Dairy Sessions

Moderator: Ken Nordlund

Will Large Dairy Herds Lead to the Revival of Metabolic Profile Testing?

T.H. Herdt, DVM, MS, Diplomate ACVN, ACVIM[1,2]; B. Dart, DVM, MS[3]; L. Neuder, DVM[2,4]
[1]*Animal Health Diagnostic Laboratory*
[2]*Dept. Large Animal Clinical Sciences*
[3]*Dept. Agricultural Economics*
Michigan State University, East Lansing, MI 48824
[4]*Green Meadows Farm, Else, MI 48831*

What is a Metabolic Profile Test (MPT)?

The term implies a battery of tests that yields information about the status of one or more metabolic functions. In dairy-cow veterinary practice the term was first made popular by the "Compton Metabolic Profile Test," which was described in the early 1970s.[16,22] The Compton MPT created interest and gave notoriety to the idea of dairy-herd MPT, but the technique as described appeared to be of limited usefulness and never became widely popular.[3] However, the interest in and the idea of MPT have never gone away. We believe this is because a need exists for a means of metabolic and nutritional assessment of dairy herds that goes beyond ration evaluation. Evaluation of ruminant diets is complex and involves considerable uncertainty, as illustrated by recently developed computerized models of ruminant digestion. Because of this uncertainty, techniques for monitoring cow responses to dietary changes are necessary complements to ration evaluation. This is because the dairy cow is the ultimate "model" in dairy nutrition. Monitoring techniques are particularly valuable if they can detect metabolic and/or nutritional changes before they are manifest in clinical disease or reduced productivity.

All techniques that monitor changes in metabolic or nutritional status could reasonably be considered part of a "metabolic profile" or MPT. This would clearly include examination of such variables as body condition score, milk composition, urine pH, and fecal consistency. These variables are monitored in many dairy herds currently and should be considered the basic MPT. The emphasis of this discussion, however, will be on blood components as variables in the MPT. We hope, however, that no one loses sight of the importance of non-hematogenous components of metabolic monitoring.

The Difference Between Disease Diagnosis and Metabolic Profile Testing

There is an important distinction between laboratory testing for disease diagnosis, and MPT as the term is used in a production-medicine context. Laboratory testing, of course, is an important aid in disease diagnosis, but the technique and objectives of laboratory testing for disease diagnosis are different than those for MPT. Disease diagnosis implies that animals being tested are clinically abnormal, *i.e.* are diseased. Disease diagnosis may require testing only a small number of animals, perhaps even one if identified at an appropriate stage of the disease. Once a diagnosis has been established, nutritional decisions about the herd may need to be made. These are based on the existence of disease, not directly on blood components, which may be widely outside of reference ranges. Metabolic profile testing, on the other hand, implies that animals being tested are clinically normal and that nutritional decisions are based directly on blood-component variables. Metabolic profile testing usually requires testing a larger number of animals than does disease diagnosis. In addition, more effort is usually required to select the optimal group of animals to test.

The Basis of Metabolic Profile Testing

The concept of measuring hematogenous variables as part of an MPT assumes that blood composition will change in response to the metabolic status of the animal. This is a sound concept supported by volumes of physiological research. Examination of journals of agricultural or physiological research will reveal that blood is frequently sampled to track and evaluate metabolic and physiological changes. The major difference between these experimental studies and the application of MPT is the ability to control variables affecting the populations from which the samples are taken. Research workers go to great length to assure that the populations studied are uniform in as many regards as possible, except for the application of some experimental treatment. Because the populations are uniform, differences among them are assumed to be due to differences in treatment. Variation that cannot be controlled by standardizing the populations is accounted for by using multiple animals and applying statistical analysis to the data. The challenges in MPT are two: 1) understanding the complex biology affecting blood composition and 2) dealing with the variation that exists in animal populations under commercial conditions.

Interpretation of MPT

Biological factors

Complex metabolic relationships determine the concentrations of various elements and metabolites in blood. These relationships may not be straightforward, and must be understood and considered when interpreting test results. For example, serum iron is affected not only by the dietary availability of iron, but also by the concentration of transferrin in the serum. Transferrin is a short-half-life protein and its production is influenced by the metabolic availability of amino acids. Therefore, low serum iron concentration might signify insufficient availability of dietary iron. Alternatively, low serum iron concentration might indicate an insufficient supply of dietary protein, leading to an insufficient supply of amino acids for transferrin production. These types of complex relationships between diet and blood-component concentrations make it imperative that considerable thought be put into the metabolic interpretation of MPT.

Statistical factors

Statistics is the science that deals with variability. It is an essential part of MPT interpretation, but the statistics of MPT require further development. In this presentation, we will introduce some new methods potentially useful in evaluation of MPT results. These methods appear to provide a simple, but fresh, outlook on the interpretation of MPT.

Values from MPT must be interpreted in some frame of reference. Clinicopathological values for disease testing are interpreted in reference to a range of "normal" values. The normal range is chosen to represent the expected range of values in clinically normal animals. Frequently, the values for diseased animals fall dramatically outside of the normal range, often making disease diagnosis reasonably straightforward. In contrast, for the purposes of MPT animals selected for testing should be clinically normal. Therefore, blood element and metabolite concentrations might be expected to fall within the normal range, as defined for clinicopathological testing. *Interpretation of MPT must then be made within the range of values observed in clinically normal animals.*

One approach to this problem is to define another type of "normal" range to be used in the interpretation of MPT. Ideally, this range should be based on some herd-level measurement, rather than on individual animals. For the Compton Metabolic Profile Test, the normal range for herd means was described as the range of two standard deviations on either side of the mean of means of a reference population of herds.[17,18] The problem with this approach is that it requires identifying a suitable population of reference herds, conducting extensive laboratory testing on them, and describing the statistical distribution of the mean values from those herds. Such information is simply not readily available.

A more common approach has been to define either empirically or epidemiologically ranges of adequate blood concentrations, based on disease risk. Herd or individual cow values are then interpreted in a discrete manner: they are classified as either "normal" or "abnormal," "adequate" or "deficient" based on whether they lay inside or outside of the reference range. This approach ignores the fact that blood concentrations are continuous variables, and their relationship to disease risk is usually continuous. For example, it is known that the postpartum risk of displaced abomasum and metritis in fresh cows is directly associated with the prepartum plasma concentration of non-esterified fatty acids (NEFA). This relationship is continuous and has been described by logistic regression.[2,10] The relationship does not say a threshold plasma NEFA concentration exists, above which the cow is almost certain to get a displaced abomasum. Rather, it says that as the plasma NEFA concentration goes up, so does the risk of displaced abomasum, without reference to a specific cutoff value. Therefore, for plasma NEFA and most other MPT variables, monitoring change is just as important, if not more important, than measuring point values in time.

An industrial concept known as "Statistical Process Control" exists to aid managers in monitoring change and variation over time in manufacturing and other commercial processes. Some of the tools of Statistical Process Control may be valuable for MPT. The major tool is called a "Process Control Chart." These charts are comparatively simple statistical tools that for construction and interpretation do not require an in-depth understanding of statistical theory.

Process Control Charts

Process Control Charts consist of two graphs, each with time as the abscissa, or 'X', axis. One of the graphs tracks the change in central tendency of the data over time, usually represented by the mean or average. The other graph tracks the change in dispersion of the data over time, usually represented by the range or standard deviation. Figures 1 and 2 are the two sections of a Process Control Chart for serum cholesterol concentrations in close-up cows in a single dairy. To create the chart, blood samples for cholesterol analysis were taken weekly from seven animals in the last two weeks of gestation. Animals were selected at random and no individual animal was sampled more than once. In Figure 1, the individual points are the averages of the seven samples at each week, referred to as the Subgroup Average. In Figure 2, the individual points are the difference between the largest and smallest values for each week, referred to as the Subgroup Range. The central solid line is referred to as the Grand Average, and the other two lines as the Upper and Lower Control Limits, respectively. The Grand Average is the arithmetic mean of all values combined over all weeks. Various methods may be used to calculate the Control Limits, but all are based on the assumption that ongoing variability in a stable system can be predicted by past variability. Computational details for the construction of Control Charts will not be covered in this discussion. Details of Control Chart construction can be found in standard textbooks on the subject.[24]

The important point for this discussion is that Control Limits are determined by the historical behavior of the data and represent the expected extent of variability in the population. The Subgroup Averages and Subgroup Ranges are expected to "bounce around" randomly within the Control Limits. When Subgroup Averages or Subgroup Ranges fall outside of the Control Limits, it indicates a significant deviation from the past, and the introduction of a new source, or sources, of variability into the system.

As an example of the use of control charts, note that in Figure 1 between Weeks 11 and 12 (points circled) the average serum cholesterol concentration fell from 70 mg/dl to about 55 mg/dl. The risk of postpartum metritis is inversely proportional to prepartum

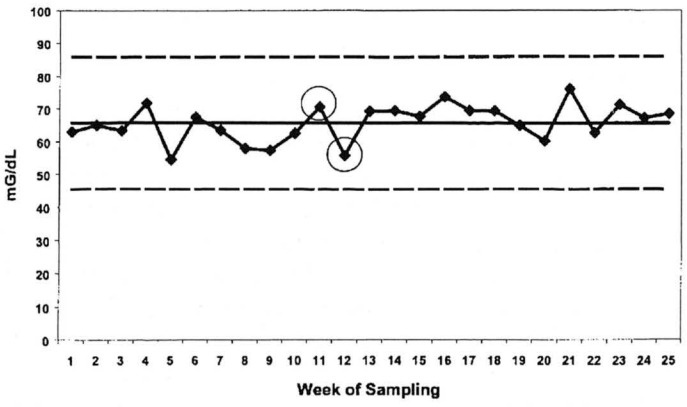

Figure 1. Average Control Chart portion of a Process Control chart for cholesterol concentrations in "close-up" cows on a single dairy. Each individual point on the graph represents the average serum cholesterol concentration from seven randomly selected cows in the last two weeks of gestation. The central solid line represents the average of all individual points. The dotted lines represent the Upper and Lower Critical Control points for the data. Points lying above or below these lines represent deviations from the historical variability in the data. Points outside the lines indicate a high likelihood that new sources of variability have been introduced into the system.

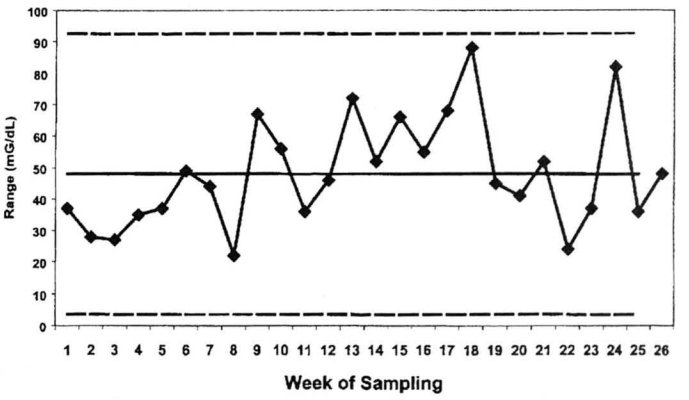

Figure 2. Range Control Chart portion of a Process Control chart for cholesterol concentrations in "close-up" cows on a single dairy. Each individual point on the graph represents the difference between the highest and lowest serum cholesterol concentration from seven randomly selected cows in the last two weeks of gestation. The central solid line represents the average of all individual points. The dotted lines represent the Upper and Lower Critical Control points for the data. Points lying above or below these lines represent deviations from the historical variability in the data. Points outside the lines indicate a high likelihood that new sources of variability have been introduced into the system.

serum cholesterol concentration[10]. So, should we be concerned about this drop in cholesterol? The chart says no. The variation is within the limits of previous variation and should be interpreted as a random event within this group of cows in this herd. Note that this says nothing about the biology of serum cholesterol concentration. The chart says only that we cannot interpret this change as being any more than expected, so we would probably be wasting our time to go looking for an explanation.

Signal-to-Noise Ratio in MPT

Variation of Subgroup Averages within the Control Limits is random variation, sometimes referred to as statistical "noise." Points outside of the Control Limits indicate the addition of non-random sources of variation, sometimes referred to as "signal." When there is a "signal" it means that something in the system has changed, and should not be ignored.

In instrument technology, reference is frequently made to the "signal-to-noise ratio." A high signal-to-noise ratio means signals are easily detected, unlikely to be lost in the noise. A low signal-to-noise ratio means there is lots of noise, or random variation, that is likely to obscure the signal and make it difficult to detect. In Process Control charts, distance between the Control Limits indicates the extent of expected "noise." The amount of noise is affected by the number of sources of variation, the amount of variation contributed by each source, and the number of animals sampled. In MPT, the objective is to maximize the signal-to-noise ratio, limiting as much as possible extraneous sources of variability. Sampling multiple animals does this.

What are Sources of Variability?

Variation is a characteristic of biological systems, but not all variation is random. Known "sources" can contribute to variation in a non-random manner. For example, in any herd of Jersey cows body weight will vary among animals, as it would also in a herd of Holstein cows. We could consider this variation as random variation in body weight within breeds. If a herd has a mixture of Jerseys and Holsteins, there will be more variation in body weight than if only one breed were present. This is because breed adds an extra, non-random source of variation. The total amount of variation in body weight within the herd will be a combination of random differences within breeds and non-random, genetic differences between breeds.

For MPT variables, several sources of variation usually exist, including

- Random biological variation
- Genetic variation
- Circadian and/or prandial variation
- Seasonal variation
- Variation associated with physiological state (growth, gestation stage, lactation stage, etc.)
- Variation associated with pathological state (the effect of existing disease)
- Artifactual variation due to sampling or sample-handling technique
- Analytical variation
- Environmental variation (influences external to the animal, including nutrition and other management factors)

It is this last source of variation in which we are generally interested for MPT interpretation, because the objective is for MPT to aid in nutritional or management decisions. The remaining sources of variation could be thought of as contributing to the "noise" that can obscure the nutritional or environmental "signal." The challenge in MPT strategy is to maximize the signal-to-noise ratio.

Quieting the Noise

Statistical noise may be due to either known or random sources of variation. Noise due to known sources of variation can be minimized by animal selection and sampling technique. For example, if lactation stage is a known source of variation for a particular blood component, then animals for testing should be grouped as closely as possible by lactation stage. Likewise, if there were an important prandial effect, sampling animals at a uniform time in relationship to feeding would reduce the effect of prandial variation on the results.

When animal grouping and sampling strategy have minimized known sources of variation, the remaining noise will be due to random variation. Sampling multiple animals can reduce noise due to random variation; the more animals sampled, the lower the amount of noise. In calculation of the Average Control Chart, the distance between the Upper and Lower Control Limits will always diminish as the number of animals in each Subgroup Average increases, assuming uniform variation in the population. Therefore, the more animals sampled, the higher the signal-to-noise ratio. The optimal number of animals to test for any particular variable is seldom known with confidence. A good thumb rule for any MPT variable is to test at least seven animals per group.[17]

Application of Process Control Charts to MPT

In industrial systems, Process Control Charts are used to monitor consistency and detect the introduction of additional sources of variation into manufacturing processes. In such systems the intended average value

is known. For example, the bags should contain 50 grams of peanuts on average, or the widget should be 37 mm thick on average. The industrial design sets the desired values. If we begin to track MPT values with Process Control Charts, the values initially measured may be desirable or undesirable. If they are desirable, the objective is to detect the introduction of additional sources of variation that move the mean value out of the desirable range. However, the situation in MPT may be that the Grand Average calculated initially will be outside a desirable range. In this case, some management action would be taken and the objective of using the Control Charts would be to detect significant movement towards the desired range, rather than to monitor for consistency. This means that for each MPT variable there must be a biologically defined adequate or desirable range. The purpose of the Process Control Chart is to determine if

- the herd control limits are within the desirable range.
- the system is stable.
- change is occurring, and if so the direction of change.

This means that a desirable or "normal" range must be defined for each MPT variable. This may seem like it puts us back into the same dilemma of comparing a herd value to a normal range. However, the advantage of using the Control Charts over comparing a point value to a normal range is that the Charts let us examine how the *variation* within the herd, as well as the point value, compares to the desirable range.

The Effect of Herd Size on MPT

Minimizing statistical noise is essential for MPT interpretation. This requires close grouping of animals to reduce known sources of variation, and sampling an adequate number of animals within groups. In many small herds at any given time there may not be sufficient numbers of animals in the groups of interest. For example, for prepartum plasma NEFA testing we recommend sampling seven animals in the last three weeks of gestation. In herds of 100 or less cows, on average one could expect there to be less than six cows in the last three weeks of gestation at any one time, thus limiting the ability to sufficiently control statistical noise.

The optimum number of animals to test will generally not change with herd size; therefore, the cost of testing will be diluted across a large number of animals in large herds. Furthermore, the cost of a bad decision can be far greater in a large herd, compared to a small herd, thus enhancing the risk-benefit of MPT in larger herds. Therefore, there are considerable advantages for large herds in the interpretation and application of MPT.

Variables in Dairy-Herd Metabolic Profile Testing

There are many potentially valuable variables for use in MPT. The selection of variables will depend on the purposes of the test. Below we've listed a number of variables we feel are valuable in monitoring dairy herds for postpartum disease risk, especially diseases associated with energy metabolism. We are not suggesting that these are the only variables of importance, but rather that these are useful blood variables that could be examined by the use of Process Control Charts. The reference ranges listed are for comparison to Control Limits. The listed ranges reflect the opinions and experiences of the authors. We want to again stress the importance of non-hematogenous variables in dairy-herd MPT, including body condition score, milk composition, urine pH and fecal characteristics.

Example MPT Variables

Hematocrit (packed cell volume)

Application: Hematocrit can be used as a general reflection of animal health. Specific nutrient deficiencies, such as iron and copper, can result in reductions in hematocrit, but in most dairy herds low hematocrit is probably a reflection of sub-optimal energy and protein nutrition.[12,23] Low hematocrit is associated specifically with subfertility,[9,21] but it is probably a general indicator of energy and protein balance, which have a strong effect on fertility. Potential sources of blood loss, such as parasites, should also be considered when interpreting low hematocrits. Cows in early lactation, prior to breeding would be the population for which the most valuable information might be gained from hematocrit testing. The low expense of sample collection and ease of analysis make hematocrit an attractive variable with which to start an MPT program.

Sampling: Samples for hematocrit determination should be taken in EDTA-treated tubes. The test is fairly robust, but some mistakes can be made. It is important to fill pre-treated tubes, such as Vacutainers™, completely. In partially filled tubes the proportion of EDTA will be too high, which can result in cell shrinkage and reduced hematocrit. Also, the samples should be refrigerated and analyzed within two days of collection to avoid artifactual changes in cell size, which will affect hematocrit measurement. Attention to these details is more important in hematocrit testing for MPT than for the usual purposes of disease diagnosis or management. This is because the relative differences in hematocrit that are important in MPT are much smaller than for disease diagnosis or management; thus, small analytical mistakes can make a difference in MPT interpretation.

Analysis: Hematocrits are usually measured in practice laboratories in microhematocrit centrifuges. It is important to be sure the centrifuge speed is accurate, and that the tubes are spun for the length of time specified for the instrument.

Non-nutritional sources of variability: Hematocrit varies with lactation stage, being highest in dry cows and in lowest for cows in early lactation. For hematocrit testing, cows should be grouped by lactation stage.

Interpretation: If hematocrit values are reduced, changes in the availability of major nutrients should be suspected. A reasonable goal value for hematocrit means for cows in the first eight weeks of lactation is between 29 and 31%.

Serum Albumin

Application: Serum albumin concentration is related to the protein status of the animal.[6,13-15,19] The relatively long half-life of serum albumin makes it a rather insensitive measure of protein status, but it may be the best blood test of protein status that is readily available.

Sampling: Serum albumin is fairly robust and requires no special sample-handling precautions. Samples should be taken into tubes without anticoagulant and serum removed after the clot has formed.

Analysis: Analytical variability can be introduced by different methods of albumin analysis. It is best to use one laboratory consistently.

Non-nutritional sources of variation: Lactation stage has a substantial effect on serum albumin. For albumin testing, animals should be grouped into dry cows, early lactation (0 to 10 weeks), and later lactation.

Interpretation: A reasonable goal for minimum values for dry cow means is from 2.9 to 3.1 G/dL, for fresh cows from 2.7 to 2.9 G/dL, and 3.0 to 3.2 G/dL for cows in later lactation.

Non-esterified fatty acids (NEFA)

Application: Non-esterified fatty acids are a sensitive indicator of energy balance.[11] They are particularly useful in monitoring energy status of dry cows in the last month of gestation, during which rapid changes in energy balance status might not be perceived from changes in body condition score.

Sampling: Either serum or plasma is suitable for NEFA analysis. Samples should be kept cold from the time of collection so that enzymatic hydrolysis of esterified lipids in the sample will not contribute to an artifactual increase in NEFA concentration. Non-esterified fatty acid concentrations are stable in frozen serum or plasma. Contrary to the indications of some instructions, heparinized plasma is a suitable sample for NEFA analysis.

Analysis: An enzymatic analysis is currently available in a kit form. This analysis is accurate, repeatable, and suitable for automated analyzers. Prior to the availability of this assay, NEFA analysis was difficult and not very accurate.

Sources of variation other than energy balance: Prandial effects on plasma NEFA are substantial, with concentrations diminishing post-feeding even in animals in net daily negative energy balance.[1] For best interpretation, samples should be taken shortly before the normal feeding time. In situations in which feed is used to catch animals in gang locks, samples for NEFA testing should be taken immediately after the animals are caught. In addition to prandial effects, there are important gestation- and lactation-stage effects. Values can be expected to increase slightly in the last two weeks of gestation, peak on the day of calving, and then drop quickly postpartum. Values in early lactation will be higher than in the dry period, but should be less than on the day of calving.

Excitement stimulates an immediate increase in blood NEFA. Working animals quietly through a chute for blood sampling causes a small increase in NEFA that is unlikely to interfere with nutritional interpretation. If cows become agitated and are running, NEFA testing should be left for another day. Supplemental fat sources in the diet will usually increase plasma NEFA slightly, but this is unlikely to interfere with interpretation.

Interpretation: The major determinant of plasma NEFA concentration is energy balance. High values are indicative of negative energy balance. Negative energy balance is expected in any animal with a poor appetite. Therefore, plasma NEFA testing is not a useful test for sick animals. They are always expected to have high NEFA if they are off feed.

For dry cows more that two weeks from calving, reasonable goals for mean plasma NEFA are < 0.3 mEq/L. In the last two weeks of gestation, reasonable goals are < 0.35 mEq/L. Some research suggests that goal values for plasma NEFA on the day of calving should be < 1.0 mEq/L. At more than three days in milk, goal values are <0.7 mEq/L.

Serum beta-hydroxybutyric acid (BHBA)

Application: Serum BHBA concentrations are affected by energy balance and glucose balance. Because of its specific relationship to glucose balance, serum BHBA is a less-specific indicator of energy balance than is plasma NEFA.[8] Testing for serum BHBA seems to be most useful in cows in the first four weeks of lactation. High values are associated with reduced milk production, increased clinical ketosis and displaced abomasum, and reduced fertility.[4]

Sampling: Beta-hydroxybutyric acid is usually measured in serum. It is stable in serum and the assay is fairly robust with respect to sample handling requirements. If samples are to be sent by courier or through

the mail, serum should be separated from the clot to avoid hemolysis.

Sources of variation other than glucose and energy balance: There are important lactation-stage effects on serum BHBA, with cows in the first six weeks of lactation normally having values higher than cows at later stages of lactation, or dry cows. There are also prandial effects, with serum BHBA values increasing within the first few hours after feeding. The postprandial BHBA increase is due to increasing ruminal butyric acid concentrations. Butyric acid is converted to BHBA as it is absorbed through the rumen epithelium. Pre-formed butyric acid in the diet, such as from silage with clostridial fermentation, is also converted to BHBA. This results in high blood BHBA concentrations, and the potential for a high ketosis rate in cows consuming these kinds of silages. When evaluating serum BHBA concentrations, samples should be taken at a uniform time in relationship to feeding.

Interpretation: For fresh cows, mean serum BHBA concentrations should be in the range of 5 to 8 mG/L. For cows in other stages of lactation, or dry cows, desirable mean values are in the range of 3 to 6 mG/dL.

Blood (Serum) urea nitrogen (SUN)

Application: Blood or serum urea nitrogen (SUN) is correlated positively with rumen ammonia concentration.[5,20] Therefore, it can be used as an estimator of rumen ammonia concentration. It is useful in cows of all lactation stages as part of the assessment of ruminal balance of energy and available protein.

Sampling: Urea is measured in serum. It is fairly robust and the samples require no special handling. It is important to remove the serum from the clot prior to shipment so as to avoid hemolysis.

Sources of variation other than dietary protein and energy characteristics: There are important prandial effects, with SUN increasing after feeding.[5] Maximum concentrations are usually seen within two hours after feeding, especially if protein supplements are included in concentrate meals. Milk urea nitrogen (MUN) concentration provides similar information to SUN. There is less of a prandial effect on MUN than on SUN, although there is a prandial effect present even for MUN.

Interpretation: A reasonable range for mean SUN concentrations is from 14 to 18 mG/dL. Serum urea nitrogen values are affected by both rumen available nitrogen and rumen available energy. Changing either of these rumen inputs will affect the SUN value. The test is useful in all classes of cattle, but may be especially useful in dry cows in which MUN values are not available.

Serum aspartate aminotransferase (AST)

Application: Aspartate aminotransferase is a cellular enzyme that escapes into blood serum in response to cellular damage. Fatty liver in dairy cows is associated with increases in the serum activity of this enzyme, although the extent of the increase is small compared to other liver diseases.[7] The enzyme is not specific to hepatocytes, thus it is not a specific indicator of liver cell damage. However, among available blood component variables, serum AST activity appears to be the most sensitive indicator of fatty liver in dairy cows.

Sampling: Aspartate aminotransferase activity is stable in serum at refrigerator temperatures for two or three days. Serum should be removed from the clot sufficiently soon to prevent hemolysis.

Sources of variation other than fatty liver: Aspartate aminotransferase is not a liver-specific enzyme. Skeletal muscle trauma associated with struggling or recumbency will elevate the serum AST activity. This is a perfect example of why samples for MPT should be collected from clinically normal animals, because diseased or recumbent animals might have elevated serum AST due to muscle damage.

Interpretation: Enzyme assays are difficult to standardize between laboratories, so reference values should be established in a single laboratory. In general, a goal range for mean values will be between 35 and 100 IU/L.

Conclusion

Methods are needed to monitor nutritional and metabolic status of dairy herds. The most valuable methods will be those that are sensitive enough to detect change before clinical or economic consequences are manifest. Analysis of blood for specific components in an MPT is a technique that, among others, may be valuable for nutritional and metabolic monitoring of dairy herds. A major challenge in the application of MPT is dealing with extraneous sources of variation. Successful management of extraneous variation requires sampling strategies based on animal grouping and testing of multiple animals. Larger herds are probably more suited for MPT because they are able to better design sampling strategies and to dilute testing costs among more animals. Furthermore, there is a greater potential cost benefit due to the high cost of bad feeding decisions in large herds. Statistical Process Control methods appear to offer a unique approach to interpretation that may increase the usefulness of MPT, but this requires further evaluation.

References

1. Blum JW, Jans F, Moses W, Frohli D, Zemp M, Wanner M, Hart IC, Thun R, Keller U: Twenty-four-hour pattern of blood hormone and metabolite concentrations in high-yielding dairy cows: effects of feeding low or high amounts of starch, or crystalline fat. *Zentralblatt fur Veterinarmedizin*, A 32:401-418, 1985.

2. Cameron RE, Dyk PB, Herdt TH, Kaneene JB, Miller R, Bucholtz HF, Liesman JS, Vandehaar MJ, Emery RS: Dry cow diet, management, and energy balance as risk factors for displaced abomasum in high producing dairy herds. *J Dairy Sci* 81:132-139, 1998.
3. Dirksen GU: Control of production disease in dairy cows in a changing agricultural environment. Proceedings, 8th International Conference on Production Diseases in Farm Animals, Berne, Switzerland, 271-282, 1992.
4. Duffield T: Subclinical ketosis in lactating dairy cattle. *Vet Clin North Am Food Anim Pract* 16:231-254, 2001.
5. Gustafsson AH, Palmquist DL: Diurnal variation of rumen ammonia, serum urea, and milk urea in dairy cows at high and low yields. *J Dairy Sci* 76:475-484, 1993.
6. Hassan A, Roussel JD: Effect of protein concentration in the diet on blood composition and productivity of lactating Holstein cows under thermal stress. *J Agri Sci*, UK 85:409-415, 1975.
7. Herdt TH, Gerloff BJ, Liesman J, Emery RS: Hepatic lipidosis and liver function in 49 cows with displaced abomasum. XIIth World Congress on Diseases of Cattle. Amsterdam, World Association for Buiatrics. 1: 522-525. 1982.
8. Herdt TH, Stevens JB, Linn J, Larson V: Influence of ration composition and energy balance on the blood beta hydroxybutyrate (ketone) and plasma glucose concentration of dairy cows in early lactation. *Am J Vet Res* 42:1177-1180, 1981.
9. Hewett C: On the causes and effects of variations in the blood profile of Swedish Dairy cattle. *Acta Vet Scand* Suppl. 50:1-152, 1974.
10. Kaneene JB, Miller RA, Herdt TH, Gardiner JC: The association of serum non-esterified fatty acids and cholesterol, management and feeding practices with peripartum disease in dairy cows. *Prev Vet Med* 1141:1-14, 1997.
11. Kunz PL, Blum JW: Relationships between energy balances and blood levels of hormones and metabolites in dairy cows during late pregnancy and early lactation. Zeitschrift fur Tierphysiologie, Tierernahrung und Futtermittelkunde 54:239-248, 1985.
12. Lister EE, Fisher LJ, Jordan WA, Wauthy JM, Comeau JE, Proulx J: Influence of shelter, level of feeding, and method of forage conservation on packed cell volume and plasma metabolite levels in pregnant beef cows. *Can J Anim Sci* 53:81-88, 1973.
13. Manston R, Russell AM, Dew SM, Payne JM: The influence of dietary protein upon blood composition in dairy cows. *Vet Rec* 96:497-502, 1975.
14. McGuffey RK, Green HB, Basson RP: Lactation response of dairy cows receiving bovine somatotropin and fed rations varying in crude protein and undegradable intake protein. *J Dairy Sci* 73:2437-2443, 1990.
15. Oldham JD, Broster WH, Napper DJ, Siviter JW: The effect of a low-protein ration on milk yield and plasma metabolites in Friesian heifers during early lactation. *Brit J Nutrition* 42:149-162, 1979.
16. Payne JM, Dew SM, Manston R, Faulks AB: The use of metabolic profile test in dairy herds. *Vet Rec* 87:150, 1970.
17. Payne JM, Rowlands GJ, Manston R, Dew SM: A statistical appraisal of the results of metabolic profile tests on 75 dairy herds. *Br Vet J* 129:370, 1973.
18. Payne JM, Rowlands GJ, Manston R, Dew SM, Parker WH: A statistical appraisal of the results of the metabolic profile tests on 191 herds in the B.V.H.I.A.D.H.S. joint exercise in animal health and production. *Br Vet J* 130:34, 1974.
19. Poso AR, Lindberg LA: Plasma protein synthesis and serum amino acids in dry and lactating dairy cows. *J Vet Med* 41:72-75, 1994.
20. Ropstad E, VikMo L, Refsdal AO: Levels of milk urea, plasma constituents and rumen liquid ammonia in relation to the feeding of dairy cows during early lactation. *Acta Vet Scand* 30:199-208, 1989.
21. Rowlands GJ, Little W, Kitchenham BA: Relationships between blood composition and fertility in dairy cows - a field study. *J Dairy Res* 44:1-7, 1977.
22. Rowlands GJ, Manston R: The potential uses of metabolic profiles in the management and selection of cattle for milk and beef production. *Livestock Production Science* 3:239-256, 1976.
23. Toharmat T, Nonaka I, Shimizu M, Batajoo KK, Kume S: Effects of prepartum energy intake and calving season on blood composition of periparturient cows. *Asian Australian J of Anim Sci* 11:739-745, 1998.
24. Wheeler DJ, Chambers DS: *Understanding Statistical Process Control* (2nd ed). Knoxville, TN, SPC Press, 1992.