Biochemical Profiling in Companion Animals: An Introduction and an Overview
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Dr. Rebar will be speaking on Clinical Pathology at the CVMA’s Spring Seminar in Yosemite, March 6-8, 2009. This article is related to his presentations there. Details on the conference can be found on page 23.

Biochemical profiling may be defined as the use of multiple blood (serum or plasma) chemistry determinations simultaneously to assess the health status of various organ systems. Organ systems most commonly assessed by standard large chemistry panels include liver, the urinary system, the exocrine pancreas, and, in a general way, the endocrine system.

Biochemical profiling in veterinary medicine first became popular in the late 1970’s-1980’s. It was during this time period that automated systems for blood chemistry determinations first became available. This in turn reduced the cost per test and per blood sample, thereby making biochemical profiling economically feasible for veterinary medicine. An additional turning point was the advent of technologies and equipment which required only very small sample sizes. Small sample size enabled veterinarians to profile even their smallest patients.

Pitfalls of Biochemical Profiling

Today, biochemical profiling is a regular part of companion animal medicine. But biochemical profiling should not be viewed as a panacea. A number of interpretive pitfalls can be cited. First, normal animals may have occasional abnormal test results. Second, ill animals may have normal test results. Finally, abnormalities in one organ system may cause abnormal results in tests used primarily to indicate disease in a different organ system. Each of these pitfalls can be explained in turn.

First, normal animals may have abnormal test results largely because of the way reference intervals are determined. Consider the liver enzyme alanine aminotransferase (ALT). To determine the reference interval, ALT is measured in a cohort of clinically normal animals. Then the mean value and standard deviation (a statistical estimation of variability around the mean) are determined mathematically. By definition, the reference interval includes all values between two standard deviations (S.D.) above and below the mean. Assuming a bell shaped distribution of results, two S.D. above and below the mean includes 95% of all the values. This definition therefore automatically excludes the values for nearly 5% of our clinically healthy population! Since this error occurs for every analyte we measure, the more analytes evaluated, the higher the number of animals that will have at least one abnormal test result. If 12 analytes are measured, over 40% of all clinically normal animals can be expected to have at least one abnormal test result.

The second major pitfall is that ill animals can actually have normal test results. Consider again the liver enzyme ALT. ALT is a cytoplasmic enzyme highly specific to hepatocytes in dogs and cats. However, it only elevates in the blood where there is active injury to hepatocyte membranes. Many chronic conditions have normal membranes.

Furthermore, circulating levels of ALT are influenced both by the number of hepatocytes with injured membranes and the circulating half-life of the enzyme (in this case 2-4 days). As a result, diffuse disease leads to higher enzyme elevations than focal or multifocal lesions which may reveal no elevations at all. Additionally, moderate elevations (2-3 fold) due to a single acute disease episode may return to normal before the animal is even presented to the veterinarian (due to ALT’s short circulating half-life).

The last pitfall of biochemical profiling is that abnormalities in one organ system may cause abnormal results in tests for a different organ system. For example, total serum calcium is used primarily as an indicator of parathormone activity. But total serum calcium is partially bound to albumin. Therefore
anything reducing albumin concentration also reduces total serum calcium, which could lead to erroneous conclusions regarding parathormone activity.

**Considerations in Interpreting Biochemical Profiles**

The preceding discussion regarding pitfalls leads to the following conclusions regarding the use and interpretation of biochemical profiles:

1. A single chemistry test should never be used to assess the total health status of an organ.
2. Understanding the factors affecting each test result in the profile is essential to proper interpretation.
3. Interactions (relationships) among tests and test results must also be considered.
4. Systematic assessment of data is essential to avoid misinterpretation.

Another key to understanding biochemical profiles is to interpret them as a part of a complete laboratory profile. Complete laboratory profiles include hemogram and urinalysis data in addition to clinical chemistry tests. Using this approach, the hemogram, urinalysis, and electrolyte/anion gap profile (sodium, potassium chloride, bicarbonate and anion gap) provide general information about the overall health status of the patient and should be interpreted first. The remainder of the chemistry tests assess various organ systems and are best interpreted last. Such an approach helps eliminate some of the ambiguity from interpreting biochemical profiles alone.

The hemogram includes white cell data (the leukogram), red cell data (the erythrogram), platelet data (the thrombogram), and total plasma protein. Leukogram data is used to recognize inflammation, stress (high circulating glucocorticoids), tissue necrosis, antigenic stimulation, and systemic hypersensitivity. Abnormal erythrogram data is used to identify either anemia (reduced circulating red cell mass) or polycythemia (increased circulating red cell mass). Anemia can be subclassified as regenerative (due to blood loss or hemolysis) or non-regenerative. Polycythemia can also be subdivided into relative polycythemia (due to hemoconcentration – elevated plasma protein) or absolute polycythemia. Absolute polycythemia can be either secondary (due to increased erythropoietin production in association with conditions such as relocation to high altitudes, renal neoplasia, pneumonia, or cardiac disease) or primary (in association with the myeloproliferative disorder, polycythemia vera).

Abnormal platelet numbers identify either thrombocytopenia (when reduced) or thrombocytosis. Thrombocytopenias can be associated with sequestration of platelets in an enlarged spleen, lack of platelet production by the marrow, peripheral destruction by circulating anti-platelet antibodies (immune-mediated thrombocytopenia) or peripheral utilization as a result of over-activation of the clotting process (DIC). Thrombocytosis can be either reactive (e.g. in response to blood loss with stimulation of both red cell and platelet production) or neoplastic (primary thrombocythemia – platelet leukemia).

Elevated total plasma protein suggests hemoconcentration/dehydration, and possible antigenic stimulation. Reduced plasma protein levels suggest possible protein loss through bleeding, glomerular disease with protein loss, loss through the gastrointestinal tract, or reduced protein production by the liver.

A complete urinalysis is essential for evaluation of the urinary system but also provides valuable information about other organ systems and general health status as well. Specific gravity assesses renal tubular concentrating ability; reagent strip chemistries shed light on glomerular (protein) and tubular (glucose) integrity, metabolic state (increased ketones indicate ketoacidosis) and liver disease (increased bilirubin usually suggests cholestasis); and sediment exam can indicate urinary tract hemorrhage (RBCs), urinary tract infection (increased leukocytes), and renal tubular degeneration (granular or waxy casts).

The electrolyte/anion gap addresses acid-base balance, total body electrolyte status, and state of hydration. Findings may help clarify urinalysis and hemogram results and provide further information about the patient’s metabolic state.
A careful integrated consideration of history, clinical signs, hemogram, urinalysis, and electrolyte/anion gap results often makes interpretation of the biochemical organ system profiles much easier. For example, if stress (high circulating glucocorticoids) is indicated by the leukogram (lymphopenia), modest to moderate increases in glucose alkaline phosphatase and ALT can be anticipated and explained in the chemistry profile. Similarly, decreases in plasma total protein in the hemogram without evidence of blood loss in the erythrogram, protein in the urine, or chronic diarrhea with weight loss suggests that lack of protein production by the liver should be strongly suspected and that liver tests in the chemistry profile should be of primary interest. Without this kind of valuable preliminary information, large biochemical profiles can be seriously misinterpreted.