parturient hypocalcaemia (clinical plus subclinical milk fever), displaced abomasum and etc. in early lactation or other times is useful in almost any dairy herd, and particularly if the herd is experiencing a high incidence of displaced abomasum or high removal rates of early lactation cows (Oetzel, 2004).

Usually the metabolic profile measures glucose, urea, albumin, cholesterol, beta-hydroxybutyric acid (BHBA) and non-esterified fatty acids (NEFA) as well as some minerals (Na^{+}, K^{+}, Cl^{-}, Ca^{2+}, Mg^{2+},P^{3-}). These parameters can help assess total protein and energy intake, the bal-ance between protein and energy, and the net energy balance. Utilising a metabolic profile also allows screening for production limiting nutrients (Puls, 1989; Lager&Jordan, 2012; Anonymous, 2018b). Some problems may not be diagnosable from a metabolic profile alone; therefore it may be necessary to add other tests such as vitamin A and E, trace minerals, or routine chemistry panels (Anonymous, 2017; 2018b).

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Samples and Analysis of Metabolic Profile Tests Results:

Urine and blood serum or plasma are the most commonly used bio fluids for metabolic-based studies for the simple reasons that they both contain hundreds to thousands of detectable metabolites and can be obtained non- or minimally invasively. A number of other fluids such as cerebrospinal fluid, bile, seminal fluid, amniotic fluid, synovial fluid, gut aspirate and saliva have also been studied (Bollard ME., *et al.* 2005). More recently, metabolic profiling of intact tissue and its lipid and aqueous metabolites extracts is gaining more importance for biomarker detection (Griffin JL., *et al*, 2007).

Serum is the required specimen for metabolic profiling and most of the trace mineral and vitamin testing's. It is essential to collect blood and harvest serum appropriately and in a timely manner to avoid sample haemolysis and obtain consistent results. A significant delay in harvesting the serum from the clot can significantly change electrolyte results. It will also increase phosphorous, potassium, albumin and magnesium levels. In addition, haemolysis is a cause of misleadingly low blood glucose. Finally, haemolysis may contribute to unreliable non-esterified fatty acids (NEFA) and betahydroxybutyric acid (BHBA) results. If possible, blood samples should be centrifuged within 2–4 h, the sera separated and stored at –20 °C (–4 °F) until shipment (Anonymous, 2017; 2018b).

After evaluation of samples, data must be statistically analysed via accurate data analysis method. The aims of data analysis in metabolic profiling will depend on the scientific objectives of the study which typically fall into one or more of the following categories. Firstly, one of aims is to reveal the relationships between groups of both samples and variables. For example, this could include clustering individuals, or detecting significant correlations between variables. A second aim could be to identify a significant difference between groups related to the effect of interest. Finally, and perhaps most importantly, metabolites responsible for these changes should be found out. There are several statistical methods for analysis of metabolic profile tests introduced by different scientists (Burnham *et al*., 1999; Butler & Denham, 2000; Trygg & Wold, 2003), also several metabolic profile analysis software packages are available (Davies, 1998). Statistical methods for analysis of metabolic profile test including principal components analysis, principal components regression, partial least squares, etc. are reviewed in details by De Iorio*et al*. (2008).

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Finally, analysed results are compared to reference values. Different reference values of metabolic profile parameters for different breed, different production level, different ages, etc. of cows were repeatedly reported in different countries (Puls, 1989; Whitaker *et al.*, 1999; Kida, 2002; Lager & Jordan, 2012; Anonymous, 2017; 2018a,b). The different steps of blood metabolic profile tests are illustrated on Fig. 1.

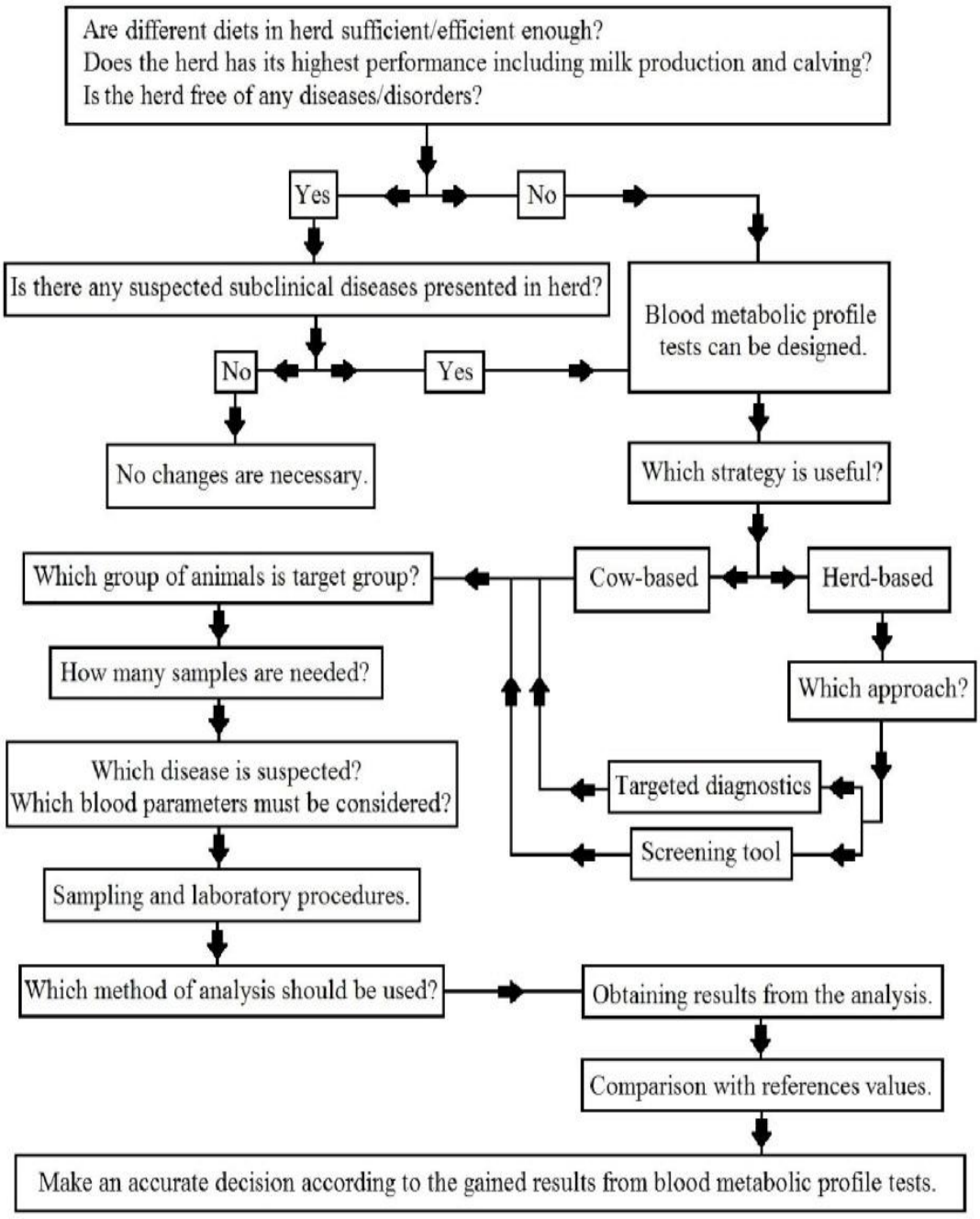

Fig. 1: Different steps of blood metabolic profile tests design

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Protein metabolism related diseases in livestock which is listed below:-

1. Ketosis:

Ketosis is one of the most prevalent metabolic diseases of dairy cows during transition period. Metabolic disturbances of ketosis involve in multi-biochemical pathways such as **gl**ycolysis, gluconeogenesis, amino acids metabolism, fatty acids metabolism, pentose phosphate pathway.

Protein Metabolites used for identification of ketosis

Metabolites	**Remarks**
Up-regulated amino acids and their catabolic products – Glycine, lysine (2-Increased piperidinecarboxylicacid),3-hydroxyvalericacid(3HV),3-hydroxy-3-methylglutaric acid (HMG), isoleucine (2-methyl-3-hydroxybutyric acid(2Me3HB)	
Leucine (3-hydroxyisovaleric acid (3HIV)), 4-aminobutyric acid (GABA) - L- Decreasedglutamic acid catabolism, melibiose from galactose metabolism, erythritol, aprecursor of fructose 6-phosphate, and l-serine (L-ser)	

2. Abomasal displacement:

Abomasal displacement [left (LDA), right (RDA) or anterioventral displacement of the abomasum] is an infrequent gastrointestinal disorder typically occurred in high producing dairy animals. The factors which responsible for the abomasal displacement are

1. Abomasalhypomotility due to mastitis, milk fever, metritis and genetic predisposition
2. Feed origin - High-concentrate, low-roughage diets
3. Other conditions – ketosis, fatty liver syndrome and phytobezoars.

Metabolites	**Remarks**
Valine, 3 β-hydroxybutyrate, alanine, glutamine andglutamate	Increased in RDA conditions
Succinate	Decreased in LDA condition

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It is demonstrated that NEFA concentration is higher in displaced abomasum cows than in healthy cows (least squares means 1.36 vs. 0.34 mmol/L), also BHBA concentration was higher in displaced abomasum cows than in healthy cows (1.56 vs. 0.90 mmol/L), same is true for aspartate aminotransferase (1.96 vs. 0.97 µkat/L), glutamate dehydrogenase (197 vs. 78 µkat/L), and haptoglobin (0.76 vs. 0.17 g/L), whereas lower concentrations of insulin (3.61 vs. 8.48 mU/L) and cholesterol (3.04 vs. 3.75 mmol/L) were iden-tifiedin displaced abomasum cows. Differences in glucose concentration (2.83 vs. 2.79 mmol/L), and most of blood parameters between displaced abomasum cows and healthy cows remained constant over time. Haptoglobin could potentially be used to detect treatable infectious or inflammatory conditions in the early post-partum period, possibly reducing the incidence of displaced abomasum. Totally, major changes in metabolic profile parameters occur in cows with displaced abomasum compared with healthy cows, which indicating a negative energy balance, liver cell damage, and an inflammatory response (Stengarde*et al*., 2010).

3. Retained placenta (RP):

Retained placenta (RP) is a common disease in dairy cattle farms which is related to immune function, with changes in neutrophil function and interleukin (IL)-8 levels at least two weeks before calving (Kimura *et al*., 2002). Cows suffering from RP had substantially higher serum cortisol for several days before parturition (Peter &Bosu, 1987) which may be one contributor to impairment of neutrophil function (Burton *et al*., 1995). Similarly, endometritis is associated with (preceded by) impaired innate immune function (Sheldon *et al*., 2009), and differences in IL-1, IL-6, and IL-10 expression (Herath*et al*., 2009), again with measurablechanges in phagocytosis, TNFα and IL-6 present prepartum (Kim *et al*., 2005), weeks before disease becomes manifest, coincident with the onset of insulin resistance and lipolysis (at least in cows at higher risk of disease). Cows in greater negative energy balance, and in particular those that go on to have metritis or endometritis have more pronounced impairment of at least some immune functions (Hammon*et al*., 2006). Cows in a greater negative energy balance prepartum, as evidenced by higher NEFA concentrations were 80% more likely to have RP, and accounting for the effect of NEFA, those with lower circulating vitamin E were at greater risk of RP (LeBlance*et al*., 2004). This supports the notion that severe negative energy balance impairs the immune function, which in turn makes

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RP more likely, but also underlines the fact that the development of RP is multifactorial (LeBlance, 2010).

4. Metritis:

Cows with severe metritis eat 2 to 6 kg/day and their dry matter intake is less than that of healthy cows in the 2 to 3 weeks preceding the clinical signs of metritis (Huzzey*et al*., 2007). Lower feed intake is associated with increased NEFA which contributes to the risk of fatty liver (Herdt, 2000), which in turn is associated with impaired neutrophil function (Zerbe*et al*., 2000). Additionally, NEFA have been shown to inhibit neutrophil function *in vitro* (Scalia *et al*., 2006).

5. Ovarian cysts:

Periodic metabolic tests also can be used for diagnosis of reproductive diseases like ovarian cysts; it is identified that ovarian cysts are associated with low serum concentrations of glucose, insulin and urea as well as high levels of cortisol. Also in addition to hormonal imbalances, metabolic disorders are involved in the formation and/or persistence of ovarian cysts. Therefore, the use of metabolic indicators in understanding and exploration of ovarian cysts is very important and useful (Mimoune *et al*., 2017). It is also identified that follicular cysts in buffaloes are associated with altered biochemical and hormonal compositions. The alterations include increased nitric oxide, progesterone, cortisol and T_3 levels with a concurrent reduction in ascorbic acid, insulin and glucose concentrations (Khan *et al*., 2011).

6. Mastitis:

Metabolic parameters and blood leukocyte profiles in cows from herds with high and/or low mastitis incidence indicate that the plasma concentrations of BHBA, glucose, insulin and urea do no change due to mastitis, but NEFA concentration is significantly higher among high mastitis in-cidence cows three weeks after parturition. The concentration of the amino acid tryptophan in plasma is also significantly lower among the high mastitis incidence cows prior to parturition. Glutamine is significantly lower in cows from high mastitis incidence herds during the first three weeks after parturition. Arginine is consistently lower in high mastitis incidence cows. Although the decrease is only significant during the period from four to fifteen weeks after parturition, there are differences in the metabolism and immune status between herds with high or low yearly mastitis treatment incidence, indicating an increased metabolic stress in high mastitis incidence cows (Holtenius *et al*., 2004).

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Conclusion:

Metabolic profile parameters are important tool for detection of important sub-clinical diseases including: ketosis, milk fever, mastitis, cystic ovaries, displaced abomasum and metritis etc. Apart from this common use of metabolic profile test is for evaluation of nutritional status, and because of easy sampling method, low fees and simple analysis of results, it also can be considered as a good choice in diagnosis of disease.

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