

THE INTERPRETATION OF CLINICAL LABORATORY TEST RESULTS

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With the advent of modern medical technology, the availability of hematological and serum biochemical data to the veterinary practitioner has become commonplace. One unfortunate side effect of this convenience is that some clinicians might tend to focus their attention on one or two abnormal laboratory abnormalities and forget to interpret the test results within the entire clinical context of the patient. The following information provides an overview of the interpretation of clinicopathological abnormalities as they apply to various clinical situations.

ANEMIA

After a thorough history and physical examination are completed, the clinician must inquire as to the basic cause of the anemia. Is it due to: (a) blood loss, (b) impaired erythropoiesis, or (c) accelerated red blood cell destruction? Acute blood loss and hemolysis are typically responsive anemias and usually have specific etiologies which are not difficult to diagnose with the aid of a good history and physical examination. Further information can be obtained from various combinations of radiographs of the chest and abdomen, and specific laboratory tests such as a reticulocyte count, Coombs test, special stains for RBC parasites, coagulogram, fecal examination, etc. Treatment is usually specific and the prognosis can range from good to grave, depending on the specific cause.

Impaired erythropoiesis is commonly associated with some other disease process such as chronic renal failure, liver disease, infections, endocrinopathies, adverse drug reactions and neoplasia. These conditions are characteristically associated with a low reticulocyte count and bone marrow changes indicating impaired RBC production. The clinician should follow up these test results with a thorough evaluation of the patient, including chest and abdominal radiographs and a complete serum biochemistry profile in order to identify the exact major pathologic process in the patient. Only through the treatment of the primary disease entity can there be hope for reversal of the anemia.

LEUKOCYTOSIS

An elevated total white blood cell count is usually interpreted as a sign of infection. More importantly, the clinician should interpret this finding merely as a sign of inflammation and/or necrosis. The differential white blood cell evaluation provides a more exact clue of the underlying cause. For instance, leukocytosis with numerous immature neutrophils and toxic vacuolization often signifies infection, but the presence of very immature cells with prominent nucleoli, abnormal nuclear-cytoplasmic ratios, and mitotic figures signifies hematopoietic neoplasia.

Leukocytosis can occur from bacterial or mycotic infections, regenerative anemias, immune-mediated disease, neoplasia, and hemoconcentration. Stress and certain pharmacologic agents such as glucocorticoids and catecholamines can also cause it. Stress leukograms are characterized with a mature neutrophilia.

If an animal has a moderate to marked leukocytosis while the history and physical examination yield no definitive findings, the clinician should search for the cause by first ordering various diagnostic tests such as a complete urinalysis, chest and abdominal radiographs, and a complete serum chemistry evaluation. A cerebral spinal fluid tap and spinal radiographs should be done if fever and neurologic signs are present. A rheumatoid factor, LE prep, ANA, and Lyme and Ehrlichia titers should be determined if fever and polyarthropathy coexist. Sometimes a bone marrow aspirate or biopsy procedure might be indicated for marked leukocytosis without any explainable cause.

AZOTEMIA

Azotemia can occur under several different circumstances. It could be of minor significance in a dehydrated animal, simply reflecting intravascular volume depletion and prerenal azotemia. Such patients characteristically have a concentrated urine specific gravity, elevated plasma solids and hemoconcentration, and resolve their azotemia with rehydration.

The clinician should determine whether the azotemia is prerenal or renal in origin. The workup should include abdominal radiographs and a complete serum chemistry screen. A complete urinalysis with a fresh urine sediment assessment is imperative. Signs compatible with primary renal failure are azotemia with inappropriately dilute urine or isosthenuria or azotemia associated with the presence of numerous cellular and/or non-cellular casts in the urine sedimentation. Simply diagnosing renal failure is only one half of the clinician's task. Next is to determine whether the animal has a treatable or non-treatable disease and to locate any other coexisting problems that can compromise the effective medical management of the patient. This is well illustrated in the patient with necrotizing pancreatitis.

Severe renal disease does not always initially cause azotemia. Glomerulonephritis and amyloid glomerulopathy, for instance, can cause severe patient debilitation due to excessive albumin losses. Quantitative urine and serum protein determinations are helpful in assessing this disorder, while renal biopsy evaluation lends a more definitive answer to the patient's problem. Renal tubular dysfunction and its accompanying azotemia will eventually ensue. A urine protein to creatinine ratio is a very practical test for assessing glomerulopathy. The normal value is < 1 .

HYPERGLYCEMIA AND HYPOGLYCEMIA

Hyperglycemia (blood glucose exceeding 200mg/dl) is the clinical hallmark sign of diabetes mellitus. In establishing this diagnosis, hyperglycemia with concomitant glycosuria should be demonstrated prior to administering insulin. In cats, psychological or pathological stress can cause temporary hyperglycemia ranging between 200-300 mg/dl. These patients rarely have glycosuria due to the transient elevation of the blood sugar; the hyperglycemia will spontaneously resolve once the stress is removed. Normal findings on a repeated blood glucose determination and urinalysis will obviate the need for insulin. However, with sustained hyperglycemia and glycosuria, insulin therapy is clearly indicated. Dogs seldom have stress-induced hyperglycemia exceeding 125-150 mg/dl.

Acute pancreatitis commonly causes hyperglycemia because of hyperglucagonemia and

hypoinsulinemia. This effect can be transient or sustained thereby requiring repeated blood and urine glucose determinations.

Diabetic patients should be thoroughly evaluated in order to identify and treat any coexisting problems such as renal failure, pyometra, Cushing's syndrome, and severe fluid and electrolyte abnormalities.

Hypoglycemia commonly occurs in the very young kitten and puppy due to transient immaturity of the liver enzyme systems responsible for gluconeogenesis and glycogenolysis. The diagnosis is usually easily achieved and successfully treated. In the middle and older aged dog, hypoglycemia is commonly associated with pancreatic beta cell adenocarcinoma (insulinoma). This diagnosis requires one or serial immunoreactive insulin and blood glucose determinations and the demonstration of inappropriate hyperinsulinemia. Hypoglycemia can also be associated with endotoxemia and septicemia, large mesenchymal neoplasms, severe prolonged hyperthermia, status epilepticus, hypoadrenocorticism, and insulin overdose.

SERUM SODIUM AND POTASSIUM

The normal serum sodium level ranges from 140-155 mEq/L. Hyponatremia basically occurs from water gain or sodium loss. It can be caused by water intoxication; ie the overzealous intravenous administration of dextrose in water solutions, ADH hypersecretion, severe gastrointestinal or renal sodium losses, or from mineralocorticoid depletion associated with hypoadrenocorticism. Unlike the preceding conditions that can actually deplete body sodium, pseudohyponatremia can occur with hyperlipidemia and hyperproteinemia by interfering with the flame photometer measurement of the true serum sodium concentration.

True hyponatremia should be corrected with saline infusions due to the hypotensive and neurological complications that can arise from this particular electrolyte abnormality. In addition, the exact underlying cause should be determined and corrected as well.

Hypernatremia is fundamentally caused by water loss or salt gain. Although it is usually benign when associated with hemoconcentration, it can become life-threatening in a water deprived patient with diabetes insipidus. Hypernatremia due to sodium gain is associated with excess sodium chloride ingestion (sea water) and from the intravenous infusion of concentrated salt solutions such as 3, 5 and 7.5% saline. Essential hypernatremia can occur from an inadequate hypothalamic response to plasma hypertonicity. The main pathologic consequence of hypernatremia is serum hyperosmolality which can lead to brain hemorrhages and infarctions and the patient's eventual demise.

Hypokalemia (serum K^+ < 3.5 mEq/L) is caused by excessive potassium loss from the body or its cellular translocation. Common causes include excessive diuretic administration, chronic renal disease (in cats), metabolic alkalosis, low potassium-containing intravenous fluid infusions, prolonged osmotic diuresis, and gastrointestinal loss. Replacement with intravenous potassium chloride while correcting the underlying cause is essential toward correcting this problem. When hypokalemia accompanies metabolic alkalosis associated with gastric outflow obstruction, the laboratory profile usually shows low serum chloride and elevated bicarbonate and

total CO₂ levels. Abdominal radiographs should also be done. With marked hypokalemia (serum K⁺ < 2.5), a lead II EKG will occasionally show characteristic changes such as elevated P wave amplitude, flattened T waves, prolonged PR interval, depressed ST segments, and a widened QRS complex.

Hyperkalemia (serum K⁺ > 5.5 mEq/L) is a life-threatening disorder due to its potential myocardial toxic effects. Various causes include acute renal failure with or without an obstructive uropathy, urinary bladder rupture, severe metabolic acidosis (pH < 7.0), hypoadrenocorticism, excessive spironolactone diuretic therapy, and iatrogenic overdose of potassium salts. The underlying abnormality should be immediately sought from the patient's history and physical findings, complete urinalysis, BUN or creatinine, serum sodium and chloride concentrations, and blood gas and pH determinations. An ACTH stimulation test should be done when Addison's disease is suspected. Serum potassium levels exceeding 7.0 mEq/l require prompt recognition and treatment. When hyperkalemia is suspected while awaiting lab test results, a lead II EKG should be done in order to detect the typical changes including shortened P wave amplitude, increased T wave amplitude, widening of the QRS complex, absence of the P wave with bradycardia, and sine wave complexes. As with other electrolyte abnormalities, the overall therapeutic success depends on identification and treatment of the underlying cause.

SERUM CALCIUM

Serum calcium exists in two main forms: (a) albumin bound (constituting about 50% of the total serum calcium) which is biologically inactive and (b) ionic calcium (contributing to the remaining 50% of the total serum calcium) which is biologically active. Blood pH influences the protein binding tendency of calcium where metabolic alkalosis increases the bound portion whereas metabolic acidosis decreases it.

Hypocalcemia (serum calcium < 9.0 mg/dl) can occur with hypoparathyroidism, chronic renal disease, malabsorption, and vitamin D deficiency. High phosphate containing enemas can cause hypocalcemia when used in the severely obstipated patient and in those with chronic renal disease. Hypocalcemia associated with hypoalbuminemia results from the loss of albumin bound calcium, but neuromuscular dysfunction seldom occurs so long as the serum ionic fraction is adequate.

Hypercalcemia (serum calcium > 12.0 mg/dl) occurs with primary hyperparathyroidism, neoplastic osteolytic metastasis, hypervitaminosis D, and hypercalcemia of malignancy. Because primary hyperparathyroidism and hypercalcemia of malignancy each cause hypercalcemia and hypophosphatemia, the medical workup should include a careful search for occult neoplasia associated with the latter condition, the more common types being lymphosarcoma and anal apocrine gland adenocarcinoma.

TOTAL CO₂

The total carbon dioxide level represents the sum of the serum bicarbonate, carbon dioxide and carbonic acid. Over 90 percent of the TCO₂ is represented by bicarbonate. Therefore, this

value can be used to approximate the acid base status of the patient. The normal range for TCO_2 in the dog and cat is 18-25 mEq/L.

In metabolic acidosis, the TCO_2 level is < 18 mEq/L. Clinically significant acidosis occurs at levels < 12 mEq/L.

Metabolic alkalosis occurs when the TCO_2 level > 25 mEq/L. Marked alkalosis occurs at levels > 40 mEq/L.

SERUM PROTEINS

Hyperalbuminemia is not associated with any particular disease entity. It merely indicates plasma water volume depletion associated with dehydration or laboratory error.

Hypoalbuminemia is associated with serious disorders. Low serum albumin is caused by loss from the body as seen in glomerulopathies and protein losing enteropathy, impaired production as found in chronic fibrosing liver disease, decreased protein ingestion associated with starvation that caused by translocation into a 3rd body space as seen in peritonitis and capillary leaks. The initial workup should include a complete history and physical examination, a complete urinalysis, and a serum biochemical profile. Additional tests such as gastrointestinal absorption studies and liver function tests can be done pending the preliminary findings.

Hyperglobulinemias can be further characterized with a serum protein electrophoresis. A monoclonal gammopathy is frequently associated with multiple myeloma. When this condition is suspected, a radiographic bone survey and an analysis for Bence-Jones proteinuria should be done. Certain macroglobulinemias associated with serum hyperviscosity can also occur and require serum viscosity and serum protein immunoelectrophoresis determinations.

Polyclonal gammopathies are rather common in the dog and cat. In the latter, it can be a feature of infectious peritonitis; however it can also be due to a benign polyclonal gammopathy associated with any chronic antigenic stimulation. Therefore, it is important to note that not all cats with polyclonal gammopathies have IFP, and not all cats with IFP have polyclonal gammopathy. Polyclonal gammopathy usually represents immune stimulation as illustrated with the beta and gamma globulin elevations accompanying dirofilariasis and skin parasitism such as demodexis.

LIVER ENZYMES

The commonly used serum chemistries to assess the liver in the dog and cat include SGOT (AST), SGPT (ALT), LDH, alkaline phosphatase, total bilirubin, albumin, and bile acids. BSP and blood NH_3 determinations can also be done. A liver biopsy provides the most definitive information.

Elevations in liver transaminase enzymes (ALT, AST) are frequently associated with hepatic necrosis, but they cannot quantitate the actual amount of liver damage. With chronic liver fibrosis, for instance, where a significant amount of hepatocellular destruction has already occurred, the liver stores of intracellular transaminase enzymes are usually depleted, thus allowing

for mild serum enzyme elevations despite extensive parenchymal damage. Serum liver transaminase elevations are commonly associated with infiltrative and inflammatory diseases such as hepatic necrosis, cholangiohepatitis, lymphosarcoma, and lipidosis. Surprisingly low levels occur with liver abscesses and metastatic tumors involving the liver. Diabetic ketoacidosis in the dog and cat and canine hyperadrenocorticism are commonly associated with elevated serum liver transaminase levels because of the accumulation of lipid and glycogen, respectively.

Increased serum alkaline phosphatase and bilirubin levels characterize cholangiostasis. When associated with markedly elevated serum transaminase levels, coexisting hepatocellular damage should be suspected. Isolated increases in serum alkaline phosphatase levels can also accompany Cushing's syndrome, metastatic tumors to the liver, and bone neoplasia. A growing puppy normally has an elevated serum alkaline phosphatase level of skeletal origin.

Hemolytic anemias can cause elevated liver enzymes and bilirubin levels. This is especially common in fulminating intravascular hemolysis where hypoxia causes cellular necrosis. Other features such as hemoglobinemia, hemoglobinuria, anemia, reticulocytosis, and polychromasia help identify this as a cause of icterus in the dog and cat.

In chronic hepatic fibrosis, the typical liver profile includes mild to moderately elevated serum alkaline phosphatase and mild to moderate elevations in serum transaminase enzymes. Bilirubinuria is common while hyperbilirubinemia will vary. The BSP and serum bile acid levels are typically elevated as well. Hypoalbuminemia, hypoglycemia and a prolonged prothrombin time signify a guarded to grave prognosis because they indicate decreased liver synthetic capability which often accompanies end-stage disease.