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Review

BLOOD METABOLIC PROFILE TESTS AT DAIRY CATTLE FARMS AS USEFUL TOOLS FOR ANIMAL HEALTH MANAGEMENT

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Summary

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Blood metabolic profile tests are simple cost-effective biochemical tests which are mostly used to identify nutritional and/or management challenges in dairy cattle herds, but they also can be simply used to find animals which are clinically healthy, but really have some hidden problems like low production performance, reproductive diseases and/or long calving intervals and other sub-clinical diseases. Routine metabolic profile tests commonly consist of blood glucose, urea, albumin, cholesterol, beta-hydroxybutyric acid and non-esterified fatty acids values, as well as sodium, potassium, chloride, calcium, magnesium and inorganic phosphate levels. Briefly, the current review discusses blood metabolic profile tests, their importance, introduces an easy method for it, emphasises on the relation between blood metabolic profile parameters and many important sub-clinical diseases including ketosis, milk fever, mastitis, cystic ovaries, displaced abomasum and etc., and indicates that because of its simplicity, low cost and easy for analysis results, it can be considered as a good method for diagnosis of important diseases at dairy cattle farms.

Key words: dairy cattle, diseases, financial damages, metabolic profile, nutritional status

INTRODUCTION OF METABOLIC PROFILE TESTS

Diagnosis and/or prevention of diseases has priority to their treatment taking into consideration financial costs, induced delay in production period etc. In this way, practitioners are always trying to monitor the health state of animals in order to prevent severe diseases which could incur financial losses. They believe that the best methods for monitoring must be

efficient, economic, easy, fast and precise and with the lowest effect and/or stress on animal's health, so they are always seeking for the best methods. One of the best ways to judge about health status of animals is monitoring their blood parameters. Each blood parameter has an important role in animal's health due to the impact of a deficiency, toxicity and/or adverse elevation. For example, when the levels of the calcium ion are low, hypocalcaemia or milk fever could be present because the cow is removing more calcium from the body for milk production than can be absorbed by the body from the diet or mobilised from calcium stores in the bones. Because of the extensive relationship between minerals within the body, an impact on calcium levels may affect phosphorous levels too, which may be seen in cows experiencing milk fever that do not respond even after successful treatment for hypocalcaemia (Goff, 2004).

For every animal species, it is possible to categorise the most important parameters with similar effect on a specific health subject in a particular group. In this way, it is not necessary to monitor all of the existing parameters for every healthy subject at the same time. For example, not all but some of blood parameters, which have effect on dairy cattle's health status during the different lactation periods, can be classified in different particular groups. For example, metabolic profile, which categorises several important parameters with influence on metabolism of animals in a specific group, is a useful tool that has evolved over time. This evolution or adaptation is necessary to account for changes in feeding management and animal genetics. The reference values of course should match the stage of lactation (Quiroz-Rocha *et al*., 2009).

ROUTINE USAGE OF METABOLIC PROFILE TESTS

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, sub-acute ruminal 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), dis-

placed 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).

HISTORY, DESIGN AND PURPOSE OF FIRST METABOLIC PROFILE TEST

For the first time in 1970, the Compton metabolic profile test was designed to monitor the metabolic health of the herd on the basis of interpretation of blood chemistry in a dairy herd. Originally it included glucose, urea, inorganic phosphate, calcium, magnesium, sodium, potassium, albumin, globulin, haemoglobin, and copper. The test was designed to detect abnormal accumulations or deficiencies of certain key metabolites. Thus considerable effort was devoted to finding the precise limits of normality and the causes of variation. For this test, to serve its intended function, it was necessary to define the limits of a normal profile as well as determine the sources of variation. To establish a profile along with the proper ranges for normal animals, a survey was conducted of 13 dairy herds encompassing 2400 blood samples focusing on three groups: early lactation, mid-lactation, and dry period. A mean and standard deviation were calculated and samples from herds were then compared to the established profile to determine the health status of the animal by evaluating the number of standard deviations from the mean (Payne *et al*., 1970).

The main purpose of the Compton metabolic profile test is to indicate whether a herd is liable to nutritional and production diseases. The test is based on a statistical appraisal of blood chemistry which reveals early signs of abnormality. It is a pre-symptomatic diagnostic aid capable of giving early warning of certain types of metabolic derangement. Also, in cases where the herd already has a high but possibly unsuspected incidence of production disease, the test can give an indication of the underlying primary cause. All the factors in metabolic profile have been shown to play an important role in animal health (Payne, 1972).

COW-BASED AND HERD-BASED METABOLIC PROFILE TESTS

Metabolic profile tests utilise the same clinical chemistry tests performed in disease diagnosis. Usually testing methods are herd-based rather than individual-based (Anonymous, 2017; 2018b). The interpretation of herd-based tests for metabolic and nutritional diseases is very different from interpreting laboratory results for metabolites from individual cows. Test results from individual cows are interpreted by comparing the laboratory result to a normal range established by the laboratory. The latter are often derived by calculating a 95% confidence interval (or a similar statistic) of test results from clinically normal animals. This approach is useful for making decisions about individual sick cows, but is not useful for interpreting herd-based test results. Interpretation of herd-based test results requires an understanding of how each test affects cow performance (regardless of whether they are within the normal range or not), a statistically-based approach to determining subsample sizes, and an emphasis on monitoring subclinical disease prevalence instead of clinical disease incidence (Oetzel, 2003; 2008).

Herd-based testing can be categorised into two approaches: targeted diagnostics and screening tool. The targeted diagnos-

tic approach utilises well defined diagnostic analysis to determine herd risk for specific "gateway" pre-parturient diseases. In other words, the targeted diagnostic approach attemps to find a disease via evaluation of specific parameters, for example: elevated prepartum non-esterified fatty acids (NEFA) concentration and postpartum beta-hydroxybutyric acid (BHBA) concentration are recognised risk factors for ketosis and left displaced abomasum. Low blood calcium concentration immediately post-calving is a risk indicator for subclinical hypocalcaemia. Blood urea nitrogen (UN) is a potential indicator for assessing herd protein status. In this approach, specific analysis concentration is determined and compared to specific threshold criteria. Percent of individuals above (NEFA and BHBA) or below (calcium) is used to interpret herd disease risk. UN values are interpreted as a mean value for the individuals within a defined group (Anonymous, 2018a,b). The screening tool approach is consistent with traditional metabolic profiling methods where multiple analyses are determined within selected group or groups of cows. Determination of multiple analyses is based on the concept that pre-parturient metabolic disease is a result of the cow's inability to maintain coordinated interrelationships between lipid, glucose and amino acid metabolism (Anonymous , 2017; 2018b).

For individual testing, lower testing costs and ease of interpretation are strengths of this approach and limitation of this approach is scope of analysis determined (Anonymous, 2018a,b). A screening tool approach can be used as a broad-based diagnostic evaluation of herd nutritive status, assessment of disease risk factors, or indicator of potential factors responsible for disease conditions. Limitations to the screening tool approach are testing costs and potential interpretation issues. A pooled-sample process has been recmmended to address cost concerns and maintain a wide analysis array in assessing herd nutritional or disease risk status. Predictive disease risk relationships have been well established with specific analysis, though multiple analysis indices or analysis combinations may provide a better indication of metabolic stability or instability (Anonymous, 2018b).

Selection of accurate approach for metabolic profile test's sampling

Which method to be used in evaluating a herd will depend upon the specific problem, herd size, and cost limitations. Smaller dairy herds (< 120 cows) will not have a large enough population of animals to be sampled within defined physiologic groups for the screening tool approach compared to large herds. With limited animal numbers, individual cow testing or collecting samples over time are possible approaches. Costs are the single most limiting factor to metabolic profiling. At this time, multiple analyses testing services range in cost from $17 to $50 per sample depending on the number of blood analysis measured and laboratory pricing structure. This makes individual testing in multiple groups nearly cost prohibitive, thus the rationale for pooled samples. Using the single analysis approach, cost may range from $3 to $10 per sample depending on the analyte. If the size of herd is large enough, then the herd testing method is recommended depending on the purpose of metabolic profile tests (Anonymous, 2018).

Selection of target animals, effective factors and number of animals

In the first step, the herd situation should be defined e.g. to find the group that has a

problem in the farm. In a dairy farm it is easy to find such a group via categorising animals according to their age, production, weight or etc. Attention should be paid to the other related factors. Diets, seasons, geographical areas, animals breed, production system, altitude of area, temperature of area, etc., are also important issues which should be considered in designing of metabolic profile tests (Jones *et al*., 1982; Ghergariu *et al*., 1984; Amano *et al*., 1992). For example, performance and biochemical parameters of animals with different genetic potential and breed are different, in addition different seasons, different production system, management level and geographical areas with different altitude and temperature and other environmental factors with obvious influence on biochemical parameters and performance of animals which should be considered in design of metabolic profile tests. One of the best categorising methods is dividing of animals to different groups according to their production status. In this way animals can be divided to far-off dry, close-up dry (pre-parturient), fresh (post-parturient) and lactation groups. Then, the health status of each group and any nutritional and/or related subclinical diseases can be simply identified. The group(s) of cows selected for analysis will depend upon the problem definition and desired sampling approach (Anonymous, 2017; 2018b).

Selected animals in groups for a metabolic profile test should be free of obvious clinical disease via selecting cows defined as "clinically normal", analyte outlier concentrations associated with disease are removed, thus better highlighting potential differences resulting from nutritional or subclinical disease problems. One may choose to sample cows affected with specific diseases for comparison to cows of similar days in milk that are not affected. Differences in blood concentrations between clinically affected and unaffected cows may provide some hints to underlying problems associated with disease pathogenesis (Anonymous, 2018b).

Size of the eligible group for testing has a limited influence on the appropriate sample size. In larger herds, there is little statistical value in testing more animals. The same sample size will yield almost the same information about the group average even when the group is large. In smaller herds, it may be possible to test the entire eligible group and still not have an adequate sample size. For example, only the pre-fresh cows (from three weeks prior to expected calving up to calving time) are eligible for urinary pH and NEFA testing. If there are only four cows in the group, then all four should be tested. However, a sample size of four cows is too small to be conclusive. So, additional cows should be tested from the eligible group, and the group results interpreted only after about eight or more test results have been accumulated. If cows are repeatedly tested for NEFA or urinary pH as they approach calving, only the last test result before actual calving for that cow should be used when interpreting test results (i.e., multiple test results from the same cow should not be used to achieve sample size goal). Sample sizes larger than the minimums recommended above are most useful when the herd's clinical problems are minimal. Larger sample sizes are usually more practical in larger herds, because there are more cows available to test and because the cost of each test is diluted across a larger number of cows. The economic cost of a bad decision based on small sample size is also greater in large herds (Oetzel, 2003; 2008).

RELEVANT ROUTINE BLOOD BIOCHEMICAL MARKERS

Metabolic profile tests can evaluate several biochemical parameters depending on the goal but the complexity of energy metabolism often makes difficult the selection of reliable indicators of the energetic status of cows (Nafikov & Beitz, 2007; García *et al*., 2017). The main blood analytes used to assess the energy profile are: glucose (GLU), which should be interpreted carefully to avoid errors related to food intake (Šamanc *et al.*, 2011; García *et al*., 2017), cholesterol (COL-T), to be used to jointly evaluate the performance of nutrition programmes (Kaneko, 2008; García *et al*., 2017), triglycerides (TAG), lipids that circulate in the blood, used by a cell to produce adenosine triphosphate (ATP) (Kaneko, 2008; García *et al*., 2017), β-hydroxybutyrate (β-HBA), which is the most important and abundant ketone body in dairy cows (Duffield *et al.*, 2009; García *et al*., 2017), and non-esterified fatty acids (NEFA), which are related to lipomobilisation and to the degree of negative energy balance (NEB) (Ospina *et al.*, 2010a; García *et al*., 2017). The essential blood analytes for assessing the protein profile are: blood urea nitrogen (BUN), a good indicator of the energy intake of the cow, in particular it is used as an indication of the synchronisation between fermentable carbohydrates and rumen degradable protein (RDP) (Van Saun, 2010; García *et al*., 2017), albumin (ALB), that can reflect hepatic insufficiency by decreasing its concentration (Whitaker, 2000; García *et al*., 2017), globulin (GLOB), that is increased in response to an inflammatory process (Kaneko, 2008; García *et al*., 2017), and total protein (PROT-T), that gives information about kidney damage, liver damage, and nutritional health (Stojević *et al.*, 2005; García *et al*., 2017). The enzyme γ-glutamyl transpeptidase (γ-GT) is an essential indicator of hepatic lesions and function (Stojević *et al.*, 2005; García *et al*., 2017).

Considering the use of body tissues in response to NEB, the produced ketone bodies (by its acidic nature) decrease the natural buffering capacity of bicarbonate (HCO^{3-}), increasing the anion gap in the blood, and causing changes in pH by movements of electrolytes, water, and carbon dioxide (CO_2) (Herdt *et al.*, 2000; García *et al*., 2017). The essential blood analytes of the mineral profile are: sodium (Na^+), the main extracellular fluid cation and an important determinant of body water homeostasis (Kume *et al.*, 2011; García *et al*., 2017), chloride (Cl^-), the most abundant anion in extracellular fluid (Soetan *et al.*, 2010; García *et al*., 2017), potassium (K^+), the principal intracellular cation in mammals (Van Saun *et al.*, 2006; García *et al*., 2017), and calcium (Ca^{2+}), phosphorus (P^{3-}), and magnesium (Mg^{2+}) due to their importance in the rapidity of metabolic reactions and their role in the transmembrane transport systems (Houillier, 2014; García *et al*., 2017).

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 balance 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, 2018a,b). 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).

SAMPLES AND ANALYSIS OF METABOLIC PROFILE TESTS' RESULTS

Serum is the required specimen for metabolic profiling and most of the trace mineral and vitamin testings. 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 beta-hydroxybutyric 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; Stein, 1999). 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).

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.

METABOLIC PROFILE TESTS AND DETECTION OF DIFFERENT DISEASES

If the parturition be considered as the start point of every production cycle in dairy cattle's life and interval between the parturitions be considered as one cycle, then four important periods for each cycle can be classically introduced and thus and cows in every dairy cattle farm can be categorized to four different groups including: fresh (transition or post-parturient period) cows, lactation cows, far-off dry cows and close-up dry (pre-parturient) cows. Biology of dairy cow health and reproductive performance is complicated and dairy cattle are experiencing different physiological conditions in these periods and different diseases can occur in each of mentioned periods due to effects of several factors. Among these periods, parturition and post-parturition period are more critical than others and

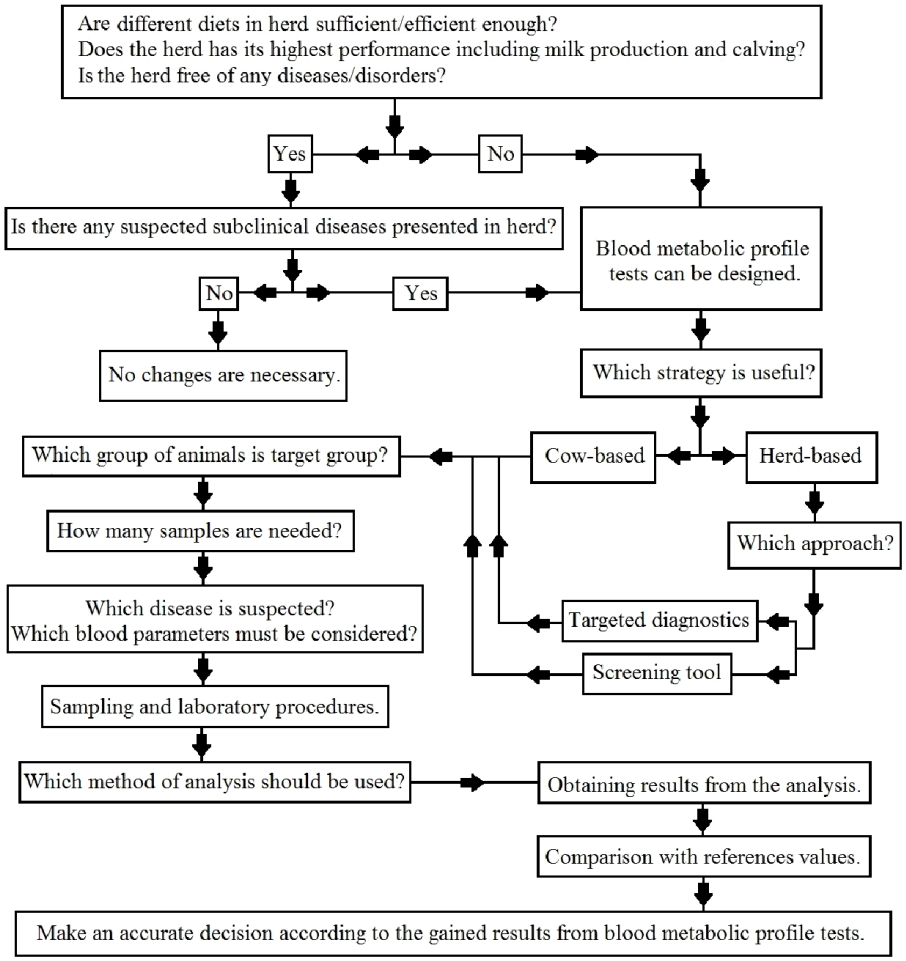

Fig. 1. Different steps of blood metabolic profile tests design.

30 to 50% of dairy cows are affected by some form of metabolic or infectious disease around the time of calving (LeBlance, 2010). In this way different diseases can be categorised according to their occurrence in two different periods: different diseases/disorders which are highly occurring in the early period after calving (transition or post-parturient period) including: retained placenta, milk fever, ketosis and/or sub-clinical ketosis, displaced abomasum, ovarian cysts, mastitis, endometritis, etc. and other diseases which occur in all other periods (fatty liver syndrome, ruminal diseases). This categorisation is used to focus on a specific group of animals and/or diseases and to facilitate metabolic profile tests designs.

There are several factors with absolute effects on interaction between different diseases and mentioned periods, on the other hand, this categorisation for diseases can be influenced by several factors including: different management, environmental stresses, different diets, prevalence of infectious diseases, etc., and may be some of these diseases can be found in the other period not exactly according to this categorisation (Jones *et al*., 1982; Ghergariu *et al*., 1984; Amano *et al*., 1992). In this review, different diseases and changes in blood metabolic profile parameters related to the both mentioned periods are discussed in details.

TRANSITION PERIOD AND/OR POST-PARTURIENT PERIOD

Transition from non-lactating pregnant state to a lactating state for the cow is recognised as the critical threshold in achieving a productively efficient lactation with potential for good reproductive performance. During this transition, cows usually experience one or more preparturient diseases (Goff & Horst, 1997). Also metabolic responses to stress can result in increased fat mobilisation leading to greater risk from fatty liver disease, wasting of muscle tissue and immune suppression (Ametaj *et al*., 2005; Bernabucci *et al*., 2005; Bertoni *et al*., 2008; 2009). Also all pre-partum dairy cattle essentially experience: a period of insulin resistance, reduced feed intake, negative energy balance, lipolysis, and weight loss in early lactation; hypocalcaemia in the days after calving; reduced immune function for 1 to 2 weeks before, and 2 to 3 weeks after calving; and, bacterial contamination of the uterus for 2 to 3 weeks after calving. These factors, as well as dramatic changes in circulating progesterone, estrogen, and cortisol concentrations contribute to a substantial reduction of immune function, in particular of neutrophils, at this time (Kehrli *et al*., 1989; Goff & Horst, 1997). Specifically, innate immunity from neutrophils is a primary means of immune response in the uterus and neutrophil migration and phagocytic and oxidative activity are associated with the risk of retained placenta (Kimura *et al*., 2002), metritis, and endometritis (Hammon *et al*., 2006). Yet, while metabolic (e.g. ketosis and fatty liver) and uterine diseases are very common, only a minority of cows experience these problems, between herds or even within a herd in which cows apparently have similar nutritional and management experiences. Prediction or early detection of cows with health problems is an important goal (LeBlance, 2010).

Application of blood testing has been shown to provide useful information for the herd relative to disease risk for postpartum disorders. Best studied and practically applied is routine measurement of blood beta-hydroxybutyric acid (BHBA) concentration in all cows at least twice within the first 7–12 days postpartum. Cows having >1.2 mmol/L BHBA can be treated to reduce hyperketonaemia. If more than 25% of sampled cows have hyperketonaemia, then blanket treatment of fresh cows should be initiated. Additionally, elevated non-esterified fatty acids (NEFA) prepartum (>0.3 mmol/L) or postpartum (>0.6 mmol/L) can be used to assess postpartum disease risk for the herd. Assessment of blood calcium concentration (<2.12 mmol/L) during the immediate postpartum period also provides another useful disease risk indicator. Other blood analysis specific to liver function, protein status, macro- and micro minerals and vitamins could be included as part of a comprehensive herd diagnos-

tic investigation of nutritional or disease factors responsible for herd's performance or health concerns. Though some variation may be masked, pooled sampling may be used as an economic approach to a herd metabolic status screening tool. Pooled samples can represent means from 5 to 20 individual samples. Empirically one can interpret pooled samples by determining how far they deviate from the midpoint of the reference range for healthy individuals. Most importantly it must be remembered that metabolic profiles are almost useless without being coupled with animal and facility evaluations, body condition scoring and ration evaluation (Van Saun, 2016).

It is identified that both prepartum NEFA and postpartum BHBA are significantly associated with development of clinical disease, postpartum serum NEFA concentration is most associated with the risk of developing displaced abomasum, clinical ketosis, metritis, or retained placenta during the first 30 days (Ospina *et al*., 2010b). Also because of the prevalence of disease within the pre-parturient period, a reference profile based on mid-lactation cows will limit the interpretation of data from cows within the transition period. By understanding the fluctuations that occur in serum biochemical analytes over the course of lactation, especially within the transition period, the value of the metabolic profile as a tool to differentiate between normal and compromised animals will be enhanced (Lager & Jordan, 2012). Important diseases which are mostly occurring in transition period or post-parturient period are described in details below.

Fatty liver syndrome

Fatty liver syndrome is not specific for post-parturition period but occurs mostly after parturition due to mentioned changes in dairy cattle's body at calving and is closely related to the poor management of diets. Lipid and lipoprotein fraction is changed, which take place simultaneously in the liver, during fatty liver. In ruminants almost no plasma lipids arise from ingested fat. Most of them are the result of *de novo* synthesis (Sevinç *et al*., 2003). Fat is stored as triglycerides and from the deposits it is transported as free fatty acids bound to albumin (Holtenius, 1989). Albumin is an important indicator for the liver's synthetic function (West, 1990). Hepatic function can be severely impaired by fatty infiltration of the liver. One of the many results of impairment of liver function is a drop in serum albumin levels (Haass & Eness, 1984). Hypoalbuminaemia is a common terminal feature of chronic liver disease, occurring when the functional hepatic mass has been reduced to 20% or less and albumin level is lower in cows with liver failure than in cows with fatty liver (Dunn, 1992). There is a negative correlation between the degree of fatty changes and albumin levels in dairy cows (West, 1990).

High serum free fatty acid concentrations and low serum triglyceride and cholesterol concentrations have been observed in cattle with fatty liver (Roberts & Reid, 1986; Herdt, 1988; Sevinç *et al*., 1998). Naturally triglyceride levels decrease in normal cattle after calving (Başoğlu *et al*., 1998). Lipoproteins are complex molecules that are heterogeneous in composition, size and biological activity. In early lactation in cows with a severe negative energy balance, the capacity of the liver to maintain the export of triglyceride in the form VLDL in balance with hepatic triglyceride production is not always adequate (Holtenius, 1989; Bauchart, 1993; Grummer, 1993). Very

low density lipoprotein (VLDL) level is extremely low two weeks after calving in cows with fatty liver (Rayssiguier *et al*., 1988). It is significantly decreased in postpartum cows (Başoğlu *et al*., 1998). There is a significant decrease in the VLDL level of fatty liver cows, also there is a negative correlation between the VLDL level and fatty liver (Sevinç *et al*., 2003). This may show that a major factor contributing to the development of fatty liver is the chronic slow output of hepatic triglyceride, which forms part of the VLDL. Other studies have already noted that the accumulation of fat in the liver cells and development of fatty liver is caused by a reduced synthesis of VLDL (Rayssiguier *et al*., 1988; Holtenius, 1989; Grummer, 1993; Başoğlu *et al*., 1998; Sevinç *et al*., 1998). Reduced VLDL synthesis is most probably associated with feeding factors (Holtenius, 1989). The decrease in LDL is especially pronounced in cows with severe fatty liver. During the same period, animals in the moderate fatty liver group were no different from the controls regarding LDL levels. In contrast, by the fourth week animals with moderate fatty liver have an LDL fraction that is significantly lower than controls (Rayssiguier *et al*., 1988; Sevinç *et al*., 1998).

Ketosis and sub-clinical ketosis

Ketosis is associated with reduced reproductive performance, which extends its impact much longer than many producers realise. It is worth emphasising that health in the weeks before and after calving influences reproduction at least 2 months later. Cows with milk BHBA >100 μmol/L in the first week postpartum were 1.5 times more likely to be anovular at 9 weeks postpartum (Walsh *et al*., 2007a; LeBlance, 2010). Cows that experienced ketosis in the first two weeks of lactation had reduced probability of pregnancy at the first insemination. Furthermore, cows that had ketosis in one or both of the first two weeks after calving had a lower pregnancy rate until 140 days in milk. The median interval to pregnancy was approximately 108 days in cows without ketosis, was significantly longer (124 days) in cows with ketosis in the first or second week postpartum, and tended to be longer still (130 days) in cows that had subclinical ketosis in both of the first weeks of lactation (Walsh *et al*., 2007b; LeBlance, 2010).

Also, more than 90% of subclinical ketosis (SCK) cases occur in the first and second months after calving. During this period, approximately 40% of all cows are affected by SCK at least once, although the prevalence is highest in the first and second weeks after calving. A monitoring programme that requires testing each cow for SCK in the first and second weeks after calving would identify nearly 90% of the SCK cases occurring the first and second months after calving (Geishauser *et al*., 2001). If cows are experiencing subclinical ketosis (SCK) within the first 3 weeks of lactation, then non-esterified fatty acids (NEFA) testing should be considered to corroborate negative energy balance (Oetzel, 2004).

The overall prevalence of SCK as determined by use of beta-hydroxybutyric acid (BHBA) threshold concentrations of 1000, 1200, and 1400 μmol/L, respectively is found to be 30.7%, 19.3% and 13.6%. Pooled sample concentrations of NEFA and BHBA are very appropriate for highly accurate herd-based detection of SCK. Also, analysis of NEFA and BHBA concentrations in pooled serum samples is useful for herd-based detection of SCK. Sample size of 10 cows/herd is deemed adequate for monitoring dairy

herds for SCK. Reference criteria specific to pooled samples should be used for this type of herd-based testing (Borchardt & Staufenbiel, 2012).

Displaced abomasum

Metabolic disease that becomes clinically manifest as displaced abomasum, typically around 10 days postpartum, is preceded by significant changes in adipose mobilisation and energy metabolism up to 3 weeks before the disease event. Periodic metabolic profile tests can also help to identify displaced abomasum syndromes. In pregnant cows with left displaced abomasum (LDA), from 14 day before calving mean NEFA serum concentrations began to diverge from mean levels in cows without left displaced abomasum, whereas mean serum BHBA concentrations do not diverge until the day of calving. Prepartum, only NEFA concentration is associated with risk of subsequent LDA. Between 0 and 6 days before calving, cows with NEFA concentration > or =0.5 mEq/L are 3.6 times more likely to develop LDA after calving. Between 1 and 7 days postpartum, retained placenta, metritis, and increasing serum concentrations of BHBA and NEFA are associated with increased risk of subsequent LDA. However, considered separately, postpartum serum BHBA is a more sensitive and specific test than NEFA concentration. Serum calcium concentration is not associated with LDA. Strategic use of metabolic tests to monitor transition dairy cows should focus on NEFA in the last week prepartum and BHBA in the first week postpartum (LeBlance *et al*., 2005).

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 identified in 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 postpartum 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).

Uterine diseases

To achieve the economic objective of pregnancy within 80 to 120 days after the previous calving, the uterus must return to a condition to support a new pregnancy, and a regular estrus cycle must be reestablished. This is the result of a complex set of interactions and endocrine signalling among the brain, liver, ovaries and uterus (Wathes *et al*., 2007; LeBlance, 2010). It is increasingly clear that uterine disease that is expressed 1 to 8 weeks after calving, and return to a normal estrus cycle and ovulation by 9 week after calving are preceded by metabolic and immunologic changes before and soon after calving. While metabolic and immune function can be studied in detail for research, there are indicators or surrogate measures that can be practical for clinical

use (LeBlance, 2010). Contamination of the uterus with potentially pathogenic bacteria is nearly universal after calving, yet only a minority of cows develop clinical disease. Similar to retained placentae (RP), development of metritis depends largely on immune function in the early postpartum period (Sheldon & Dobson, 2004; Hammon *et al*., 2006; LeBlance, 2010).

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

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). Healthy cows clear the uterus of bacteria by approximately 3 weeks postpartum but important gaps remain in understanding of the immunobiology of the reproductive tract of cattle. Approximately 17% of cows fail to clear bacterial infection and have clinical endometritis (LeBlance *et al*., 2002) and an additional 15 to 20% have chronic subclinical inflammation (Gilbert *et al.,* 2005). Uterine infection predominated by *Escherichia coli* in the first week postpartum and *Trueperella pyogenes* (formerly *Actinomyces pyogenes*) in the third week is associated with subsequent endometritis (LeBlance, 2008). Both forms of endometritis are closely associated with substantial decreases in pregnancy rate (LeBlance, 2010). It is also identified that endometritis makes lower albumin concentrations throughout the calving transition period; perhaps indicating impaired liver function, with lower plasma magnesium and evidence of hepatocellular damage in early lactation. Similar profiles of non-esterified fatty acids (NEFA) and glucose indicate that energy status is not a risk factor for endometritis (Burke *et al*., 2010).

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).

LACTATION, FAR-OFF DRY AND CLOSE-UP DRY PERIODS

In these periods, health status of dairy cattle becomes normal and usually they do not have severe problem/diseases in these periods, but even in this condition some diseases can occur, which are described below. Note that these diseases can also occur in transition period but with lower probability than other above mentioned transition period diseases.

Milk fever

Some of the animals, diagnosed as having milk fever, show a high frequency of hypocalcaemia within the general range from 0.69 to 2.73 mmol Ca/liter. Also blood osteocalcin level is significantly lower in hypocalcaemic animals, indicating that synthesis of bone is arrested during hypocalcaemia (Larsen *et al*., 2001). Assessment of blood calcium concentration (< 2.12 mmol/L) during the immediate postpartum period provides useful disease risk indicator for occurrence of clinical or subclinical milk fever (Van Saun, 2016). The critical margin concentration for calcium in dairy cattle is ≤2.0 mmol/L and concentrations below this can make firstly subclinical milk fever in dairy cattle herds which subsequently can shift to severe milk fever (Mulligan *et al*., 2006). Periodic metabolic profile tests help to find and treat them before their complication. Also, monitoring of cows on the day of calving for parturient hypocalcaemia can provide early detection of diet-induced problems in calcium homeostasis (Oetzel, 2004).

Ruminal diseases

There are little data about the relationship between occurrence of ruminal disorders like sub acute ruminal acidosis (SARA) and metabolic profile parameters. SARA occurs without common clinical signs and most of times it is undiagnosed. Most of scientists were focused on blood gas analysis for diagnosis of SARA and reported that blood gas analysis is a valuable tool to diagnose acidosis in dairy cows because it provides good assessment of acidosis while being less invasive than rumen pH analysis. Moreover, blood gas analysis can help to differentiate respiratory acidosis from metabolic acidosis, especially in a sub-acute form such as SARA. Blood gas analysis has many limitations like high costs, it is unavailable in most of farms, etc. It is suggested that more researchers focus on ruminal diseases and their specific effects on metabolic profile parameters (Gianesella *et al*., 2010), for example, it is indicated that SARA increases blood concentrations of haptoglobin and serum amyloid-A. It is

reported that inducing SARA by feeding wheat-barley pellets activated a systemic inflammatory response in the steers (Gozho *et al*., 2005).

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 incidence 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).

CONCLUSION

Briefly, the current review shows the relationships between metabolic profile parameters and many important sub-clinical diseases including: ketosis, milk fever, mastitis, cystic ovaries, displaced abomasum and etc.. Apart the common use of metabolic profile test 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 important/costly diseases in dairy cattle farms.

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REFERENCES

Amano, H., Y. Takesima, M. Nitta, T. Mabuti, T. Tokuti & T. Yagi, 1992. Relationship of haematocrit values with age, lactation stage, nutrition levels of dairy cows and temperature. *Journal of the Japan Veterinary Medical Association*, **45**, 467–470.

Ametaj, B. N., B. J. Bradford, G. Bobe, R. A. Nafikov, Y. Lu, J. W. Young & D. C. Beitz, 2005. Strong relationships between mediators of the acute phase response and fatty liver in dairy cows. *Canadian Journal of Animal Science*, **85**, 165–175.

Anonymous, 2017. Collecting blood to perform metabolic profiling. Guide Catalog. Texas A&M Veterinary Medical Diagnostic Laboratory. https://tvmdl.tamu. edu/wp-content/uploads/2017/09/ED-Collecting-Blood-for-Metabolic-Profiling-0917-1.pdf (3 June 2018, date last accessed).

Anonymous, 2018a. Reference ranges. biochemistry reference interval. Oregon State University, College of Veterinary Medicine, Veterinary Diagnostic Laboratory, http://vetmed.oregonstate.edu/sites/vetmed.oregonstate.edu/files/biochemistry_reference_intervals_1.pdf (3 June 2018, date last accessed).

Anonymous, 2018b. Metabolic profiling. Penn State University https://extension.psu.edu/metabolic-profiling (3 June 2018, date last accessed).

Başoğlu, A, M. Sevinç, O. K. Mahmut & M. Gökçen, 1998. Peri and postparturient concentrations of lipid lipoprotein insulin and glucose in normal dairy cows. *Turkish Journal of Veterinary and Animal Sciences*, **22**, 141–144.

Bauchart, D., 1993. Lipid absorption and transport in ruminants. *Journal of Dairy Science*, **76**, 3864–3881.

Bernabucci, U., B. Ronchi, N. Lacetera & A. Nardone, 2005. Influence of body condition score on relationships between metabolic status and oxidative stress in periparturient dairy cows. *Journal of Dairy Science*, **88**, 2017–2026.

Bertoni, G., E. Trevisi, X. Han & M. Bionaz, 2008. Effects of inflammatory conditions on liver activity in puerperium period and consequences for performance in dairy cows. *Journal of Dairy Science*, **91**, 3300–3310.

Bertoni, G., E. Trevisi & R. Lombardelli, 2009. Some new aspects of nutrition, health conditions and fertility of intensively reared dairy cows. *Italian Journal of Animal Science*, **8**, 491–518.

Borchardt, S. & R. Staufenbiel, 2012. Evaluation of the use of nonesterified fatty acids and β-hydroxybutyrate concentrations in pooled serum samples for herd-based detection of subclinical ketosis in dairy cows during the first week after parturition. *Journal of the American Veterinary Medical Association*, **240**, 1003–1011.

Burke, C. R., S. Meier, S. McDougall, C. Compton, M. Mitchell & J. R. Roche, 2010. Relationships between endometritis and metabolic state during the transition period in pasture-grazed dairy cows. *Journal of Dairy Science*, **93**, 5363–5373.

Burnham, A. J., J. F. MacGregor & R. Viveros, 1999. A Statistical framework for multivariate latent variable regression methods based on maximum likelihood. *Journal of Chemometrics*, **13**, 49–65.

Burton, J. L., M. E. Kehrli, S. Kapil & R. L. Horst, 1995. Regulation of L‐selectin and CD18 on bovine neutrophils by glucocorticoids: Effects of cortisol and dexamethasone. *Journal of Leukocyte Biology*, **57**, 317–325.

Butler, N. A. & M. C. Denham, 2000. The peculiar shrinkage properties of partial least squares regression. *Journal of the Royal Statistical Society, Series B (Methodological)*, **62**, 585–593.

Davies, T., 1998. The new automated mass spectrometry deconvolution and identification system (AMDIS). *Spectroscopy*, **10**, 24–27.

De Iorio, M., T. M. D. Ebbels & D. A. Stephens, 2008. Statistical techniques in metabolic profiling. In: *Handbook of Statistical Genetics*, eds D. J. Balding, M. Bishop, C. Cannings, John Wiley & Sons, Ltd, New Jersey, pp. 347–373.

Duffield, T. F., K. D. Lissemore, B. W. McBride & K. E. Leslie, 2009. Impact of hyperketonemia in early lactation dairy cows on health and production. *Journal of Dairy Science*, **92**, 571–580.

Dunn, J., 1992. Assessment of liver damage and dysfunction. *In Practice*, 193–200.

García, C. A. C., F. M. G. Prado, L. L. Galicia & T. F. Borderas, 2017. Reference values for biochemical analytes in Mexican dairy farms: interactions and adjustments between production groups. *Arquivo Brasileiro de Medicina Veterinária e Zootecnia*, **69**, 445–456.

Geishauser, T., K. Leslie, D. Kelton & T. Duffield, 2001. Monitoring for subclinical ketosis in dairy herds. *Compendium on Continuing Education for the Practising Veterinarian*, **23**, S65–S70.

Gianesella, M., M. Morgante, C. Cannizzo, A. Stefani, P. Dalvit, V. Messina & E. Giudice, 2010. Subacute ruminal acidosis and evaluation of blood gas analysis in dairy cow. *Veterinary Medicine International*, **10**, 1–4.

Ghergariu, S., G. J. Rowlands, A. L. Pop, N. Danielescu & N. A. Moldovan, 1984. A comparative study of metabolic profiles obtained in dairy herds in Romania. *British Veterinary Journal*, **140**, 600–608.

Gilbert, R. O., S. T. Shin, C. L. Guard, H. N. Erb & M. Frajblat, 2005. Prevalence of endometritis and its effects on reproductive performance of dairy cows. *Theriogenology*, **64**, 1879–1888.

Goff, J. P. & R. L. Horst, 1997. Physiological changes at parturition and their relationship to metabolic disorders. *Journal of Dairy Science*, **80**, 1260–1268.

Goff, J. P., 2004. Macromineral disorders of the transition cow. *Veterinary Clinics: Food Animal Practice*, **20**, 471–494.

Gozho, G. N., J. C. Plaizier, D. O. Krause, A. D. Kennedy & K. M. Wittenberg, 2005. Subacute ruminal acidosis induces ruminal lipopolysaccharide endotoxin release and triggers an inflammatory response. *Journal of Dairy Science*, **88**, 1399–1403.

Grummer, R. R., 1993. Etiology of lipid-related metabolic disorders in periparturient dairy cows. *Journal of Dairy Science*, **76**, 3882–3896.

Hammon, D. S., I. M. Evjen, T. R. Dhiman, J. P. Goff & J. L. Walters, 2006. Neutrophil function and energy status in Holstein cows with uterine health disorders. *Veterinary Immunology and Immunopathology*, **113**, 21–29.

Haass, C. L. & P. G. Eness, 1984. Bovine fatty liver syndrome. *Iowa State University Veterinarian*, **46**, 108–111.

Herath, S., S. T. Lilly, N. R. Santos, R. O. Gilbert, L. Goetze, C. E. Bryant, J. O. White, J. Cronin & I. M. Sheldon, 2009. Expression of genes associated with immunity in the endometrium of cattle with disparate postpartum uterine disease and fertility. *Reproductive Biology and Endocrinology*, **7**, 55.

Herdt, T. H., 1988. Fatty liver in dairy cows. *Veterinary Clinics of North America: Food Animal Practice*, **4**, 269–287.

Herdt, T. H., W. Rumbeiha & W. E. Braselton, 2000. The use of blood analyses to evaluate mineral status in livestock. *Veterinary Clinics of North America: Food Animal Practice*, **16**, 423–444.

Herdt, T. H., 2000. Ruminant adaptation to negative energy balance: Influences on the etiology of ketosis and fatty liver. *Veterinary Clinics: Food Animal Practice*, **16**, 215–230.

Holtenius, P., 1989. Plasma lipids in normal cows around partus and in cows with metabolic disorders with and without fatty liver. *Acta Veterinaria Scandinavica*, **30**, 441–445.

Holtenius, K., K. P. Waller, B. Essen-Gustavsson, P. Holtenius & C. H. Sandgren, 2004. Metabolic parameters and blood leukocyte profiles in cows from herds with high or low mastitis incidence. *The Veterinary Journal*, **168**, 65–73.

Houillier, P., 2014. Mechanisms and regulation of renal magnesium transport. *Annual Review of Physiology*, **76**, 411–430.

Huzzey, J. M., D. M. Veira, D. M. Weary & M. A. G. Von Keyserlingk, 2007. Prepartum behavior and dry matter intake identify dairy cows at risk for metritis. *Journal of Dairy Science*, **90**, 3220–3233.

Jones, G. M., E. E. Wildman, H. F. Troutt, T. N. Lesch, P. E. Wagner, R. L. Boman & N. M. Lanning, 1982. Metabolic profiles in Virginia dairy herds of different milk yields. *Journal of Dairy Sciences*, **65**, 683–688.

Kaneko, J. J., 2008. Blood analyte reference values in large animals. In: *Clinical Biochemistry of Domestic Animals*, eds J. J. Kaneko, W. J. Harvey, L. M. Bruss, Academic Press, California, pp. 882–888.

Kehrli, M. E., B. J. Nonnecke & J. A. Roth, 1989. Alterations in bovine neutrophil function during the periparturient period. *American Journal of Veterinary Research*, **50**, 207–214.

Khan, F. A., G. K. Das, M. Pande, M. K. Pathak & M. Sarkar, 2011. Biochemical and hormonal composition of follicular cysts in water buffalo (*Bubalus bubalis*). *Animal Reproduction Science*, **124**, 61–64.

Kida, K., 2002. Use of every ten-day criteria for metabolic profile test after calving and dry off in dairy herds. *Journal of Veterinary Medical Science*, **64**, 1003–1010.

Kim, I. H., K. J. Na & M. P. Yang, 2005. Immune responses during the peripartum period in dairy cows with postpartum endo-

metritis. *Journal of Reproduction and Development*, **51**, 757–764.

Kimura, K., J. P. Goff, M. E. Kehrli & T. A. Reinhardt, 2002. Decreased neutrophil function as a cause of retained placenta in dairy cattle. *Journal of Dairy Science*, **85**, 544–550.

Kume, S., T. Sato, I. Murai, M. Kitagawa, K. Nonaka & T. Oshita, 2011. Relationships between urine pH and electrolyte status in cows fed forages. *Animal Science Journal*, **82**, 456–460.

Lager, K. & E. Jordan, 2012. The metabolic profile for the modern transition dairy cow. In: *Proceedings of Mid-South Ruminant Nutrition Conference*, Grapevine, Texas, p. 9–16.

Larsen, T., G. Moller & R. Bellio, 2001. Evaluation of clinical and clinical chemical parameters in periparturient cows. *Journal of Dairy Science*, **84**, 1749–1758.

LeBlance, S. J., T. F. Duffield, K. E. Leslie, K. G. Bateman, G. P. Keefe, J. S. Walton & W. H. Johnson, 2002. Defining and diagnosing postpartum clinical endometritis and its impact on reproductive performance in dairy cows. *Journal of Dairy Science*, **85**, 2223–2236.

LeBlance, S. J., T. Herdt, W. Seymour, T. Duffield & K. Leslie, 2004. Factors associated with peripartum serum concentrations of vitamin E, retinol, and β-carotene in Holstein dairy cattle, and their associations with periparturient disease. *Journal of Dairy Science*, **87**, 609–619.

LeBlance, S. J., K. E. Leslie & T. F. Duffield, 2005. Metabolic predictors of displaced abomasum in dairy cattle. *Journal of Dairy Science*, **88**, 159–170.

LeBlance, S. J., 2008. Postpartum uterine disease and dairy herd reproductive performance: A review. *The Veterinary Journal*, **176**, 102–114.

LeBlance, S., 2010. Monitoring metabolic health of dairy cattle in the transition period. *Journal of Reproduction and Development*, **56** (**Suppl**), S29–S35.

Mimoune, N., R. Kaidi, M. Y. Azzouz, S. Zenia, M. H. Benaissa & G. England, 2017. Investigation on diagnosis and metabolic profile of ovarian cysts in dairy cows. *Kafkas Universitesi Veteriner Fakultesi Dergisi*, **23**, 579–586.

Mulligan, F., L. O. Grady, D. Rice & M. Doherty, 2006. Production diseases of the transition cow: Milk fever and subclinical hypocalcaemia. *Irish Veterinary Journal*, **59**, 697–702.

Nafikov, R. A. & D. C. Beitz, 2007. Carbohydrate and lipid metabolism in farm animals. *Journal of Nutrition*, **137**, 702–705.

Oetzel, G. R., 2003. Herd-based biological testing for metabolic disorders. In: *Preconvention Seminar 7: Dairy Herd Problem Investigation Strategies, 36th Annual Conference*, Columbus, American Association of Bovine Practitioners, Ohio, pp. 1–16.

Oetzel, G. R., 2004. Monitoring and testing dairy herds for metabolic disease. *Veterinary Clinics: Food Animal Practice*, **20**, 651–674.

Oetzel, G. R., 2008, Herd-based evaluations for nutritional and metabolic disease in dairy herds. https://www.vetmed.wisc.edu/dms/fapm/fapmtools/2nutr/Herd-Testing-070926.pdf (3 June 2018, date last accessed).

Ospina, P. A., D. V. Nydam, T. Stokol & T. R. Overton, 2010a. Associations of elevated nonesterified fatty acids and beta-hydroxybutyrate concentrations with early lactation reproductive performance and milk production in transition dairy cattle in the northeastern United States. *Journal of Dairy Science*, **93**, 1596–1603.

Ospina, P. A., D. V. Nydam, T. Stokol & T. R. Overton, 2010b. Evaluation of nonesterified fatty acids and β-hydroxybutyrate in transition dairy cattle in the northeastern United States: Critical thresholds for prediction of clinical diseases. *Journal of Dairy Science*, **93**, 546–554.

Payne, J. M., S. M. Dew, R. Manston & M. Faulks, 1970. The use of a metabolic pro-

file test in dairy herds. *The Veterinary Record*, **87**, 150–158.

Payne, J. M., 1972. The Compton metabolic profile test. *Royal Society of Medicine*, **65**, 181.

Peter, A. T. & W. T. K. Bosu, 1987. Peripartal endocrine changes associated with retained placenta in dairy cows. *Theriogenology*, **28**, 383–394.

Puls, R., 1989. Mineral levels in animal health: Diagnostic data. In: *Minerals in Animal Nutrition,* 2nd edn, Sherpa Int., Clearbrook, BC, Canada. http://www.cofemer.gob.mx/expediente/v99/_B001002200.pdf (3 June 2018, date last accessed).

Quiroz-Rocha, G. F., S. J. LeBlance, T. F. Duffield, D. Wood K. E. Leslie & R. M. Jacobs, 2009. Reference limits for biochemical and hematological analytes of dairy cows one week before and one week after parturition. *The Canadian Veterinary Journal*, **50**, 383–388.

Rayssiguier, Y., A. Mazur, E. Gueux, I. M. Reid & C. J. Roberts, 1988. Plasma lipoproteins and fatty liver in dairy cows. *Research in Veterinary Science*, **45**, 389–393.

Roberts, C. J. & I. M. Reid, 1986. Fat cow syndrome and subclinical fatty liver. *Current Veterinary Therapy, Food Animal Practice*, **2**, 324–326.

Šamanc, H., D. Kirovski, V. Stojic, D. Stojanovic, I. Vujanac, R. Prodanovic & S. Bojkovic-Kovacevic, 2011. Application of the metabolic profile test in the prediction and diagnosis of fatty liver in Holstein cows. *Acta Veterinaria (Beograd)*, **61**, 543–545.

Scalia, D., N. Lacetera, U. Bernabucci, K. Demeyere, L. Duchateau & C. Burvenich, 2006. In vitro effects of nonesterified fatty acids on bovine neutrophils oxidative burst and viability. *Journal of Dairy Science*, **89**, 147–154.

Sevinç, M., A. Başoğlu, İ. Öztok, M. Sandikçi & F. Birdane, 1998. The clinical-chemical parameters, serum lipoproteins and fatty infiltration of the liver in ketotic cows. *Turkish Journal of Veterinary and Animal Sciences*, **22**, 443–448.

Sevinç, M. , A. Başoğlu, H. Güzelbektaş & M. Boydak, 2003. Lipid and lipoprotein levels in dairy cows with fatty liver. *Turkish Journal of Veterinary and Animal Sciences*, **27**, 295–299.

Sheldon, I. M. & H. Dobson, 2004. Postpartum uterine health in cattle. *Animal reproduction science*, **82**, 295–306.

Sheldon, I. M., J. Cronin, L. Goetze, G. Donofrio & H. J. Schuberth, 2009. Defining postpartum uterine disease and the mechanisms of infection and immunity in the female reproductive tract in cattle. *Biology of Reproduction*, **81**, 1025–1032.

Soetan, K. O., C. O. Olaiya & O. E. Oyewole, 2010. The importance of mineral elements for humans, domestic animals and plants: A review. *African Journal of Food Science*, **4**, 200–222.

Stein, S. E., 1999. An integrated method for spectrum extraction and compound identification from GC/MS data. *Journal of the American Society of Mass Spectrometry*, **10**, 770–871.

Stengarde, L., K. Holtenius, M. Traven, J. Hultgren, R. Niskanen & U. Emanuelson, 2010. Blood profiles in dairy cows with displaced abomasum. *Journal of Dairy Science*, **93**, 4691–4699.

Stojević, Z., J. Piršljin, S. Milinković-Tur, M. Zdelar-Tuk & B. B. Ljubić, 2005. Activities of AST, ALT and GGT in clinically healthy dairy cows during lactation and in the dry period. *Veterinarski Arhiv*, **75**, 67–73.

Trygg, J. & S. Wold, 2003. O2-pls, a two-block (x-y) latent variable regression (LVR) method with an integral osc filter. *Journal of Chemometrics*, **17**, 53–64.

Van Saun, R. J., 2010. Indicators of dairy cow transition risks: metabolic profiling revisited. In: *World Buiatrics Congress* (Abstract), Santiago, Proceedings XXV World Buiatrics Congress, Santiago, pp. 65–77.

Van-Saun, R. J., 2016. Indicators of dairy cow transition risks: metabolic profiling revisited. *Tierarztliche Praxis Großtiere*, **44**, 118–126.

Walsh, R. B., D. F. Kelton, T. F. Duffield, K. E. Leslie, J. S. Walton & S. J. LeBlance, 2007a. Prevalence and risk factors for postpartum anovulatory condition in dairy cows. *Journal of Dairy Science*, **90**, 315–324.

Walsh, R. B., J. S. Walton, D. F. Kelton, S. J. LeBlance, K. E. Leslie & T. F. Duffield, 2007b. The effect of subclinical ketosis in early lactation on reproductive performance of postpartum dairy cows. *Journal of Dairy Science*, **90**, 2788–2796.

Wathes, D. C., M. Fenwick, Z. Cheng, N. Bourne, S. Llewellyn, D. G. Morris, D. Kenny, J. Murphy & R. Fitzpatrick, 2007. Influence of negative energy balance on cyclicity and fertility in the high producing dairy cow. *Theriogenology*, **68**, S232–S241.

West, H. J., 1990. Effect on liver function of acetonaemia and the fat cow syndrome in cattle. *Research in Veterinary Science*, **48**, 221–227.

Whitaker, D. A., W. J. Goodger, M. Garcia, B. M. Perera & F. E. Wittwer, 1999. Use of metabolic profiles in dairy cattle in tropical and subtropical countries on smallholder dairy farms. *Preventive Veterinary Medicine*, **38**, 119–131.

Whitaker, D. A., 2000. Use and interpretation of metabolic profile. In: *The Health of Dairy Cattle*, ed. A. H. Andrews, Wiley Blackwell, Oxford, pp. 89–107.

Zerbe, H., N. Schneider, W. Leibold, T. Wensing, T. A. M. Kruip & H. J. Schuberth, 2000. Altered functional and immunophenotypical properties of neutrophilic granulocytes in postpartum cows associated with fatty liver. *Theriogenology*, **54**, 771–786.

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