

Biochemical Profiling in the Dog and Cat

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 Nestlé PURINA
Clinical Handbook Series

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Introduction



The goal of this text, *Biochemical Profiling in the Dog and Cat*, is to outline a systematic approach to the interpretation of large clinical chemistry profiles. It is not designed as an in-depth treatise on interpretive clinical chemistry but rather as an adjunct to such texts. To accomplish these objectives, an organ system and case-oriented format is used, following the style first introduced to veterinary medicine by Duncan and Prasse.³² The book is divided into four sections, as described below.

Part I (Chapters 1 through 4) covers basic information on biochemical profiling as well as interpretation of the hemogram, urinalysis, and acid-base balance. Many of the tests used to evaluate acid-base balance are part of most large biochemical profiles; however, because acid-base disturbances are non-specific and can occur in diseases of many organ systems, acid-base balance is considered along with hemogram and urinalysis data.

In Part II (Chapters 5 through 9), each major organ system is discussed independently and a specific test panel is outlined for each. The specific panel represents a subset of the standard large chemistry profile and consists of those tests which should be evaluated first and as a unit whenever involvement of the given organ is suspected on the basis of history, clinical signs, and physical examination. The rationale for the use and interpretation of each test in the organ system panel is briefly outlined and a series of cases that illustrate the principles of interpretation for each organ system is then provided. (In some instances, the data have been modified for teaching purposes.)

Part III (Chapter 10) consists of a series of case studies presented as “unknowns.” The reader is encouraged to apply the principles outlined in Parts I and II to interpret the data presented. For each case, the authors’ interpretations are included.

Part IV includes important reference material:

- ❑ Table 1. Chemistry Reference Ranges for the Dog and Cat*
- ❑ Table 2. Hematology Reference Ranges for the Dog and Cat*
- ❑ Subject Index
- ❑ Suggested Reading
- ❑ Glossary of Terms

** Reference values listed herein are from the Purdue University Veterinary Clinical Pathology Laboratory and are not intended as general reference values. Reference ranges may vary among other institutions and laboratories.*



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Chapter 1: Biochemical Profiling Defined

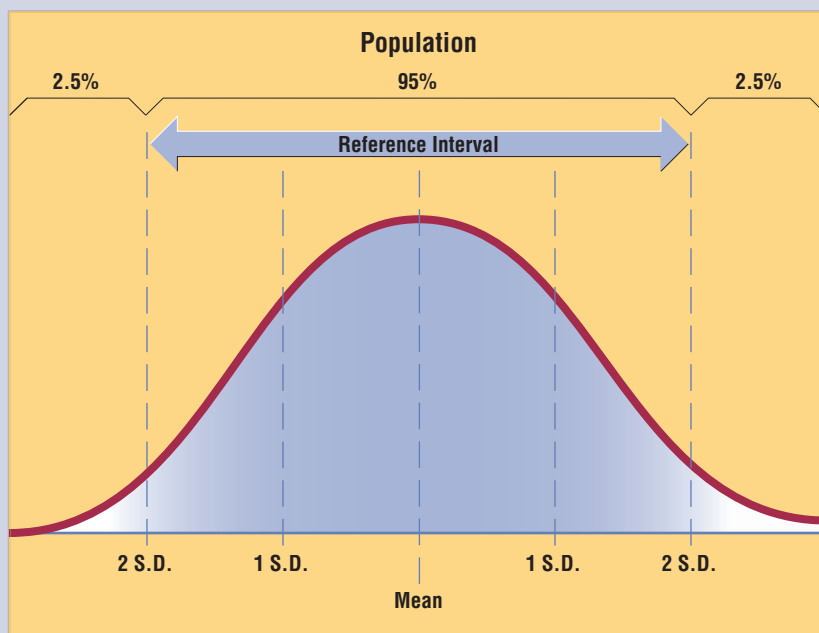
Biochemical profiling is defined as the use of multiple blood chemistry determinations to simultaneously assess the health status of various organ systems. In addition to standard chemistry tests, other parameters (ie, hemograms, urinalysis) are measured to give a more accurate and complete picture of the overall health status of the patient. Strictly speaking, hemograms and urinalysis are not part of clinical biochemical profiles; however, biochemical profiles cannot be accurately interpreted without simultaneous evaluation of the complete blood count (CBC) and urinalysis.

Biochemical profiling is a powerful diagnostic and monitoring device used in ill patients and those receiving therapy. It is also an important component of regular wellness evaluations in healthy dogs and cats. Although biochemical profiling offers exciting potential as a clinical tool, it is not a panacea. The following paragraphs illustrate some of the more important difficulties encountered in the interpretation of clinical chemistry data.

Since standard chemistry screens may include from 12 to 30 different test results, interpretation of these data may

be extremely complex. Furthermore, interpretation of results is often clouded by the fact that perfectly normal animals may have, indeed are expected to have an occasional abnormal test result. It is estimated that in a standard panel of 12 chemistry tests, approximately 46% of all normal subjects will have at least one abnormal test result. Such abnormalities are usually associated with the way in which reference (or normal) values are determined.

In order to establish the “normal range” reference values for a given test, the procedure is performed on samples from a large population of clinically normal individuals. The central 95% of the given results is identified and, if the data have a Gaussian distribution, a mean and a standard deviation are determined based on the central 95%. The reference values are then defined as those values falling within the central 95%, ie, within 2 standard deviations above and below the mean (*see Fig. 1*). Therefore, 5% of the values from a normal (ie, healthy) population fall outside the defined “normal” reference interval for any given parameter.



Reference intervals are established as all values falling between 2 standard deviations above and below the mean. By convention, therefore, 5% of the results from clinically normal individuals fall outside the reference interval for any given parameter.

Figure 1. Establishment of reference intervals based on a Gaussian distribution

Just as healthy individuals may have occasional abnormal test results, patients with severe organ disease can have test results that lie within the normal reference intervals. For example, elevated alanine aminotransferase (ALT)—an enzyme normally found in the cytosol of hepatocytes—has long been considered an important indicator of liver disease in dogs. However, serum ALT levels will only be elevated under specific circumstances, eg, in conditions where there is injury to hepatocyte plasma membranes causing release of cytoplasm from membrane bound vesicles. In more chronic liver disease, plasma membrane characteristics may be near normal. Additionally, ALT levels reflect the number of hepatocytes with injured membranes; therefore, marked elevations are more commonly seen in diffuse rather than localized liver disease. ALT levels also will vary with the stage of organ disease at the time of sample collection. This enzyme has a circulating half-life of 2 to 4 days; therefore, a 2-fold elevation in ALT due to acute liver necrosis may be expected to return to near normal within a week.

The clinician must also be aware that physical compromise of one organ system may cause abnormal chemistry

values in tests that are used primarily to indicate disease in a different organ system. For example, calcium levels are used primarily as indicators of parathormone activity. However, serum calcium is partially bound to albumin filtrate. Consequently, anything that reduces albumin concentration may result in reduced calcium concentration, which could lead to erroneous conclusions about parathormone activity.

Key points in the practice of biochemical profiling:

- ❑ A single chemistry test should never be used to assess the total health status of an organ.
- ❑ Understand the factors affecting a given test result, such as the causes of elevations, circulating half-lives of components being measured, and routes of excretion.
- ❑ Consider the interactions between different organ systems and how that interaction can affect various test results.
- ❑ Only through the systematic assessment of data can misinterpretation and confusion be avoided.

Chapter 2: Hemogram Interpretation

The hemogram, or complete blood count (CBC), is not by definition part of the large chemistry profile. However, hemogram data provide important indicators that can support chemistry findings and assist in diagnosis and treatment of disease.

The CBC includes both quantitative and qualitative hematologic data. Quantitative data include total red cell, white cell, and platelet counts; differential white cell count; total plasma protein (TP); hemoglobin (Hb); hematocrit (HCT); reticulocyte count; and red cell indices (*See Red blood cells*). Qualitative data are the morphologic findings on the blood film. The following paragraphs touch upon the highlights of hemogram interpretation, particularly as they relate to the interpretation of chemistry data.

More detailed discussions on hemograms as well as numerous case illustrations can be found in the Purina Clinical Handbook *Hemogram Interpretation for Dogs and Cats*.⁹⁸

Total protein

Total plasma protein (TP) can be determined by either a refractometer or chemical methods. In the CBC, it is usually measured by refractometry. Plasma protein is a conglomerate of over 200 protein fractions including albumin, alpha globulins such as haptoglobin, beta globulins such as hemopectin, fibrinogen, transferrin, and all classes of immunoglobulins. Because TP levels are a crude estimation of plasma protein alterations, only very basic and general interpretations are possible.

Elevated TP levels are most often associated with either dehydration or chronic antigenic stimulation with hypergammaglobulinemia. Total protein elevations influence interpretation of other laboratory data. For example, elevated TP levels in conjunction with elevated HCT suggest that the animal is probably dehydrated with relative polycythemia as a result. If normal hydration were restored, HCT would most likely be normal. On the other hand, an elevated TP in conjunction with a low HCT is alarming because dehydration may well be masking a more severe anemia. When TP is elevated secondarily to dehydration, other chemistry changes are to be anticipated. For example, electrolyte levels should be higher due to simple concentration (*see Chapter 6, case 2*). Prerenal azotemia secondary to hypovolemia and characterized by mild to moderate eleva-

tions in blood urea nitrogen (BUN) and creatinine is often present. If renal tubular function has remained normal, elevated urine specific gravity is expected.

Decreased TP levels (hypoproteinemia) are also significant and further evaluation of specific organ systems is necessary. Hypoproteinemia may result from protein-losing enteropathy, protein-losing nephropathy, decreased protein production by the liver, or severe blood loss anemia. The pattern of hypoproteinemia, determined from clinical chemistry evaluation of TP and albumin, may be helpful in differentiating underlying etiology. Protein-losing enteropathy and blood loss are typically characterized by panhypoproteinemia (decreased TP, albumin, and globulins). Protein-losing nephropathy is often characterized by hypoproteinemia with low albumin and normal globulins. Proteinuria is generally detected with urine reagent strips. Reduced protein production by the liver is most commonly characterized by hypoproteinemia with hypoalbuminemia and usually hypergammaglobulinemia.

Red blood cells

Red blood cell (RBC) measurements in the CBC include HCT, RBC count, Hb determination, and red cell morphology as seen on the peripheral blood film.

From these standard measurements, the red cell indices—mean cell volume (MCV) and mean cell hemoglo-

The CBC

- ❑ Total plasma protein (TP)
- ❑ Red cell parameters
 - Hematocrit
 - Red cell count (RBC)
 - Hemoglobin
 - Morphology
- ❑ White cell parameters
 - White cell count (WBC)
 - Differential cell count
 - Morphology
- ❑ Platelets

bin concentration (MCHC)—can be computed (*Table 2.1*). In anemic dogs and cats a reticulocyte count can be helpful. Absolute reticulocyte counts of greater than 80,000/ μ l in either dogs or cats suggest increased production of RBCs in the bone marrow. With these data, the principal RBC abnormalities, polycythemia and anemia, can be recognized and subclassified.

Anemia is by far the most common red cell disturbance in animals and can be classified as regenerative or non-regenerative on the basis of the CBC and reticulocyte count. Regenerative anemias are characterized by decreased HCT, increased reticulocyte count, and polychromasia and anisocytosis on the blood film. Markedly regenerative anemias have elevated MCV values and reduced MCHC values (macrocytic and hypochromic anemias). Regenerative anemias include the acute and subacute blood loss anemias, and intravascular and extravascular hemolytic anemias. Further differentiation of the specific types of regenerative anemias is beyond the scope of this discussion and the reader is referred to more in depth hematology references. (*See Suggested Reading; 10, 22, 23, 25, 32, 41, 42, 50, 55, 57, 60, 71, 98, 110.*)

Rapidly developing blood loss or hemolytic anemias may profoundly affect other laboratory data. Acute anemias are associated with rapidly developing hypoxia, which causes damage to cell membranes in parenchymal organs (eg, the liver) and the release of cytoplasmic enzymes. Enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) all may be elevated. Hemolysis in general may cause elevations in serum bilirubin levels because of increased hemoglobin turnover. Intravascular hemolysis causes hemoglobinemia and hemoglobinuria. Hemoglobinemia may interfere with many colorimetric chemistry determinations.

Non-regenerative anemias are characterized by decreased HCT without evidence of response; that is, no reticulocytosis. Non-regenerative anemias can only be subclassified by bone marrow examination. Generally, non-regenerative anemias are either maturation defect anemias characterized by ineffective erythropoiesis^{32,98,110} or anemias associated with RBC marrow hypoplasia. Hypoplastic non-regenerative anemias may be caused by general marrow damage, reduced erythropoietin, marrow invasion by neo-

plasia, or marrow depression associated with chronic disease. The vague non-regenerative “anemia of chronic disease” is the most commonly encountered anemia in veterinary medicine and can develop in a week or less (in cats). In terms of MCV and MCHC, maturation defect anemias may be macrocytic normochromic, normocytic normochromic, or microcytic hypochromic. Hypoproliferative anemias are usually normocytic normochromic. Because of the prevalence of the anemia of chronic disease, other evidence of chronicity should be considered in evaluating chemistry data from patients with normocytic normochromic anemias.

White blood cells

White blood cell (WBC) measurements in the CBC are the WBC count and differential cell count from the peripheral blood film. Although the differential cell count is always evaluated as a percentage, it should only be interpreted in terms of absolute numbers. Specific interpretation of leukogram data relies heavily upon an understanding of granulocyte kinetics, and for a complete discussion the reader is referred to other more detailed references. (*See Suggested Reading; 1, 15, 24, 32, 73, 74, 80, 81, 86, 98.*) Leukogram data are used to determine whether a disease process is inflammatory or non-inflammatory. The role of stress (ie, exogenous or endogenous steroids) in the disease process also can be partially assessed. Acute to subacute inflammation is suggested by a left shift, ie, the presence of increased numbers of immature neutrophils (band cells) in the circulation. In dogs and cats, most inflammatory processes are also accompanied by a leukocytosis with neutrophilia and possible monocytosis, but leukopenia with neutropenia and left shift (degenerative left shift) may be seen with severe overwhelming inflammatory disease. Chronic inflammatory diseases are usually low grade and therefore characterized by normal to elevated leukocyte counts with mature neutrophilia, no left shift, and often a monocytosis. Stress (endogenous steroid secretion) or exogenous glucocorticoid administration results in the presence of a lymphopenia. Thus, in dogs and cats suffering from acute to subacute inflammatory disease processes accompanied by stress, a leukocytosis with neutrophilia, left shift (regenerative left shift), monocytosis, and lym-

Table 2.1 Red Cell Indices

$$\text{Mean cell volume (MCV)} = \frac{\text{HCT} \times 10}{\text{RBC (in millions)}} \text{ expressed in femtoliters (fl)}$$

$$\text{Mean cell hemoglobin concentration (MCHC)} = \frac{\text{Hb} \times 100}{\text{HCT}} \text{ expressed in grams per deciliter (g/dl)}$$

phopenia can be expected. A stress leukogram without accompanying inflammation is usually characterized as a mild leukocytosis with a mature neutrophilia, no left shift, lymphopenia, eosinopenia, and a marginal monocytosis.

A suggestion of stress in the CBC has important implications for the clinical chemistry panel. Physiologic increases in glucocorticoids associated with stress can cause moderate elevations in blood glucose (> 135 mg/dl but < the renal threshold of 180 mg/dl). Increases of greater than physiologic levels (eg, Cushing's disease, exogenous steroids) can additionally cause marked increases in alkaline phosphatase (ALP) or interfere with renal tubular concentrating ability.

Platelets

Platelet parameters in the CBC include assessment of platelet numbers and evaluation of platelet morphology on the peripheral blood film. The most frequently recognized platelet abnormality in animals is thrombocytopenia. Thrombocytopenia may be associated with immune-mediated disease, bone marrow hypoproliferation, or splenic sequestration. In addition, thrombocytopenia may be a feature of disseminated intravascular coagulopathy (DIC), a syndrome that is almost always secondary to severe underlying systemic disease and that usually produces numerous chemistry profile abnormalities.

Chapter 3: Urinalysis Interpretation

Although urinalysis is not part of the large chemistry profile, it is a recommended accompanying test for two important reasons. First, like the CBC, urinalysis provides valuable information concerning general health status and state of hydration. Second, renal parameters in the large chemistry profile (eg, blood urea nitrogen (BUN) and creatinine) can only be accurately interpreted by including urinalysis data.

Urinalysis is comprised of three components: physical examination, chemical examination, and urine sediment examination. Physical examination includes evaluation of color, turbidity, and specific gravity. Chemical evaluation includes semiquantitative evaluation of urine protein, ketones, glucose, bilirubin, urobilinogen, occult blood, and pH. Urine sediment examination is the microscopic evaluation of the formed elements of the urine—casts, crystals, cells, and other elements such as bacteria.

For a more detailed discussion on urinalysis, including numerous case studies, please see the Purina Clinical Handbook *Interpretation of Canine and Feline Urinalysis*.¹¹⁸

Physical Examination

Color

Normal urine is yellow to amber. In general, the more dilute the urine, the less intense the color. Numerous abnormalities result in color changes. Frank hemorrhage will color urine red. Hemoglobinuria or myoglobinuria gives urine a deep red-brown discoloration. Bilirubin gives urine an orange-brownish cast. Drug therapy may also alter urine color.

Turbidity

Normal feline and canine urine is clear; increased turbidity is generally a reflection of increased particulate matter in the urine. Such particulates will be identified during the microscopic examination of the sediment.

Specific gravity

Specific gravity is used to estimate the ability of the renal tubules to concentrate or dilute the urine; therefore, it is a true renal function test. There is no “normal” value for urine specific gravity and measurements can range from 1.001 to 1.070 in the dog and up to 1.080 in the cat. Normal animals may have urine specific gravity values in

the dilute, isosthenuric, or concentrated range, depending upon the state of hydration. Animals that are diuresing are expected to have urine specific gravity values in the fixed or dilute range. In contrast, dehydrated animals are expected to concentrate urine.

Urine specific gravity of 1.008 to 1.012—the normal specific gravity of plasma—is considered to be in the fixed or isosthenuric range. (In practice, this fixed range is often extended up to 1.017). Urine specific gravity of greater than 1.030 in the dog and 1.035 in the cat suggests renal tubular concentration; specific gravity levels below 1.008 indicate dilution.

Urine specific gravity is of particular value in the evaluation of azotemia (increased circulating nitrogenous wastes as reflected by elevations in BUN and creatinine). Prerenal azotemia is the result of reduced renal perfusion seen with conditions such as dehydration and shock, and elevated BUN and creatinine should be accompanied by a high urine specific gravity. In contrast, primary renal azotemia (renal failure) is usually associated with inability of the tubules either to concentrate or to dilute; therefore, the marked elevation in BUN is generally accompanied by a

Urinalysis

- Physical examination
 - Color
 - Turbidity
 - Specific gravity
- Chemical examination
 - Protein
 - Ketones
 - Glucose
 - Bilirubin
 - Occult blood
 - Urine pH
- Sedimentation
 - Casts
 - Crystals
 - Cells
 - Bacteria

specific gravity in the isosthenuric range. Even inadequately concentrated urine (≤ 1.030 in dogs, < 1.035 in cats) in the face of azotemia is consistent with renal azotemia. A fixed or inadequately concentrated specific gravity with azotemia or dehydration indicates that at least two-thirds of the tubules are nonfunctional.

Certain caution must be exercised in the interpretation of urine specific gravity. Because even normal animals have occasional urine samples with specific gravity values in the fixed range, the significance of a single demonstration of isosthenuria must be questioned. If the animal is in a normal state of hydration and not azotemic, further evaluation may be necessary to determine renal function.

Urine specific gravity should also be interpreted in light of certain historical information as well as the physical exam. For example, postrenal azotemia is a consequence of retaining the nitrogenous wastes due to postrenal obstruction and/or the loss of integrity of the excretory route. Depending on the nature of the lesion and the timing of sampling, azotemia may be present with either concentrated or inadequately concentrated urine. Therefore, postrenal azotemia cannot be readily distinguished from prerenal or renal azotemia based on laboratory data alone. Azotemia in conjunction with stranguria, dribbling urine, history of recent trauma and/or ascites should raise concerns for a postrenal mechanism of azotemia. Other diagnostic modalities (imaging, fluid analysis, etc.) are needed for confirmation.

Furthermore, urine chemistry measurements must be considered in conjunction with urine specific gravity. Concentrations of urine protein or glucose of greater than 4+ on reagent dip strips can falsely elevate urine specific gravity from the isosthenuric or ambiguous range into the concentrating range.

Chemical Examination

Urine protein

Urine protein levels are easily determined with reagent dip strips. Like most renal parameters, urine protein levels must be evaluated in light of urine specific gravity. A 1+ to 2+ proteinuria is far more significant in a dilute urine sample than in a concentrated one.

There are many causes of proteinuria and in most cases differentiation depends upon other reagent dip strip results or sediment findings. Hemorrhage or inflammation in the

urinary tract may cause proteinuria and is recognized by the increased number of cells in the sediment.

Myoglobinuria or hemoglobinuria, detected as occult blood, also may be a cause of proteinuria. If the preceding causes of proteinuria are lacking, glomerular leakage must be considered. However, conditions such as shock or fever may cause a mild nonspecific proteinuria.

Ketones

The presence of ketones in the urine is readily established with reagent dip strips. Ketone bodies are found in the urine when fat metabolism has replaced carbohydrate metabolism as the principal energy-producing pathway. This occurs in several conditions, including starvation and diabetes mellitus. Ketonuria is usually associated with a metabolic acidosis. False negatives can occur when urine is not fresh.

Glucose

In normal animals, circulating glucose is filtered into the glomerular filtrate and then reabsorbed into general circulation by the proximal renal tubules. Glycosuria is seen in association with either hyperglycemia when the tubular reabsorption maximum of the kidney has been exceeded (180 mg/dl in dogs; 280 mg/dl in cats), or when the renal tubules have reduced resorptive capabilities. The latter condition is seen occasionally in renal disease as a nonspecific finding and, rarely, in congenital renal glycosuria. Glycosuria is commonly seen in cases of diabetes mellitus, a condition where the glucose in the urine predisposes to bacterial cystitis. If urine is allowed to stand after collection from a patient with diabetes mellitus, glycosuria may not be detected because of bacterial metabolism. Cats with stress hyperglycemia also commonly present with glycosuria. False positives may be seen in cats with hematuria. False negatives may be seen in animals excreting ascorbic acid in their urine as occurs in diabetes mellitus.

Bilirubin

See Chapter 6, Clinical Pathology of Hepatic Disease.

Urobilinogen

Urobilinogen is produced in the intestine by bacterial reduction of bilirubin. Approximately 10% of the urobilino-

gen produced is recirculated to the liver by portal circulation and back into the intestine via bile. Ten percent of that recirculated to the liver reaches general circulation, becomes a part of the glomerular filtrate, and is excreted in the urine. Because urobilinogen is produced only from bilirubin that has entered the intestinal tract, the presence of urinary urobilinogen indicates that the bile duct is at least partially patent. Similarly, in theory, the absence of urinary urobilinogen indicates bile duct obstruction. Unfortunately, the test for urobilinogen is of little interpretive value. The test for measuring urobilinogen is of low sensitivity and is further complicated by the fact that urobilinogen converts to an inert form almost immediately upon exposure to light. In addition, a decrease in urobilinogen cannot be measured by reagent dip strips.

Occult blood

The test for the presence of myoglobin or hemoglobin in the urine may be positive when there is hematuria, hemoglobinuria, or myoglobinuria. Myoglobinuria is seen with muscle disease, hemoglobinuria may be seen with overwhelming hemolysis, and hematuria is seen with hemorrhage anywhere in the urogenital tract. Hematuria is confirmed by the presence of RBCs in the urine sediment. Myoglobin may be distinguished from hemoglobin by the associated clinical signs and serum chemistry measurements (ie, creatine kinase).

Urine pH

Normally, urine pH of carnivores is acidic (< 7.0). In cystitis, pH may be alkaline because of the presence of urea-splitting bacteria. Also, urine that stands for some time before testing may turn alkaline due to bacterial action (*see Chapter 4, Acid-Base Balance*).

Urine Sediment Examination Cells

Three kinds of cells may be found in the urine sediment: WBCs, RBCs, and epithelial cells. In cystocentesis or midstream samples the following results are considered within normal limits: 0 to 5 RBC/high power field (HPF, 40× objective), 0 to 5 WBC/HPF, and occasional epithelial cells/HPF. These values will vary with the volume of urine used for sediment preps (5 ml to 10 ml is recommended).

Slightly higher numbers may be seen in catheterized samples.

Increased numbers of RBCs (hematuria) indicate hemorrhage in the urogenital tract and may be the result of either inflammation (eg, pyelonephritis, cystitis) or trauma (eg, traumatic catheterization).

White cell numbers must be interpreted in relation to RBC numbers. If WBCs are disproportionately increased compared to numbers in the peripheral blood, inflammation is present. Inflammation is rarely seen in the absence of hematuria.

Increased numbers of epithelial cells in the sediment are more difficult to interpret. Three types of epithelial cells may be found in urine: squamous epithelium from the vagina or prepuce, transitional cells from the lower urinary tract, and smaller renal epithelial cells. The type of sample collection influences the numbers and types of epithelial cells seen in normal samples. Midstream urine samples have higher numbers of squamous cells while catheterized samples from normal animals may contain increased numbers of transitional cells (in some cases, cohesive rafts) or clusters. In general, pathologically increased numbers of epithelial cells in the sediment are associated with inflammation, degeneration, or neoplasia of the urogenital tract. For malignancy determination, cytologic evaluation of an air-dried, stained sediment smear is recommended in cases where markedly increased numbers of epithelial cells are seen.

Crystals

Urine of healthy dogs and cats contains the following types of crystals: triple phosphate, calcium oxalate hydrate, occasional calcium carbonate, urate, and accumulations of amorphous phosphate. Crystals of pathologic significance in dogs and cats include ammonium biurate and tyrosine crystals (associated with liver disease), bilirubin crystals (associated with cholestasis or hemolysis), calcium oxalate monohydrate crystals (associated with ethylene glycol toxicosis), and cystine crystals (associated with an inherited aminoaciduria). The morphology of these crystals is discussed in other texts.³²

Casts

Casts are probably the most important diagnostic find-

ing in the urine sediment because they localize injury to the kidney. With the exception of hyaline casts, any casts in the urine are abnormal and usually imply some degree of renal damage. The morphology of casts is described and illustrated elsewhere³⁹; only the interpretive significance will be considered here.

Casts may be hyaline, cellular, granular, or waxy. Hyaline casts are composed of mucoprotein and are primarily seen with mild renal injury and glomerular leakage. However, very low numbers may be present in otherwise healthy animals. Mildly increased numbers may be observed with exercise, dehydration, or fever. Large numbers of the hyaline casts indicate significant glomerular damage and usually are found concomitantly with elevated urine protein. Hyaline casts are common in cases of the nephrotic syndrome.

Cellular casts may be composed of RBCs, WBCs, or epithelial cells. Red cell casts indicate renal hemorrhage or inflammation, white cell casts indicate renal inflammation, and epithelial cell casts indicate acute tubular degeneration.

Granular casts are simply older epithelial cell casts in which the epithelial cells have degenerated to the point that they can no longer be identified as individual cells.

Granular casts are of 2 forms: coarsely granular (early stage) and finely granular (late stage). Both forms are interpreted as evidence of tubular degeneration. With time, the finely granular cast is further modified to form a fairly homogeneous cast called a waxy cast. Waxy casts indicate intrarenal stasis of granular casts and must be distinguished from hyaline casts.

It is possible to see epithelial cell, granular, and waxy casts simultaneously in the urine sediment of an animal with ongoing tubular degeneration.

Bacteria

Bacteria in urine are only significant in aseptically collected samples that are immediately evaluated. Immediacy is especially important; bacteria multiply readily in standing urine samples, which can affect other parameters measured.

Chapter 4: Acid-Base Balance

Abnormalities in acid-base balance are not diagnostically specific since they can occur in many diseases of various organ systems. For this reason, acid-base evaluation is an important secondary profile for most of the organ systems covered in this text. Although essential for complete characterization of acid-base status, blood gas analysis is not discussed since it is not readily available to most veterinary practices; this discussion covers only clinical chemistry and urinalysis, parameters that are more commonly assayed. Hence, interpretations are limited since blood pH (necessary for identification of acidemia and alkalemia) and $p\text{CO}_2$ (used to identify respiratory disorders) are only found on blood gas analysis.

In the absence of blood pH measurements, only processes (acidosis, alkalosis) that lead to abnormal blood pH are identified. *Acidosis* is a process that, if continued unchecked, will lead to acidemia (a decrease in blood pH). *Alkalosis* is a process that, if continued unchecked, will lead to alkalemia (an increase in blood pH). Significant changes in blood pH are often associated with secondary changes in electrolyte concentrations and/or urine pH (described below). The presence of acidosis or alkalosis does not necessarily imply that a significant change in blood pH has occurred, which helps explain why secondary changes are not evident with every acid-base disturbance.

Primary Acid-Base Profile Total carbon dioxide

Total carbon dioxide (TCO_2) is used as an estimate of serum bicarbonate concentration, an important buffer in the blood stream. The assay involves measuring the amount of CO_2 produced when a sufficient volume of strong acid is added to serum (the acid consumes all of the bicarbonate present in the serum and produces CO_2 gas). The amount of CO_2 released is directly proportional to the amount of bicarbonate that reacted with the acid. Total carbon dioxide levels above the reference range indicate the presence of metabolic alkalosis, whereas TCO_2 levels below the reference range indicate metabolic acidosis.

Metabolic acidosis generally occurs by one of two mechanisms, either loss of bicarbonate from the body (“secretional” acidosis) or consumption of bicarbonate through titration with increased amounts of acids (“titrational” aci-

dosis). Distinguishing between these two mechanisms is important when characterizing and localizing a disease process and can only be done by integrating information from other acid-base parameters (described below).

Metabolic alkalosis results from increased production of bicarbonate (eg, as compensation for respiratory acidosis) and/or increased loss of acids relative to bicarbonate (gastric vomiting or sequestration). Loss of gastric HCl by vomiting is by far the most common cause of metabolic alkalosis. However, the presence of vomiting does not necessarily imply alkalosis since duodenal contents rich in bicarbonate may also be lost in vomiting.

Anion gap

The anion gap, although reported with other serum chemistry measurements, is actually a calculated value $[(\text{Na} + \text{K}) - (\text{TCO}_2 + \text{Cl})]$. The electrolytes used in the formula are called *measured cations* (Na^+ , K^+) and *measured anions* (TCO_2^- , Cl^-). Ions not included in the formula are called *unmeasured cations* and *unmeasured anions*. There are always equivalent numbers of total cations and total anions in the body since electroneutrality is essential. The relationship between cations and anions, including examples of ions comprising the unmeasured cation and unmeasured anion compartments, is illustrated in *Figure 4.1*.

Intuitively, it may at first appear that the anion gap is a reflection of primary disturbances in the measured ions. However, in reality, the anion gap is an indirect measure of changes in the unmeasured cation or anion compartments that, in turn, have an impact on circulating levels of the

Acid-Base Panel

- Primary acid-base profile
 - TCO_2
 - Anion gap
- Secondary acid-base profile
 - Sodium, chloride
 - Potassium
 - Urine pH

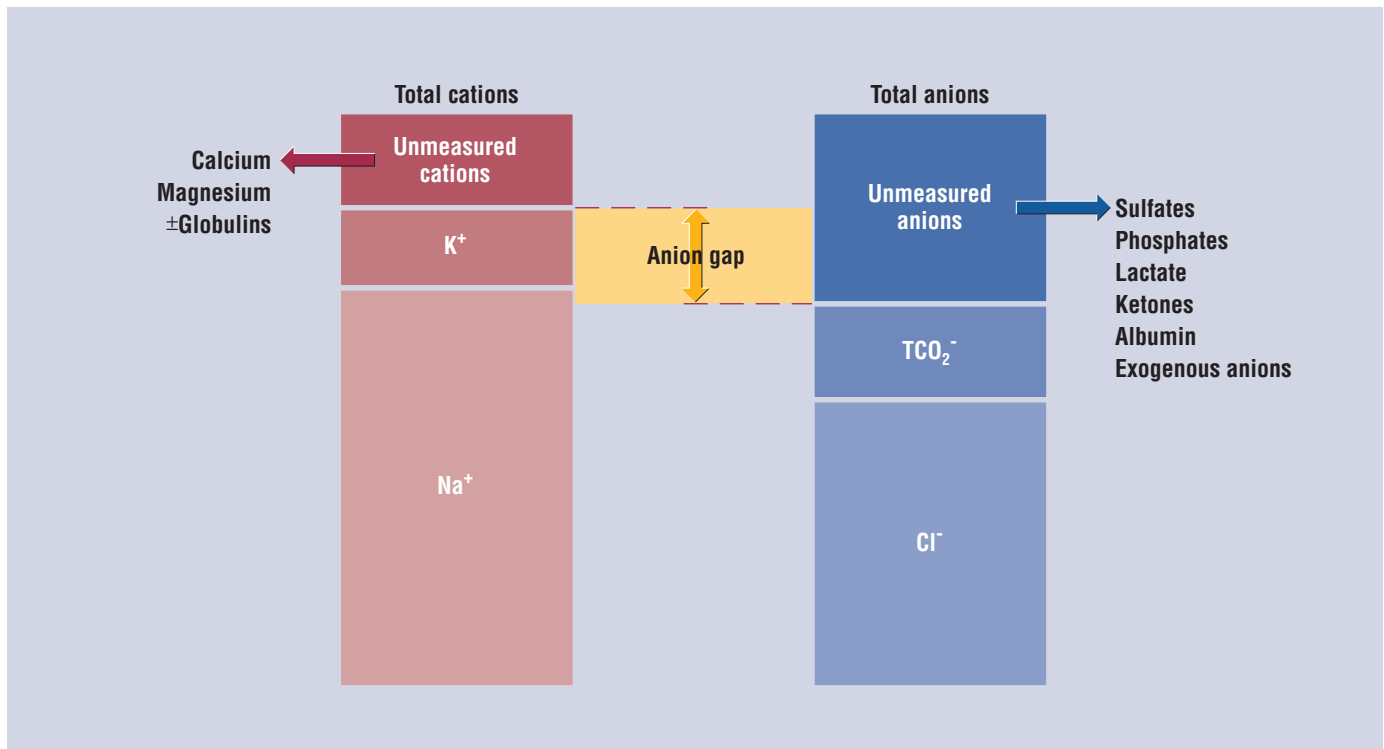


Figure 1. Ions comprising total cations and total anions

measured ions. Alterations that can be identified by evaluating the anion gap are not always readily apparent when evaluating the individual ion values. Furthermore, in practice, large changes in unmeasured cations (eg, Ca^{++}) are generally incompatible with life; therefore, clinically significant changes in the anion gap are generally restricted to changes in the unmeasured anion compartment. A modified diagram that emphasizes the role of unmeasured anions in anion gap interpretation is found in *Figure 4.2*. This diagram illustrates key patterns of acid-base disorders.

The anion gap may be avoided by some because the mechanisms involved in anion gap changes can be somewhat confusing. Fortunately, the anion gap can be a very useful diagnostic parameter even if its biochemical basis is not well understood. The majority of clinical applications for anion gap evaluation can be mastered if the following facts are remembered.

- 1) **The formula.** If the anion gap is not reported, the formula for calculation should be used.

$$[(\text{Na} + \text{K}) - (\text{TCO}_2 + \text{Cl})]$$
- 2) **The primary interpretation for an increased anion gap.** An increase in the anion gap provides evi-

dence for titrational metabolic acidosis. The major causes for an increased anion gap are due to an increase in organic acids that titrate (consume) bicarbonate with subsequent formation of increased unmeasured anions.

- 3) **The differential list for an increased anion gap.** The diseases/conditions causing titrational metabolic acidosis are limited and should be memorized as a specific differential list for an increased anion gap (see *Table 4.1*). Briefly, these can be divided into endogenous conditions (uremic acids of renal failure, ketoacidosis, and lactic acidosis) and exogenous organic acids (ethylene glycol metabolites, salicylate toxicity, etc.).
- 4) **The significance of a decreased anion gap.** Although conditions that cause an increased anion gap are strongly associated with metabolic acidosis, decreases in the anion gap are not necessarily associated with acid-base disturbances (eg, alkalosis). In fact, the most common cause for a decreased anion gap is hypoalbuminemia (an unmeasured anion). Thus, a decreased anion gap has no particular significance

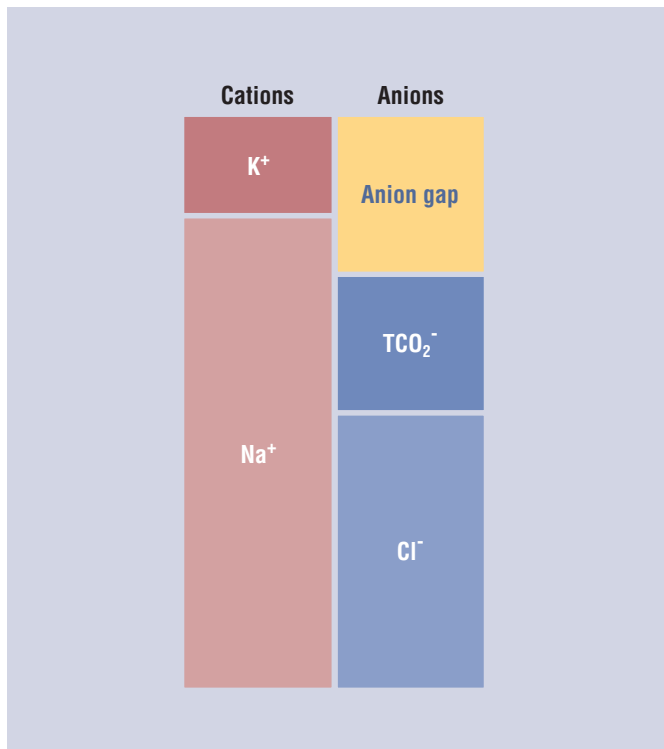


Figure 4.2. Normal distribution of acid-base parameters

in evaluating acid-base status and should not be interpreted as evidence of metabolic alkalosis.

Secondary Acid-Base Profile Sodium, chloride

Sodium and chloride should always be evaluated with respect to acid-base balance, even when TCO_2 and the anion gap appear to be normal. Changes in sodium concentration are not directly indicative of an acid-base disturbance. However, sodium concentrations are required in interpreting changes in chloride, an electrolyte that can be very important in identifying subtle or mixed acid-base disorders. Normally, chloride levels change in concert with sodium, since chloride stays associated with sodium to maintain electroneutrality. Thus, disorders of fluid balance and/or sodium homeostasis typically show closely proportional chloride changes.

Sodium and chloride levels are related in that the two will be within approximately ± 3 units of the respective reference ranges. That is, when sodium is 10 units above the center of the sodium reference range, for example, a normal chloride value would be approximately 10 ± 3 units above

Table 4.1 Causes of Increased Anion Gap

- Endogenous sources
 - Renal failure (uremic acids)
 - Ketoacidosis
 - Lactic acid
- Exogenous sources
 - Ethylene glycol toxicity
 - Salicylate toxicity (eg, aspirin)
 - Others

the center of the chloride reference range. In this case, although the chloride is elevated, it is an appropriate change relative to the change in sodium.

When chloride levels are not parallel to sodium levels there is strong evidence for an acid-base disturbance. Specifically, it can generally be assumed that whichever direction chloride is moving away from sodium, bicarbonate values are moving in the opposite direction. This occurs because chloride and bicarbonate are two of the major negatively charged ions in circulation. Loss or retention of one will often lead to a compensatory change in the other to maintain electroneutrality. Thus, a decrease in chloride *relative to sodium* provides evidence for increased TCO_2 (metabolic alkalosis); an increase in chloride *relative to sodium* provides evidence for decreased TCO_2 (metabolic acidosis). It must be emphasized that these interpretations cannot be based solely on changes in chloride with respect to the reference range. These interpretations only hold true when chloride is increased or decreased *relative to sodium*.

Potassium

Alterations in serum potassium are frequently seen as a compensatory response to changes in acid-base status. With acidemia, excess hydrogen ions in blood are moved into cells for buffering. To maintain electroneutrality, intracellular potassium is exchanged for the incoming hydrogen, which could lead to hyperkalemia. With alkalemia, the shortage of hydrogen ions in blood leads to a shift of hydrogen out of cells into the blood. Blood potassium moves intracellularly in exchange for hydrogen, potentially

leading to hypokalemia. Since acidosis or alkalosis may not be associated with a significant change in blood pH, potassium shifts may or may not be observed in these conditions. Therefore, with acidosis, serum potassium should either be unchanged or increased. With alkalosis, serum potassium should be either unchanged or decreased.

Since the vast majority of body potassium is found within cells rather than in the blood, serum potassium is generally considered to provide an unreliable estimate of total body potassium. However, an important exception to this principle is seen when hypokalemia is observed in the face of acidemia (acidemia being suspected based on the presence of acidosis). The presence of hypokalemia at a time when the shift of intracellular potassium to the blood stream should be leading to hyperkalemia suggests that intracellular stores of potassium are depleted. It is critically important to recognize this pattern since such depletion can exacerbate clinical signs and could be life threatening.

Urine pH

Urine pH provides a crude indication of body acid-base status since the kidney typically excretes ions that are in excess. Thus, with acidemia, excretion of hydrogen ions and retention of bicarbonate leads to acidification of urine, while the converse response occurs with alkalemia. For most acid-base disorders, urine pH is near neutral or tends to follow the acid-base change (eg, acidemia leads to aciduria). Unfortunately, other factors such as eating (ie, post-prandial alkaline tide), diet composition (carnivores have more acidic urine), etc., also influence urine pH, which is why there is a broad range for normal pH of urine. It would be an over interpretation, for example, to conclude that every acidic urine indicates a metabolic acidosis. Rather, it is important to recognize patterns of discrepancy, for example, when urine pH is clearly inconsistent with clinical chemistry data indicating an acid-base disorder. Two examples of this scenario are metabolic alkalosis with paradoxical aciduria (discussed below) and renal tubular acidosis. The latter condition is characterized by metabolic acidosis with alkaline (or inadequately acidified) urine and, because of its relative infrequency in veterinary medicine, will not be discussed here.

Acid-Base Patterns

Normal

A diagram of the relationship between various parameters in the acid-base profile is found in *Figure 4.2*. This will be used for comparative purposes in the following pathologic conditions.

Secretional metabolic acidosis

Secretional metabolic acidosis occurs when bicarbonate is lost (secreted) from the body (as opposed to being consumed in a titration process). Such losses can occur with GI/pancreatic secretions that are sequestered (obstruction) or lost (diarrhea), or through renal tubular losses.

Key biochemical features of secretional acidosis are a decrease in TCO_2 , a normal anion gap, and an increase in chloride relative to sodium. Since unmeasured anions (reflected in the anion gap) are unchanged, shifts in chloride relative to sodium are essential for electroneutrality (ie, to maintain the total anions in equilibrium with total cations). If the changes lead to a significant change in blood pH, it is likely that hyperkalemia and acidic urine will also be present. Therefore, normal to increased potassium and neutral to acidic urine are consistent secondary findings. These changes are illustrated in *Figure 4.5* and sample data are presented in *Case 4.1*.

Titritational metabolic acidosis

Titritational metabolic acidosis occurs when there are increased amounts of organic acids that titrate (consume) bicarbonate (*see Anion gap, above*). The differential list for conditions leading to this change are given in *Table 4.1* and should be committed to memory.

Key biochemical features of titritational acidosis are a decrease in TCO_2 , an increased anion gap, and a normal chloride relative to sodium. Since equimolar shifts are occurring between unmeasured anions and bicarbonate, total anions are maintained in equilibrium with total cations such that shifts in chloride are unnecessary to maintain electroneutrality. If the changes lead to a significant change in blood pH, it is likely that hyperkalemia and acidic urine will also be present. Therefore, normal to increased potassium and neutral to acidic urine are consistent secondary findings. These changes are illustrated in *Figure 4.4* and sample data are presented in *Case 4.2*.

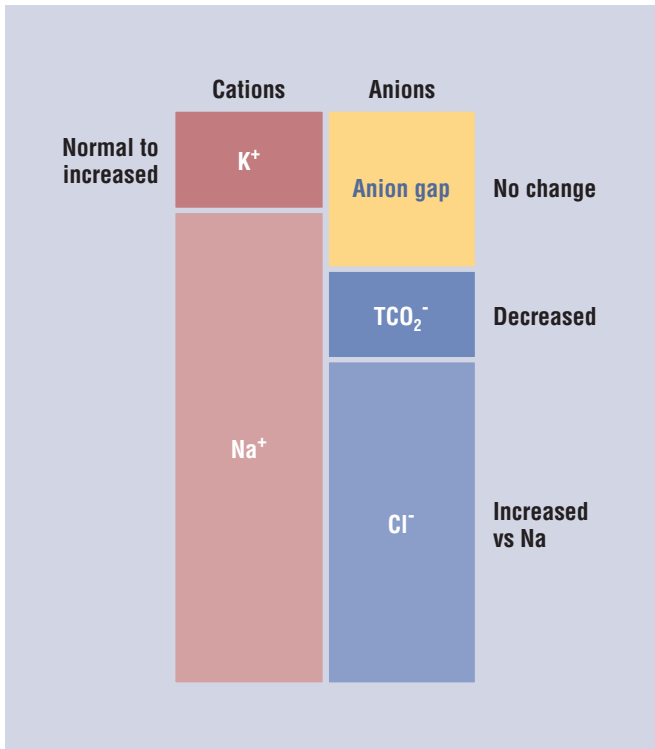


Figure 4.3. Secretional metabolic acidosis

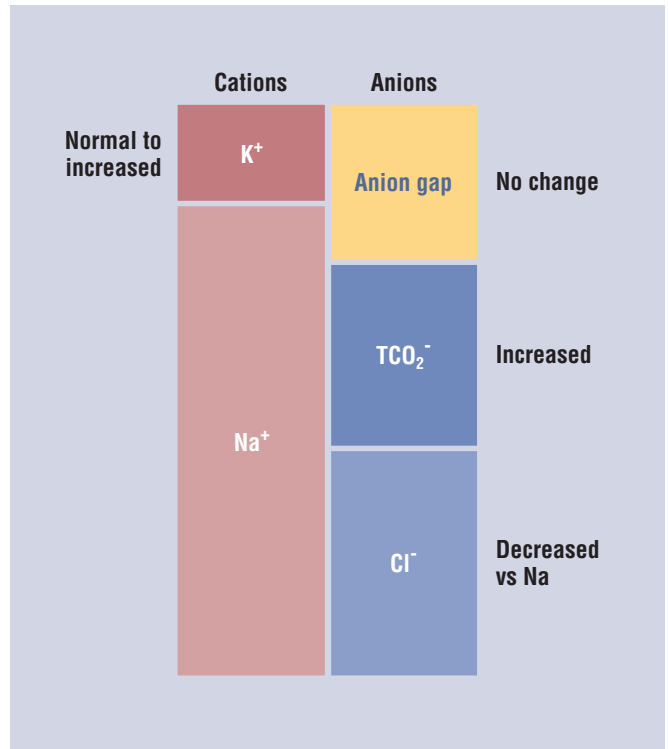


Figure 4.5. Metabolic alkalosis

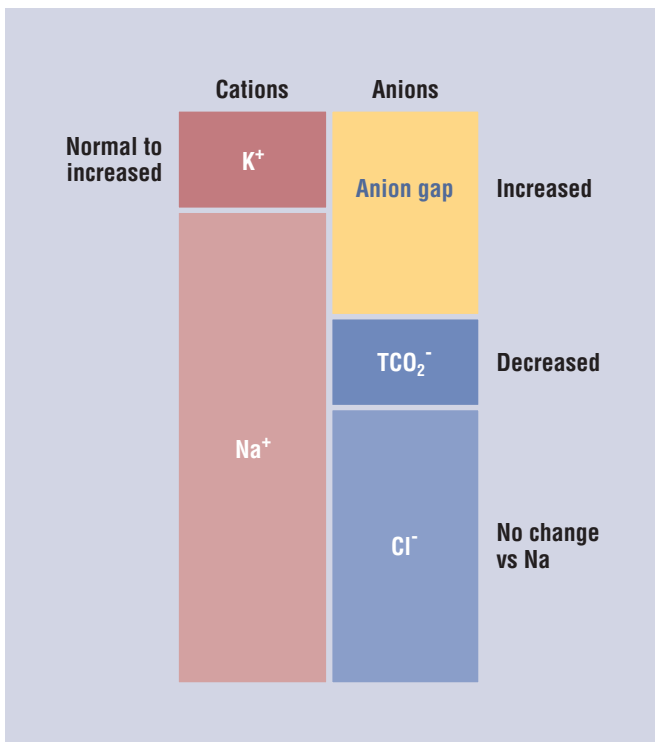


Figure 4.4. Titrational metabolic acidosis

Metabolic alkalosis

Metabolic alkalosis occurs by loss of acid and/or retention of bicarbonate (see TCO_2 , above). The most common cause is gastric vomiting or sequestration of gastric contents (obstruction).

Key biochemical features of metabolic alkalosis are an increase in TCO_2 , a normal anion gap, and a decrease in chloride relative to sodium. If the changes lead to a significant change in blood pH, it is likely that hypokalemia and alkaline urine will also be present. Therefore, normal to decreased potassium and neutral to alkaline urine are consistent secondary findings. These changes are illustrated in *Figure 4.5* and sample data are presented in *Case 4.3*.

Mixed titrational metabolic acidosis and metabolic alkalosis

This state represents a mixture of the findings for these two conditions individually. Therefore, any cause for titrational acidosis that has concurrent gastric vomiting could present with this type of mixed disorder (eg, renal failure, diabetic ketoacidosis, or ethylene glycol toxicity with gas-

tric vomiting). Conversely, the alkalosis could be primary with the titrational acidosis following as a component of metabolic derangement. (GI foreign body obstruction with gastric vomiting and subsequent shock and lactic acidosis).

Biochemical features of a mixed titrational metabolic acidosis and metabolic alkalosis are quite variable and often require very careful and systematic evaluation. The potential biochemical changes are illustrated in *Figure 4.6*.

Although TCO_2 is the most important parameter for identifying acidosis or alkalosis in simple disorders, it can be misleading in mixed disorders depending on which process is predominating. Therefore, the only biochemical changes that will consistently confirm that each component of this mixed disorder is present include an increased anion gap (titrational acidosis) and a decrease in chloride relative to sodium (metabolic alkalosis). Three case examples, listed below (*see Case Studies at the end of this chapter*), illustrate the increasingly difficult task of identifying this mixed disorder unless these criteria are consistently evaluated, as established in the preceding acid-base patterns.

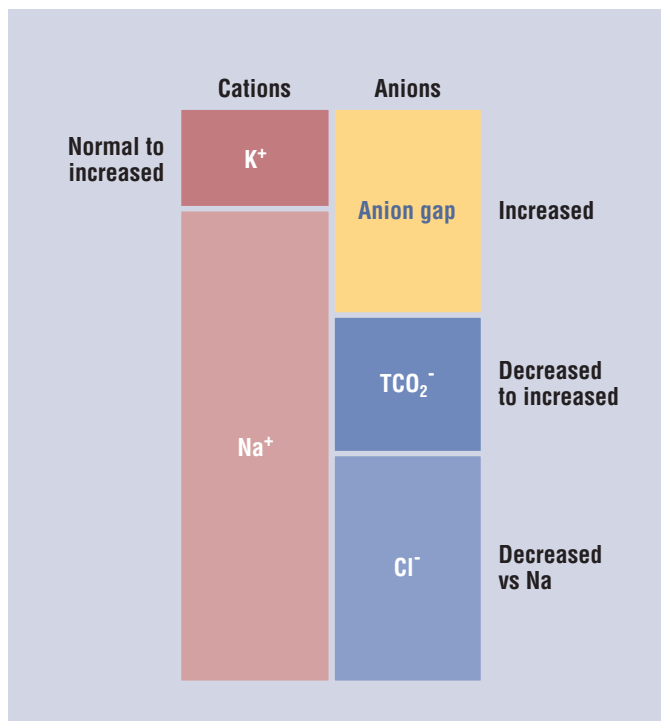


Figure 4.6. Mixed titrational metabolic acidosis and metabolic alkalosis

Case 4.4a: Increased TCO_2 , increased anion gap, decreased chloride relative to sodium

A mixed disorder is readily identified in this case since the increase in TCO_2 indicates alkalosis and the increased anion gap indicates metabolic acidosis (titrational type). The decrease in chloride relative to sodium simply confirms the alkalosis that was already obvious from the TCO_2 value.

Case 4.4b: Normal TCO_2 , increased anion gap, decreased chloride relative to sodium

This mixed disorder is subtle since the TCO_2 is within the reference range. The appropriate finding for a metabolic acidosis (identified from the anion gap) is a decreased TCO_2 ; a lack of TCO_2 decrease in the face of an acidosis provides fairly straightforward support for a mixed disorder. The normal TCO_2 value suggests that an alkalosis is generating bicarbonate that is offsetting the consumption (titration) of TCO_2 by the acidosis. Importantly, the presence of alkalosis is confirmed by the decrease in chloride relative to sodium.

Case 4.4c: Decreased TCO_2 , increased anion gap, decreased chloride relative to sodium

A decrease in TCO_2 with an increase in the anion gap constitutes the classic primary pattern for a titrational metabolic acidosis (see above). Unless the decrease in chloride relative to sodium is identified as evidence for a metabolic alkalosis, the mixed nature of this disorder will be missed. This finding is significant because it tells us that (1) the severity of acidosis is being masked by the alkalosis (the TCO_2 would have been lower without the alkalosis) and, (2) the clinical condition causing alkalosis (eg, vomiting) is of significant severity to cause biochemical alterations. With mixed disorders of this type, serum potassium and urine pH may be high low or intermediate depending on the predominating disorder. Since almost any potassium or urine pH value can conceivably be consistent with a mixed disorder, they are of little value in these scenarios.

Metabolic alkalosis with paradoxical aciduria

The normal compensatory response of renal tubules to

alkalemia is to excrete bicarbonate and to conserve hydrogen. This results in urine that is more alkaline and blood that is less alkaline. Unfortunately, conditions where this occurs are often associated with volume depletion and loss of electrolytes such as sodium, chloride, and potassium. Paradoxical aciduria accompanies metabolic alkalosis when there is a strong drive to restore fluid volume through sodium retention by the tubules, yet there are other electrolyte depletions that prevent the tubules from making the appropriate compensations. In this situation the body will attempt to maintain/correct the fluid disturbance at the expense of acid-base balance.

The resorption of sodium by the renal tubules is normally accomplished by either exchanging tubular sodium with blood potassium or by concurrent resorption of chloride. These processes are designed to retain fluid while maintaining electroneutrality. If potassium depletion is present, hydrogen ions will then make the swap with sodium. This decreases blood hydrogen ions (alkalosis) while increasing urine hydrogen ions (acidic urine). If chloride depletion is present, another negatively charged ion (bicarbonate) will co-migrate with sodium. The removal of bicarbonate from urine makes it more acidic, while rendering the blood even more alkaline. Each process contributes to a vicious cycle of increasingly alkaline blood and acidic urine. It is critical to recognize this pattern as the condition will exacerbate

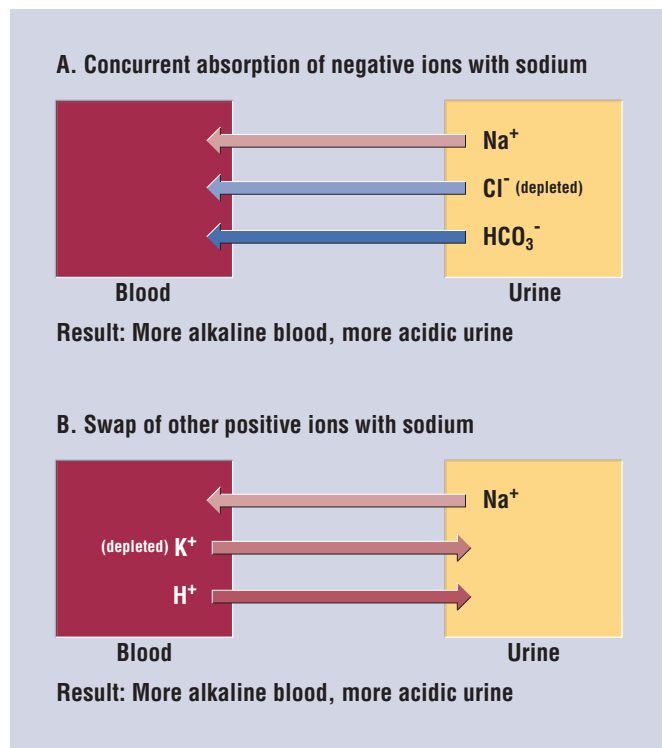


Figure 4.7. Metabolic alkalosis with paradoxical aciduria

until fluid and/or electrolyte abnormalities are corrected. These changes are illustrated in *Figure 4.7* and sample data are presented in *Case 4.5*.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

† Deviation of the sample value from the middle value of this reference range (143 for sodium, 111 for chloride). Under normal conditions, chloride should match sodium within ± 3 units.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

Case Studies

Case 4.1

		Ref. Ranges	
* TCO ₂ (mmol/L)	9 L	(13-24)	
Anion gap (mmol/L)	14	(9-18)	
Sodium (mmol/L)	145	(138-148)	(+2) [†]
* Chloride (mmol/L)	127 H	(105-117)	(+16) [†]
Potassium (mmol/L)	4.8	(3.5-5.0)	
Urine pH	6.1		

A decrease in TCO₂ indicates a metabolic acidosis. The lack of an increase in the anion gap suggests the decrease in TCO₂ is a secretional acidosis. The increase in chloride relative to sodium by greater than 3 units (14 units) strongly supports a secretional process. The high normal serum potassium value is consistent a metabolic acidosis where potassium should be normal or increased. Acidic urine is consistent with the above findings.

Summary: Secretional metabolic acidosis. Sources of bicarbonate loss through the GI tract or kidneys should be evaluated.

Case 4.2

		Ref. Ranges	
* TCO ₂ (mmol/L)	10 L	(13-24)	
* Anion gap (mmol/L)	25 H	(9-18)	
Sodium (mmol/L)	143	(138-148)	(0) [†]
Chloride (mmol/L)	113	(105-117)	(+2) [†]
* Potassium (mmol/L)	5.1 H	(3.5-5.0)	
Urine pH	6.5		

A decrease in TCO₂ indicates a metabolic acidosis. This is supported by an increased anion gap, which additionally indicates a titrational acidosis. Chloride is normal relative to sodium (ie, within ± 3 units deviation), which is consistent with a titrational acidosis. The mild hyperkalemia and acidic urine are findings consistent with metabolic acidosis.

Summary: Titrational metabolic acidosis. Conditions associated with increased amounts of organic acids should be assessed. (See Table 4.1)

Case 4.3

		Ref. Ranges	
* TCO ₂ (mmol/L)	28 H	(13-24)	
Anion gap (mmol/L)	15	(9-18)	
Sodium (mmol/L)	141	(138-148)	(-2) [†]
* Chloride (mmol/L)	101 L	(105-117)	(-10) [†]
* Potassium (mmol/L)	3.2 L	(3.5-5.0)	
Urine pH	7.6		

The increase in TCO₂ indicates metabolic alkalosis. The normal anion gap is consistent with this, since it is not typically altered with alkalosis. The decrease in chloride relative to sodium (8 units) strongly supports metabolic alkalosis. An intracellular shift of blood potassium in exchange for hydrogen leading to hypokalemia and alkaline urine are both consistent with alkalosis.

Summary: Metabolic alkalosis. The most common cause for this is loss of gastric contents (HCl) through vomiting.

Case 4.4a

		Ref. Ranges	
* TCO ₂ (mmol/L)	26 H	(13-24)	
* Anion gap (mmol/L)	22 H	(9-18)	
Sodium (mmol/L)	141	(138-148)	(-2) [†]
* Chloride (mmol/L)	97 L	(105-117)	(-14) [†]
Potassium (mmol/L)	4.0	(3.5-5.0)	
Urine pH	7.1		

The increase in TCO₂ indicates metabolic alkalosis. Interestingly, an increased anion gap indicates a concurrent titrational acidosis. Chloride is unaffected by a titrational acidosis. However, the decrease in chloride relative to sodium (12 units) is a classic change that strongly supports the presence of alkalosis. The normal potassium value and near

neutral urine are acceptable findings since, in a mixed disorder of this type, these values can either increase or decrease depending on blood pH (which is unknown).

Summary: Mixed titrational metabolic acidosis and metabolic alkalosis. Differentials for titrational acidosis are given in Table 4.1. Metabolic alkalosis is most often due to gastric vomiting.

Case 4.4b

		Ref. Ranges	
TCO ₂ (mmol/L)	20	(13-24)	
* Anion gap (mmol/L)	23 H	(9-18)	
Sodium (mmol/L)	140	(138-148)	(-3) [†]
* Chloride (mmol/L)	101 L	(105-117)	(-10) [†]
Potassium (mmol/L)	4.2	(3.5-5.0)	
Urine pH	6.9		

TCO₂ is within the reference range. This is an abnormal finding in the face of an increased anion gap, which signals the presence of titrational metabolic acidosis. Since TCO₂ should be decreased because of titration with organic acids, this represents a relative increase in TCO₂ (ie, a concurrent metabolic alkalosis). The chloride is decreased 7 units relative to sodium, which strongly supports the presence of metabolic alkalosis. Potassium within the reference range and near neutral urine are consistent findings for a mixed titrational acidosis and alkalosis. These values could also be either increased or decreased depending on the blood pH (which is unknown).

Summary: Mixed titrational metabolic acidosis and metabolic alkalosis. Differentials for titrational acidosis are given in Table 4.1. Metabolic alkalosis is most often due to gastric vomiting.

Case 4.4c

		Ref. Ranges	
* TCO ₂ (mmol/L)	10 L	(13-24)	
* Anion gap (mmol/L)	37 H	(9-18)	
Sodium (mmol/L)	148	(138-148)	(+5) [†]
Chloride (mmol/L)	106	(105-117)	(-5) [†]
* Potassium (mmol/L)	5.2 H	(3.5-5.0)	
Urine pH	6.2		

A decrease in TCO₂ combined with an increased anion

gap indicates a titrational metabolic alkalosis. Although both sodium and chloride are within the respective reference ranges, chloride is decreased 10 units relative to sodium, indicating the presence of a metabolic alkalosis. Mild hyperkalemia and acidic urine are consistent with a predominating acidosis with probable acidemia.

Summary: Mixed titrational metabolic acidosis and metabolic alkalosis. Differentials for titrational acidosis are given in Table 4.1. Metabolic alkalosis is most often due to gastric vomiting.

Comment: Note that without careful and systematic biochemical profiling habits (ie, interpreting chloride relative to sodium even when they are within reference ranges), the comparatively subtle alkalosis would have been missed.

Case 4.5

		Ref. Ranges	
* TCO ₂ (mmol/L)	33.1 H	(13-24)	
Anion gap (mmol/L)	11	(9-18)	
Sodium (mmol/L)	136 L	(138-148)	(-7) [†]
Chloride (mmol/L)	95 L	(105-117)	(-16) [†]
* Potassium (mmol/L)	3.1 L	(3.5-5.0)	
Urine pH	6.0		

The increase in TCO₂ indicates metabolic alkalosis. Anion gap is typically unaffected by alkalosis. Sodium, chloride and potassium are decreased. The chloride is decreased by 9 units relative to sodium, supporting the finding of metabolic alkalosis. Hypokalemia is consistent with metabolic alkalosis, particularly with alkalemia, as potassium shifts to the intracellular compartment in exchange for hydrogen. In this moderately severe metabolic alkalosis, acidic urine is unusual (paradoxical), since the kidneys should be excreting bicarbonate and retaining hydrogen in a compensatory effort.

Summary: Moderately severe metabolic alkalosis with paradoxical aciduria. Restoration of blood volume (to reduce the drive for sodium resorption) and supplementation with electrolytes will provide the tubules with the components needed to resume appropriate compensation for the acid-base disturbance.

Part II

Chapter 5: Clinical Pathology of the Urinary System

The kidney is a vitally important organ that performs a variety of functions to maintain homeostasis. It is involved in the excretion of wastes and the regulation of acid-base balance, electrolyte balance, and state of hydration.

The performance of these functions depends upon both normal glomerular filtration and normal renal tubular integrity. The primary urinary panel assesses both. It is important to note that urinalysis, although not a part of our large chemistry profile, is an essential part of the primary renal panel. The secondary urinary panel is primarily designed to evaluate changes that may occur secondary to renal disease.

Primary Urinary Panel Blood urea nitrogen (BUN)

Urea is a nitrogenous waste that is excreted by the kidney via glomerular filtration. Blood urea nitrogen (BUN) level is primarily used as an indicator of glomerular filtration rate. Azotemia (elevations in circulating nitrogenous waste and therefore BUN) may be prerenal due to reduced renal perfusion, renal due to primary kidney disease, or postrenal due to ureter, bladder, or urethral obstruction or rupture.

Blood urea nitrogen should only be interpreted in light of urine specific gravity (*see Chapter 5*). If BUN is elevated and urine specific gravity indicates that the renal tubules are concentrating, then the azotemia is most likely prerenal. If BUN is elevated but urine specific gravity is isosthenuric (between 1.008 and 1.017, the concentration of plasma), then primary renal disease is suspected.

Despite the value of BUN as a test of renal function, it is not a terribly sensitive or specific test. In primary renal disease, approximately 3/4 of both kidneys must be non-functional before BUN will elevate. Also, circulating levels of urea nitrogen are influenced by many other factors. To better understand how to interpret BUN values, it is first necessary to understand how urea is produced.

The primary source of blood urea is dietary protein. Ingested protein is converted to ammonia by bacteria in the gut. The ammonia diffuses across the gut wall into the portal circulation and is carried to the liver. In the liver, ammonia is converted to urea by enzyme activity.

Minor elevations in BUN can be caused by high protein diets or gastrointestinal (GI) hemorrhage (which also increases intestinal protein load). Liver disease may cause

low circulating BUN levels (and high ammonia levels) because of reduced hepatic conversion of ammonia. Reduced BUN levels also may occur when the ammonia produced in the gut is not carried to the liver, as in the case of portosystemic shunts. Finally, diuresis may reduce circulating BUN levels by increasing glomerular filtration rate.

Creatinine

Creatinine, a by-product of muscle metabolism, is excreted almost exclusively by glomerular filtration. Therefore, serum creatinine levels, like BUN levels, are used as estimates of glomerular filtration rate. Interpretations of elevated serum creatinine and elevated BUN are nearly identical; however, creatinine is less influenced by nonrenal factors than is BUN. For this reason, some authors have suggested that sequential serum creatinine determinations may be used for prognostic purposes. When factors such as diet and hydration are constant, patients with renal disease and sequentially elevating serum creatinine levels have a much more guarded prognosis than patients with diagnosed renal disease and decreasing serum creatinine levels.

Occasionally, creatinine levels may be elevated when BUN levels are normal. Such occurrences should be interpreted cautiously; substances known as non-creatinine chromogens are sometimes present in the blood and may interfere with the test for creatinine, giving false elevated levels.

Urinary Disease Panel

- Primary urinary panel
 - Blood urea nitrogen (BUN)
 - Creatinine
 - Urinalysis
- Secondary urinary panel
 - Electrolytes
 - Calcium, phosphorus
 - Sodium, potassium, chloride
 - Acid-base balance and anion gap
 - Cholesterol

Urinalysis

Urinalysis is an essential part of the primary urinary tract panel and is discussed in Chapter 3. BUN and creatinine cannot be interpreted appropriately without urinalysis, particularly specific gravity. In addition, because of the relative insensitivity of BUN and creatinine measurements, reagent dip strip and/or sediment findings may be the first indicators of urinary tract disease.

Secondary Urinary Panel

Electrolytes

Calcium, phosphorus

Circulating calcium levels are regulated by the interaction of parathyroid hormone, calcitonin, activated vitamin D, GI absorption and renal tubular function. The kidney is responsible for converting inactive vitamin D to its active form. Therefore in renal disease, available activated vitamin D is decreased which in turn decreases calcium absorption from the gut. Furthermore, renal tubules also become increasingly refractory to active vitamin D, causing decreased calcium resorption and increased loss of calcium in the urine. These hypocalcemic effects are counterbalanced by parathyroid hyperplasia, increased production of parathyroid hormone, and resorption of calcium from bone. The net effect is that renal failure (including chronic renal failure) is usually associated with normal or only mildly reduced serum calcium. Approximately 10% of patients with chronic renal failure may have mild increases in serum calcium.

In contrast, serum phosphorus levels are often markedly elevated. Phosphorus is excreted primarily by glomerular filtration; therefore anything which reduces glomerular filtration rate will cause hyperphosphatemia. In general, phosphorus elevations in renal disease correlate with BUN elevations.

Sodium, potassium, and chloride

Diseases of the kidney can cause profound electrolyte disturbances. In renal disease, total body sodium is usually reduced because of failure of the distal tubules to excrete potassium and reabsorb sodium. However, serum sodium levels are usually in the normal range; animals with renal disease are usually dehydrated due to excessive water loss, which results from the inability of the kidneys to concen-

trate. Serum chloride levels tend to follow serum sodium. The most profound electrolyte disturbance seen with renal disease is hyperkalemia, which occurs for two reasons. First, as stated above, failing kidneys are often incapable of excreting potassium (and conserving sodium). Second, patients with severe renal disease are nearly always acidotic (see following discussion on acid-base balance). The relationship of hyperkalemia to acidosis is discussed in Chapter 4.

Acid-base balance and anion gap

Disturbances in acid-base balance in renal disease are variable and can be quite complex. There is almost always titration metabolic acidosis because of increased circulating organic and inorganic acids (sulfates and phosphates). These are unmeasured anions that contribute to an increased anion gap. With simple titration acidosis chloride levels are normal. Acid-base balance is discussed in Chapter 4.

If there is concomitant duodenal emesis or diarrhea (loss of sodium bicarbonate) a secretory component is present. Combined titration and secretion acidosis has low bicarbonate levels, normal to elevated anion gap, and high normal to elevated chloride levels as a result of increased chloride resorption (in place of bicarbonate).

Finally, there may be a superimposed metabolic alkalosis as a result of gastric emesis and loss of hydrochloric acid (HCl). Furthermore, any increase in anion gap may be moderated by proteinuria. Albumin is an unmeasured anion and the primary source of the normal anion gap. Any reduction in circulating albumin therefore reduces the anion gap. Obviously, the changes in electrolytes, bicarbonate, and anion gap must be carefully considered on a case by case basis to understand the range of potential metabolic disturbances in patients with renal disease.

Cholesterol

Hypercholesterolemia may be a feature of renal disease, particularly when hypoalbuminemia is present. The relationship of hypercholesterolemia to hypoalbuminemia has never been clearly established. However, hypoalbuminemia triggers increased albumin synthesis by the liver. A current theory suggests that albumin metabolism and lipid metabolism are linked and hypercholesterolemia and hypertriglyceridemia may result.

Chapter 5: Case Studies

Case 1

SIGNALMENT: Three-year-old female mixed-breed dog
HISTORY: The dog's abdomen has been enlarging for 2 to 3 weeks.

P.E.: T = 101.2°F P = 84 R = 15

The dog is bright, alert, and in good general condition except for an enlarged abdomen.

Percussion of the abdomen reveals a fluid wave.

INITIAL ASSESSMENT: Ascites can be exudative due to tumors or inflammatory diseases of the peritoneum or transudative secondary to portal hypertension or hypoalbuminemia. Portal hypertension is most commonly seen with chronic liver disease and congestive heart failure while hypoalbuminemia can be associated with liver, kidney, or intestinal disease. Examination of the ascites fluid, plus hepatic, GI, and renal panels should be very helpful in localizing the problem.

LABORATORY DATA:

Hematology

HCT (%)	40	WBC (/μl)	14,200
Hb (g/dl)	13.7	Neutrophils (/μl)	9,500
RBC (× 10 ⁶ /μl)	5.92	Lymphocytes (/μl)	3,400
* TP (g/dl)	4.8 L	Monocytes (/μl)	600
Platelets	Adequate	Eosinophils (/μl)	700

Chemistry

BUN (mg/dl)	15	Lipase (IU/L)	1,000
Creatinine (mg/dl)	0.5	Sodium (mmol/L)	146
Glucose (mg/dl)	120	Potassium (mmol/L)	4.4
T. bilirubin (mg/dl)	0.5	Chloride (mmol/L)	114
* TP (g/dl)	3.6 L	* Calcium (mg/dl)	8.1 L
* Albumin (g/dl)	0.9 L	Phosphorus (mg/dl)	3.8
ALT (IU/L)	19	* Cholesterol (mg/dl)	430 H
ALP (IU/L)	21	Triglycerides (mg/dl)	78
GGT (IU/L)	7	TCO ₂ (mmol/L)	24
Amylase (IU/L)	946	Anion gap (mmol/L)	12.4

Urinalysis

Color	dark yellow	Occ. blood	neg.
Turbidity	sl. cloudy	Urobilinogen (units/dl)	0.5
Sp. gr.	1.031	WBC (/HPF)	0-1
pH	7.0	RBC (/HPF)	0-1
Protein	4+	Epithelial (/HPF)	5-10
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	2-3 hyaline
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: *Hypoproteinemia*. With evidence of ascites, hypoproteinemia suggests that the underlying cause relates to hypoalbuminemia rather than inflammatory or neoplastic lesions. It must be kept in mind that a mild to moderate hypoproteinemia can result from congestive heart failure. Determinations of albumin and globulin are needed for better discrimination.

WBC: No abnormalities.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)
(see Chapter 6)

Hypoproteinemia. The refractometric measurement used in the CBC is confirmed.

Hypoalbuminemia. The profound hypoalbuminemia resulting in a consequent decreased plasma oncotic pressure is undoubtedly responsible for the ascites. The pattern of hypoalbuminemia and normal globulin level seen here is most consistent with glomerular loss but can occasionally be seen in chronic hepatic disease.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride) *(see Chapter 8)*

Hypoproteinemia and hypoalbuminemia. Discussed under the hepatic panel.

Urinary panel (BUN, creatinine, protein, casts)

Marked proteinuria. Marked proteinuria without evidence of urinary tract inflammation strongly suggests glomerular disease. Hyaline casts are consistent with glomerular leakage. *Adequate renal function*. Creatinine and BUN values within normal limits do not rule out renal disease as these parameters are elevated only when glomerular filtration rate is 25% or less of normal. A urine specific gravity of 1.031 indicates the presence of at least 33% of normal tubular function, not a lack of renal disease.

Additional findings:

Hypocalcemia. Decreased calcium levels are associated with the hypoalbuminemia.

Hypercholesterolemia. The elevated cholesterol may be due to increased production by the

liver. Increased hepatic production of cholesterol is linked to increased hepatic albumin production. In this patient, albumin production (and therefore cholesterol production) may be occurring as a compensatory response to albumin loss in the urine.

Abnormal fluid analysis:

Color	colorless
Turbidity	clear
TP (g/dl)	2.5
RBC	500
WBC	50
Cytology	no cells seen

Summary and outcome:

Protein-losing glomerular disease was diagnosed on the basis of hypoalbuminemia and proteinuria. Analysis of the ascitic fluid revealed a transudate compatible with that diagnosis. A renal biopsy was necessary to arrive at a specific diagnosis and revealed an immune complex glomerulonephritis. The combination of proteinuria, hypoproteinaemia, hypercholesterolemia and effusion indicates the presence of nephrotic syndrome.

Case 2

SIGNALMENT: Four-year-old male Irish Setter

HISTORY: Sudden onset of emesis, anorexia, and depression 2 days ago.

P.E.: T = 100.4°F P = 90 R = 25

The dog is severely depressed and 8% dehydrated.

INITIAL ASSESSMENT: Vomiting, anorexia, and depression are nonspecific signs that can be caused by diseases of many organ systems including kidney, liver, pancreas, and GI tract.

LABORATORY DATA:

Hematology

HCT (%)	49	* WBC (/μl)	19,700 H
Hb (g/dl)	16.8	* Neutrophils (/μl)	15,900 H
RBC (× 10 ⁶ /μl)	7.56	Lymphocytes (/μl)	2,900
* TP (g/dl)	7.8 HN	Monocytes (/μl)	900
Platelets	Adequate		

Chemistry

* BUN (mg/dl)	240 H	* Lipase (IU/L)	3,000 H
* Creatinine (mg/dl)	5.2 H	Sodium (mmol/L)	147
Glucose (mg/dl)	120	Potassium (mmol/L)	4.9
T. bilirubin (mg/dl)	0.4	* Chloride (mmol/L)	102 L
* TP (g/dl)	7.5 H	Calcium (mg/dl)	9.2
* Albumin (g/dl)	4.3 H	* Phosphorus (mg/dl)	12.4 H
ALT (IU/L)	42	Cholesterol (mg/dl)	278
ALP (IU/L)	35	Triglycerides (mg/dl)	94
GGT (IU/L)	14	TCO ₂ (mmol/L)	18
* Amylase (IU/L)	2,780 H	* Anion gap (mmol/L)	64 H

Urinalysis

Color	light yellow	Occ. blood	neg.
Turbidity	cloudy	Urobilinogen (units/dl)	0.5
Sp. gr.	1.011	WBC (/HPF)	0-5
pH	6.0	RBC (/HPF)	0-5
Protein	1+	Epithelial (/HPF)	0-5
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	many granular
		Crystals	many oxalates

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Hemoconcentration.* A high normal PCV supports dehydration.

TP: *Hyperproteinemia.* High normal to marginally elevated protein in this case is very likely secondary to dehydration.

WBC: *Mild mature neutrophilia.* This degree of neutrophilia without alterations in other cell types is nonspecific. Mild inflammation or physiologic leukocytosis could be responsible.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel (primary and secondary – BUN, creatinine, sodium, potassium, chloride, calcium, phosphorus, cholesterol, total CO₂, anion gap, specific gravity, casts, crystals)

Renal azotemia. A markedly elevated BUN combined with an isosthenuric urine specific gravity indicates renal failure.

Urinary casts. Granular casts indicate renal tubular degeneration.

Oxalate crystalluria. Oxalate crystals suggest oxalate nephrosis. However, oxalate dihydrate crystals can be seen in healthy dogs whereas oxalate monohydrate crystals are more specific for ethylene glycol toxicity. It also must be remembered that oxalate crystals are an inconsistent finding in oxalate nephrosis so that their absence would not rule out that disease.

Mixed metabolic acidosis and alkalosis.

Hypochloridemia relative to sodium suggests either simple metabolic alkalosis or mixed metabolic acidosis/alkalosis. In simple metabolic alkalosis, total CO₂ (bicarbonate) is elevated and anion gap is normal. In this patient, anion gap is elevated and bicarbonate is normal. This combination of changes suggests mixed acidosis/alkalosis. Based on the signs, history, and laboratory data, the alkalosis is the result of gastric emesis and the acidosis is the result of renal failure.

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hyperproteinemia, hyperalbuminemia. These changes are consistent with dehydration, not liver disease.

Pancreatic panel (BUN, creatinine, amylase, lipase) (see Chapter 7)

Hyperamylasemia and hyperlipasemia. Mild elevations in serum amylase and lipase are not specific for pancreatic damage. Additionally, renal function must be examined since amylase and lipase are eliminated by the kidney. There is evidence of primary renal disease. (***See Renal panel.***)

Renal azotemia. See Renal panel.

Summary and outcome:

Oxalate nephrosis due to ethylene glycol ingestion was considered likely on the basis of the laboratory data. Further questioning of the owner revealed access to ethylene glycol and a renal biopsy confirmed the diagnosis.

Case 3

SIGNALMENT: Three-year-old female Miniature Poodle

HISTORY: Pollakiuria and stranguria for 1 week.

P.E.: T = 102.1°F P = 120 R = panting

The dog is nervous and seems tender in the posterior abdomen. Otherwise no abnormalities are apparent.

INITIAL ASSESSMENT: The history suggests cystitis, or urethritis; however, since pyelonephritis can complicate cystitis, a renal panel is justified.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: No abnormalities.

WBC: No abnormalities. A normal leukogram is expected with cystitis. Pyelonephritis may produce an inflammatory leukogram if sufficient renal tissue is involved.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel (BUN, creatinine, specific gravity, protein, occult blood, WBC, RBC, bacteria)

Urinary tract infection. All of the abnormalities seen in the urinalysis can be explained by the presence of bacteria and the inflammatory response. However, it is not possible to localize the inflammation to any area of the urinary tract..

Normal renal function. Normal BUN and creatinine levels indicate that at least 25% of the normal glomerular filtration is present. Concentrated urine indicates that at least 33% of normal tubular function is present. Neither of these statements rules out the possibility of renal involvement.

Summary and outcome:

Bacterial cystitis was diagnosed on the basis of the urinalysis. Since the leukogram and renal function were normal, it was decided that pyelonephritis was either not present or of a minor degree. To be completely sure of the presence or absence of pyelonephritis, an intravenous pyelogram, or renal biopsy, or both, would be necessary. These options were rejected as unjustifiably expensive and invasive and the dog was placed on antibiotic therapy.

LABORATORY DATA:

Hematology

HCT (%)	42	WBC (/µl)	13,400
Hb (g/dl)	13.4	Neutrophils (/µl)	8,300
RBC (× 10 ⁶ /µl)	6.67	Lymphocytes (/µl)	4,000
TP (g/dl)	6.8	Monocytes (/µl)	400
Platelets	Adequate	Eosinophils (/µl)	700

Chemistry

BUN (mg/dl)	18	Lipase (IU/L)	725
Creatinine (mg/dl)	0.9	Sodium (mmol/L)	143
Glucose (mg/dl)	115	Potassium (mmol/L)	4.4
T. bilirubin (mg/dl)	0.4	Chloride (mmol/L)	112
TP (g/dl)	6.8	Calcium (mg/dl)	9.8
Albumin (g/dl)	3.9	Phosphorus (mg/dl)	3.4
ALT (IU/L)	37	Cholesterol (mg/dl)	278
ALP (IU/L)	45	Triglycerides (mg/dl)	94
GGT (IU/L)	11	TCO ₂ (mmol/L)	18
Amylase (IU/L)	657	Anion gap (mmol/L)	17.4

Urinalysis

Color	yellow	Occ. blood	1+
Turbidity	cloudy	Urobilinogen (units/dl)	1.0
Sp. gr.	1.038	WBC (/HPF)	100-150
pH	7.0	RBC (/HPF)	40-50
Protein	3+	Epithelial (/HPF)	5-10
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	3+
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

† Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

Case 4

SIGNALMENT: Nine-year-old male Labrador Retriever
HISTORY: Malaise and weight loss for 2 months.

Recent vomiting

P.E.: T = 103.9°F P = 92 R = 20

The dog is thin and moderately depressed.

INITIAL ASSESSMENT: The history of malaise, weight loss, and vomiting are not specific for any organ system. Therefore, evaluation of a variety of systems including hepatic, pancreatic, renal, and GI panels is justified.

LABORATORY DATA:

Hematology

* HCT (%)	32	L	* WBC (/μl)	33,300	H
* Hb (g/dl)	11.1	L	* Neutrophils (/μl)	26,900	H
* RBC (× 10 ⁶ /μl)	4.92	L	Lymphocytes (/μl)	4,000	
* TP (g/dl)	8.2	H	* Monocytes (/μl)	1,700	H
Reticulocytes (%)	1.2		Eosinophils (/μl)	700	
Platelets	Adequate				

Chemistry

* BUN (mg/dl)	145	H	Lipase (IU/L)	1,700	
* Creatinine (mg/dl)	3.9	H	Sodium (mmol/L)	146	
Glucose (mg/dl)	125		Potassium (mmol/L)	4.7	
T. bilirubin (mg/dl)	0.6		Chloride (mmol/L)	116	
* TP (g/dl)	7.7	H	Calcium (mg/dl)	10.8	
Albumin (g/dl)	3.2		* Phosphorus (mg/dl)	13.2	H
ALT (IU/L)	44		Cholesterol (mg/dl)	236	
ALP (IU/L)	25		Triglycerides (mg/dl)	72	
GGT (IU/L)	9		TCO ₂ (mmol/L)	19	
* Amylase (IU/L)	1,864	H	Anion gap (mmol/L)	16	

Urinalysis

Color	yellow	Urobilinogen (units/dl)	1.0
Turbidity	cloudy	WBC (/HPF)	100-125
Sp. gr.	1.013	RBC (/HPF)	20-30
pH	6.0	Epithelial (/HPF)	2-4
Protein	3+	Sperm	neg.
Glucose	neg.	Bacteria	2+
Ketones	neg.	Casts (/LPF)	4-6 granular
Bilirubin	neg.	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Anemia, non-regenerative.* A HCT of 32% indicates anemia. The RBC indices (MCV 65 fl, MCHC 35 g/dl) reveal a normocytic, normochromic anemia, while the absolute reticulocyte count is 59,000/μl. If the elevated TP is due to dehydration, the anemia is more severe than is apparent. There is no evidence as to the pathogenesis of the anemia at this point.

TP: *Hyperproteinemia.* Elevated TP is most commonly a result of dehydration. Without evidence of dehydration in this dog, however, hyperglobulinemia and hyperfibrinogenemia must be considered. Measurement of albumin will be necessary to clarify this protein abnormality.

WBC: *Inflammatory leukogram.* A mature neutrophilia of nearly 27,000, a monocytosis, and normal lymphocyte level are most consistent with a tissue demand for phagocytes.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)
Hyperglobulinemia. A normal albumin and elevated TP indicate hyperglobulinemia. This can be caused by several globulin abnormalities, which can best be differentiated by electrophoresis. The most likely possibility is a polyclonal gammopathy secondary to chronic antigenic stimulation. There is no evidence of active hepatic disease or decreased functional hepatic mass.

Pancreatic panel (BUN, creatinine, amylase, lipase)

There is no evidence of pancreatic disease. The slight elevation in amylase is insignificant.

Urinary panel (BUN, creatinine, specific gravity, protein, WBC, RBC, bacteria, casts)

Renal azotemia. Elevated BUN and creatinine with an isosthenuric urine specific gravity indicate renal failure.

Urinary tract infection. All of the abnormalities in the urinalysis can be explained by bacterial infection and the associated inflammatory response. The presence of granular casts indicates that there is renal disease. In addition, the inflammatory leukogram would not be expected in uncomplicated cystitis, further suggesting renal inflammatory disease.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

Hyperglobulinemia. Discussed under hepatic panel.

Summary and outcome:

Pyelonephritis was diagnosed on the basis of renal failure,

urinary bacterial infection, and an inflammatory leukogram. An intravenous pyelogram confirmed this diagnosis and the dog was placed on antibiotic therapy based on urine culture and sensitivity testing. After successful treatment of the pyelonephritis, the HCT returned to normal, suggesting that the anemia was caused by chronic inflammation.

Case 5

SIGNALMENT: Three-year-old male DSH cat

HISTORY: Sudden onset of dysuria 1 day ago. The cat continually strains as if to defecate and is now becoming depressed.

P.E. T = 99.8°F P = 160 R = 28

The cat is moderately depressed and 5% dehydrated. The bladder is large and firm on palpation.

INITIAL ASSESSMENT: The diagnosis of urethral obstruction in this case is not challenging. However, to evaluate the severity of the condition and to aid in treatment and prognosis, a renal panel may be examined.

LABORATORY DATA:

Hematology

HCT (%)	44	* WBC (/μl)	19,100	H
Hb (g/dl)	14.2	* Neutrophils (/μl)	17,700	H
RBC (× 10 ⁶ /μl)	8.65	Lymphocytes (/μl)	1,000	
TP (g/dl)	7.5	Monocytes (/μl)	400	
Platelets	Adequate			

Chemistry

* BUN (mg/dl)	225	H	Lipase (IU/L)	900	
* Creatinine (mg/dl)	9.2	H	Sodium (mmol/L)	157	
* Glucose (mg/dl)	156	H	* Potassium (mmol/L)	7.2	H
T. bilirubin (mg/dl)	0.2		Chloride (mmol/L)	126	
TP (g/dl)	7.2		Calcium (mg/dl)	9.6	
Albumin (g/dl)	3.8		* Phosphorus (mg/dl)	11.0	H
ALT (IU/L)	22		Cholesterol (mg/dl)	112	
ALP (IU/L)	30		Triglycerides (mg/dl)	82	
GGT (IU/L)	4		* TCO ₂ (mmol/L)	8	L
Amylase (IU/L)	1,200		* Anion gap (mmol/L)	30.2	H

Urinalysis

Color	red	Occ. blood	4+
Turbidity	cloudy	Urobilinogen (units/dl)	0.5
Sp. gr.	1.022	WBC (/HPF)	10-20
pH	7.0	RBC (/HPF)	TNTC
Protein	3+	Epithelial (/HPF)	20-30
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	many triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: No abnormalities.

WBC: *Stress leukogram.* A mild leukocytosis, characterized by a mature neutrophilia, marginal lymphopenia, and eosinopenia, is an indicator of stress.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel (BUN, creatinine, specific gravity)

Azotemia. Azotemia is to be expected with urethral obstruction of almost any duration.

Inadequate urine concentration. Interpretation of urine specific gravity is fraught with uncertainty. Since it is below 1.035 it would seem to indicate greater than two-thirds loss of tubular function. However, some of this urine was undoubtedly produced before obstruction occurred and we do not know the state of water balance at that time. It would be safest to assume that obstructive tubular nephropathy is present.

Additional findings:

Metabolic acidosis. Increased circulating organic acids (sulfates, phosphates) are causing a titrational metabolic acidosis characterized by increased anion gap, normal chloride relative to sodium, and reduced TCO₂ (bicarbonate). *Hyperkalemia.* Elevated potassium levels are also expected in obstruction uropathy due to acidosis and anuria and are often the cause of death. Relief of the obstruction and fluid therapy for the acidosis will quickly return the potassium to normal levels.

Hyperglycemia. Blood glucose elevations of this degree (not exceeding renal threshold) are common in stressed cats.

Summary and outcome:

After relief of the urethral obstruction and treatment with intravenous fluids for dehydration and acidosis, the renal parameters and potassium quickly returned to normal.

Case 6

SIGNALMENT: Eleven-year-old male Dachshund

HISTORY: Polyuria, polydipsia, and nocturia have been noticed for several months. Anorexia has developed in the past week.

P.E.: T = 101.4°F P = 128 R = 24

The dog is thin, slightly depressed, and 5% dehydrated. Mucous membranes are slightly pale and there are shallow ulcerations on the buccal mucosa.

INITIAL ASSESSMENT: Polyuria and polydipsia can be associated with diseases of the liver, kidney, and some endocrine organs, as well as some specific conditions such as pyometra and hypercalcemia. With the history and physical findings of this dog, certainly the renal panel must be examined and scrutiny of the hepatic panel, glucose, and calcium may be helpful.

LABORATORY DATA:

Hematology

* HCT (%)	23	L	WBC (/μl)	16,200
* Hb (g/dl)	7.6	L	* Neutrophils (/μl)	14,300 H
* RBC (× 10 ⁶ /μl)	3.24	L	Lymphocytes (/μl)	1,300
* TP (g/dl)	8.2	H	Monocytes (/μl)	600
Platelets	Adequate			

Chemistry

* BUN (mg/dl)	165	H	Lipase (IU/L)	1,650
* Creatinine (mg/dl)	4.9	H	Sodium (mmol/L)	143
* Glucose (mg/dl)	135		* Potassium (mmol/L)	6.0 H
T. bilirubin (mg/dl)	0.5		Chloride (mmol/L)	110
* TP (g/dl)	7.8	H	Calcium (mg/dl)	10.9
* Albumin (g/dl)	4.3	H	* Phosphorus (mg/dl)	14.2 H
ALT (IU/L)	43		Cholesterol (mg/dl)	232
ALP (IU/L)	47		Triglycerides (mg/dl)	97
GGT (IU/L)	10		* TCO ₂ (mmol/L)	8 L
* Amylase (IU/L)	2,330	H	* Anion gap (mmol/L)	31 H

Urinalysis

Color	light yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen (units/dl)	0.5
Sp. gr.	1.016	WBC (/HPF)	8-10
pH	6.5	RBC (/HPF)	0-5
Protein	1+	Epithelial (/HPF)	0-5
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	occ. granular
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Anemia, non-regenerative.* A HCT of 23% establishes a moderate anemia. Indices (MCV 71 fl, MCHC 33 g/dl) indicate that it is a normochromic normocytic anemia. With no report of polychromasia and a history of disease of several months' duration, it seems likely that this is a hypoproliferative anemia. Further evaluation of this anemia would require bone marrow examination and iron studies, both of which are unwarranted until the available information has been more fully examined.

TP: *Hyperproteinemia.* With clinical evidence of dehydration, elevated protein levels are likely to be associated with this condition. As with other cases, however, measurement of albumin will be helpful for confirmation.

WBC: *Stress leukogram.* Even with a normal total WBC count, a mild neutrophilia and low normal lymphocyte count are compatible with the action of glucocorticoids.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel (BUN, creatinine, specific gravity, WBC, protein, casts)

Renal azotemia. Elevated BUN and creatinine combined with an isosthenuric urine specific gravity indicate renal failure. No statement regarding etiology or prognosis can be made from these data.

Renal tubular disease. Granular casts originate in the renal tubules and indicate that there is disease involving those structures.

Mild urinary inflammation. The slight elevations in WBCs and protein in the urine indicate that there is a mild inflammation somewhere in the urinary tract. In interpreting these parameters, it is important to note the method of sample collection, as contamination from the external genitalia may cause such elevations.

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hyperproteinemia. Both the albumin and TP are elevated. This is most compatible with the dehydration seen on physical examination. There is no evidence of active hepatic disease or decreased functional hepatic mass.

Additional findings:

Mild hyperglycemia. A blood glucose of 135 mg/dl establishes the presence of a very mild

hyperglycemia. Interpretation of this abnormality must be approached with caution. A non-fasted sample and stress are two very common causes of this type of abnormality. The presence of a stress leukogram suggests that stress may be the underlying cause in this case.

Hyperphosphatemia. In combination with a normal calcium, hyperphosphatemia is most likely secondary to decreased glomerular filtration and is an expected finding in renal failure.

Hyperamylasemia. This is probably an accompaniment of reduced glomerular filtration.

Metabolic acidosis. High anion gap and low bicarbonate confirm metabolic acidosis. The high anion gap coupled with the normal chloride relative to sodium confirms that the acidosis is titrational and is probably associated with the renal failure and increased circulating sulfates and phos-

phates. (Both sodium and chloride are in the middle of the reference range but are probably falsely elevated due to hemoconcentration. It is possible that both are actually low due to solute diuresis.)

Hyperkalemia. The hyperkalemia is probably associated with the acidosis. The potassium value is still elevated even after accounting for the effect of dehydration.

Summary and outcome:

Renal failure was diagnosed on the basis of serum chemistries and urinalysis. Further diagnostic work including radiology and biopsy was necessary to reach a more specific diagnosis. Radiographs revealed shrunken kidneys, suggesting end-stage renal disease, which was confirmed by histopathology. This diagnosis readily accounts for the anemia seen in this dog as a secondary phenomenon.

Chapter 6: Clinical Pathology of Hepatic Disease

The liver performs a wide variety of different and seemingly unrelated functions. For example, it plays a central role in plasma protein synthesis, carbohydrate metabolism, lipid metabolism, and detoxification of both endogenous and exogenous substances. In addition, the liver is the site of bilirubin metabolism and bile synthesis, as well as synthesis of most circulating coagulation factors. The Kupffer cells of the hepatic sinusoids form one of the major elements of the monocyte-macrophage continuum (mononuclear phagocyte system).

The diversity of hepatic function suggests that a chemistry organ panel assessing the liver must also be diverse (see side bar). The screening panel listed here includes tests of primary importance as well as a group of additional tests to be more closely evaluated when abnormalities are present in any of the screens.

Primary hepatic panel

Serum alanine aminotransferase (ALT)

Serum alanine aminotransferase (ALT) is probably the most accurate indicator of liver disease in small animal medicine. However, it is important to realize that ALT is *not* a liver function test but rather an indicator of hepatocyte injury. ALT is a liver-specific enzyme present in high concentrations within the cytoplasm of hepatic parenchymal cells. As such, serum ALT activity is obviously increased with necrosis. However, a common response to non-lethal hepatocellular injury involves membrane blebbing with subsequent release of cytoplasmic-rich vesicles such that increased ALT activity is seen in the serum. Therefore, in a general way, the degree of elevation correlates not with the severity of hepatocellular damage but rather with the number of hepatocytes involved. In other words, diffuse fatty change may result in more extreme ALT activity elevations than focal hepatic necrosis.

As with other serum enzymes, interpretation of ALT values is largely dependent upon circulation dynamics. Serum alanine aminotransferase activity reaches maximal elevation approximately 48 hours after acute injury. The half-life of ALT is approximately 2 to 4 days in the dog and approximately 6 hours in the cat. Consequently, elevations of ALT activity following single episodes of hepatocellular damage will be transient; continuous and persistent elevations imply ongoing hepatocellular damage.

Serum alkaline phosphatase (ALP)

Serum alkaline phosphatase (ALP) is a membrane-bound enzyme produced at the bile canalicular surface of hepatocytes. Increased ALP production is induced whenever cholestasis occurs with resultant elevation in circulating enzyme activities. Thus, ALP is *not* an indicator of hepatocellular leakage, as is ALT; instead ALP is used as an indicator of either intrahepatic or extrahepatic biliary obstruction.

Unfortunately, ALP is not liver-specific; the enzyme is also found in bone, placenta, intestine, kidney, and leukocytes. In addition, both exogenous steroid administration and endogenous adrenal glucocorticoid production can induce the production of a second isozyme of ALP in the dog (but not in the cat). Furthermore, drugs such as primidone and phenobarbital can directly induce ALP production. In general, in dogs 2- to 3-fold elevations of ALP activity are regarded as non-specific and may be the result of liver disease, bone disease, or drug/exogenous steroid administration. Also in dogs, 4-fold elevations or greater are virtually always the result of cholestasis or induction of the corticosteroid isozyme of alkaline phosphatase.

Interpretation of serum ALP activity in cats is quite different. First, normal ALP activity in the liver of cats is much lower than in dogs. In addition, the circulating half-life of ALP in cats is significantly shorter than that of dogs. As a consequence, any elevation in ALP activity in cats is

Hepatic Disease Panel

- Primary hepatic panel
 - Alanine aminotransferase (ALT)
 - Alkaline phosphatase (ALP)
 - Gamma glutamyltransferase (GGT)
 - Total protein (TP)
 - Albumin
- Secondary hepatic panel
 - Blood urea nitrogen (BUN)
 - Serum bilirubin, urine bilirubin
 - Delta bilirubin
 - Cholesterol, triglycerides
 - Glucose

regarded as suggestive of cholestasis.

ALP elevations secondary to cholestasis may occur with or without concurrent elevations of ALT. Many acute conditions causing hepatocellular injury and ALT release also cause hepatocellular swelling and intrahepatic cholestasis. In contrast, many more chronic hepatic disorders are characterized by periportal fibrosis with resultant cholestasis and elevated ALP levels but little active hepatocellular degeneration.

Serum gamma glutamyl transferase (GGT)

Serum gamma glutamyl transferase (GGT) is a second membrane bound enzyme associated with bile duct epithelium. Both ALP and GGT are indicators of cholestasis. It has been suggested that GGT may be more useful than ALP because GGT activity elevations are not directly induced to a significant magnitude by glucocorticoids and drugs such as primidone. However, in most cases, this distinction is academic; most drugs that directly induce ALP also cause hepatocellular swelling which secondarily causes intrahepatic cholestasis and elevated GGT activity.

Measuring both GGT and ALP activities is probably most useful in cats where elevations in ALP are often more subtle. Elevations of both enzymes simultaneously provides supportive evidence that cholestasis is present. In cats, a relatively greater increase in ALP than GGT is suggestive of hepatic lipidosis.

Total protein (TP) and albumin

As mentioned in previous chapters, the majority of the plasma proteins are produced in the liver and severe liver disease may be a cause of hypoproteinemia due to decreased production. Due to the relatively long half-lives of plasma proteins (7-10 days), such alterations are usually seen only in chronic liver disease. Hypoproteinemia of this type is usually predominantly the result of hypoalbuminemia.

If only total protein (TP) is measured (and not albumin), the hypoproteinemia of liver disease may be missed. This is because hepatic disease is sometimes accompanied by hypergammaglobulinemia (gamma globulins are produced by cells of the immune system rather than hepatocytes), which may keep TP levels in the normal range. Hypergammaglobulinemia can develop in chronic liver disease because there are increased levels of circulating for-

eign proteins which have not been removed by the liver; this results in systemic antigenic stimulation.

Secondary hepatic panel Blood urea nitrogen (BUN)

In the liver, ammonia is metabolized to urea, the principal nitrogenous waste product of mammalian systems. The blood carries urea to the kidneys, where it is excreted as a part of the glomerular filtrate. In cases of reduced hepatic blood flow (congenital or acquired portosystemic shunts) and possibly with reduced functional hepatic mass, urea production from ammonia may be markedly reduced with a resultant *decrease* in circulating blood urea nitrogen (BUN) levels. It should be emphasized that a decreased BUN is not specific for liver disease of this nature; on the contrary, a common cause of decreased BUN is diuresis. Establishing liver disease as a cause of decreased BUN is best accomplished by demonstrating a concomitant elevation in circulating ammonia, by measuring pre and postprandial ammonia levels, or by measuring pre and postprandial bile acid levels. Both serum ammonia and serum bile acids are special tests not usually included in the large chemistry profile and therefore beyond the scope of this text. For a more complete understanding of these tests and their interpretation the reader is referred to other resources. (*See Suggested Reading; 16,17,19,32,104,105.*)

Serum bilirubin, urine bilirubin

When senescent RBCs are phagocytized and degraded by macrophages, the hemoglobin they contain is converted to heme and globin. The protein moiety, globin, is degraded to its amino acid constituents and recycled. The tetrapyrrole ring, heme, is enzymatically cleaved with release of iron and, following further degradation, is converted to free (unconjugated) bilirubin. Unconjugated bilirubin is complexed to albumin and circulated to the liver where it is conjugated with glucuronic acid and excreted in bile as bilirubin diglucuronide.

Sera from normal individuals contain a small amount of both conjugated and unconjugated bilirubin. Increases in total circulating bilirubin may result from prehepatic, intrahepatic, or posthepatic causes. Prehepatic elevations are the result of hemolysis; increased breakdown RBCs leads to increased levels of circulating bilirubin. As might be

expected in the acute phase of hemolysis, the majority (more than 75%) of the elevations in bilirubin are usually the result of elevation in unconjugated (indirect) bilirubin. Elevations due to intrahepatic cholestasis are usually the result of increases in both conjugated (direct) and unconjugated bilirubin. Elevations resulting from posthepatic cholestasis usually feature predominant (75%) elevations in conjugated bilirubin acutely, although levels of unconjugated bilirubin may also be increased. However, the reader is cautioned that these patterns of elevation are suggested as general guidelines and become increasingly less reliable as disease processes progress.

Circulating conjugated bilirubin passes the glomerulus with the glomerular filtrate and is excreted in the urine. Therefore elevated urine bilirubin levels may also be used as an indicator of hepatic disease with cholestasis particularly in the dog, which normally has a low normal renal threshold for bilirubin. In the dog, normal urine contains only small amounts of bilirubin when evaluated by standard reagent dip strip methods; an increased amount is therefore a significant finding. However, occasional increased urine bilirubin with no evidence of liver disease is seen in some dogs. The cause of this phenomenon is uncertain. In other cases, bilirubinuria may precede bilirubinemia in the progression of liver disease. Since only conjugated bilirubin passes the glomerulus, urine bilirubin levels do not usually reflect presence of prehepatic bilirubinemia.

The normal cat has a high renal threshold for bilirubin; the reagent dip strip test is almost always negative even when serum bilirubin levels are significantly elevated. Positive urine bilirubin tests in cats are only obtained in the most severe cases of liver disease, usually after clinical icterus is apparent.

Urine bilirubin and serum bilirubin are included only as secondary liver screening tests because they are less sensitive indicators of cholestasis than ALP or GGT. As a general rule in dogs, ALP and GGT elevate earlier than urine bilirubin levels, which in turn can be detected earlier than elevations in serum bilirubin levels.

Delta bilirubin

Delta bilirubin is conjugated bilirubin that has been bound to albumin. In previously used diazo reagent meth-

ods, all conjugated bilirubin, whether protein-bound (delta) or not, was measured as direct or conjugated bilirubin. Some newer assays are specific for non-protein-bound conjugated bilirubin, the fraction that most closely parallels active cholestasis. The delta bilirubin fraction is then calculated by subtracting unconjugated and conjugated bilirubin values from total bilirubin (*note: cases in this chapter report the direct value only and do not separate the delta fraction*).

Delta bilirubin is not readily excreted and therefore has nearly the same circulating half-life as albumin. In contrast, both conjugated and unconjugated bilirubin are readily cleared. Consequently, when liver disease resolves, delta bilirubin persists while conjugated and unconjugated fractions are rapidly excreted. In people with liver disease, if total bilirubin is elevated and the major form is delta bilirubin, the prognosis is favorable. Although less is known with regard to animals, there is some evidence to suggest that the same is true in dogs.

Cholesterol and triglycerides

Because the liver is central to lipid metabolism, hepatic disease greatly influences circulating lipid levels. It is well established that serum cholesterol and triglycerides are often elevated in liver diseases in both man and animals. However, these tests are listed only as components of the secondary liver screen because they are far from specific for hepatic disease. Elevations occur in a large number of diseases such as pancreatitis, diabetes mellitus, hypothyroidism, etc. These two tests are therefore considered a part of several organ system panels. In contrast, very few conditions result in decreased serum cholesterol. The primary differential for hypocholesterolemia is reduced synthesis secondary to hepatic insufficiency.

Glucose

Chronic severe liver disease can cause hypoglycemia or hyperglycemia. This is a reflection of reduced glycogen storage capacity and reduced functional hepatic mass. The presence of hypoglycemia in cases of obvious liver disease is therefore a poor prognostic sign. Hyperglycemia in liver disease is a postprandial event also due to reduced functional hepatic mass where there is no longer a place for glucose storage.

Chapter 6: Case Studies

Case 1

SIGNALMENT: Eight-year-old male DSH cat

HISTORY: Intermittent vomiting, anorexia, and jaundice of 3 weeks' duration.

P.E.: Scleral membranes are icteric and hepatomegaly is present.

INITIAL ASSESSMENT: Vomiting and anorexia are nonspecific signs most commonly associated with hepatic, pancreatic, renal, or intestinal disease. Presence of icterus and hepatomegaly suggests that the liver and the hematopoietic system are of particular interest. Hematology and chemistry profiles are warranted with particular emphasis on aforementioned organ systems.

LABORATORY DATA:

Hematology

* HCT (%)	25	L	* WBC (/μl)	39,800	H
* Hb (g/dl)	8.3	LN	* Neutrophils (/μl)	35,800	H
* RBC (× 10 ⁶ /μl)	5.0	LN	* Bands (/μl)	400	H
TP (g/dl)	6.8		Lymphocytes (/μl)	2,400	
Reticulocytes (%)	1.3		* Monocytes (/μl)	1,200	H
Platelets	Adequate				

Chemistry

BUN (mg/dl)	17		Lipase (IU/L)	400	
Creatinine (mg/dl)	1.0		Sodium (mmol/L)	150	
Glucose (mg/dl)	85		Potassium (mmol/L)	4.5	
* T. bilirubin (mg/dl)	4.6	H	Chloride (mmol/L)	118	
Direct bilirubin (g/dl)	3.9		Calcium (mg/dl)	10.2	
TP (g/dl)	7.0		Phosphorus (mg/dl)	4.2	
Albumin (g/dl)	2.8		* Cholesterol (mg/dl)	480	H
* ALT (IU/L)	449	H	* Triglycerides (mg/dl)	180	L
* ALP (IU/L)	200	H	TCO ₂ (mmol/L)	18	
GGT (IU/L)	18		Anion gap (mmol/L)	14.5	
Amylase (IU/L)	568				

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.021	WBC	neg.
pH	6.5	RBC	neg.
Protein	neg.	Epithelial	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts	neg.
Bilirubin	1+	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* Presence of anemia is established by HCT of 25%. Reticulocyte count of 1.3% indicates that the anemia is non-regenerative. Computed MCV is 50 fl, MCHC is 33 g/dl; the anemia is normocytic normochromic.

TP: Normal.

WBC: *Chronic active inflammatory leukogram.* Moderate leukocytosis with moderate neutrophilia and slight left shift suggestive of active inflammation. Monocytosis and degree of neutrophilia suggest chronicity. Monocytosis indicates increased tissue demand for macrophages. No evidence of stress; lymphocyte count is normal.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (primary and secondary – total bilirubin, direct bilirubin, TP, albumin, ALT, ALP, GGT, cholesterol, triglycerides, glucose, urine bilirubin)

Hepatocellular injury. Marked elevation in ALT suggests that many hepatocytes are affected. It does not necessarily provide information on the severity or reversibility of the injury.

Cholestasis. Two-fold elevation of alkaline phosphatase in the cat and elevated GGT are highly suggestive of cholestasis. This is supported by moderate elevations in serum bilirubin. The 1+ urine bilirubin is also supportive.

Altered lipid metabolism. Mild hypercholesterolemia and hypertriglyceridemia in the secondary hepatic panel support the interpretation of altered lipid metabolism due to liver disease.

Pancreatic panel (BUN, amylase, lipase)

No abnormalities noted.

Urinary panel (BUN, creatinine, specific gravity)

No abnormalities noted.

Intestinal panel (TP, albumin, sodium potassium, chloride)

No abnormalities noted.

Summary and outcome:

The clinical signs and laboratory data strongly suggest primary chronic inflammatory liver disease with a prominent

cholestatic component and an associated non-regenerative anemia. Hepatic biopsy and culture led to the specific diagnosis of bacterial cholangiohepatitis.

Case 2

SIGNALMENT: Four-month-old male mixed-breed dog

HISTORY: Acute-onset vomiting, anorexia, and evidence of abdominal pain.

P.E.: Tender abdomen, icteric mucous membranes, high fever (104.5°F).

INITIAL ASSESSMENT: Acute abdomen with icterus in a puppy strongly suggests the possibility of infectious canine hepatitis (ICH), but other causes of acute abdomen (eg, pancreatitis, gastroenteritis, acute renal disease) must be ruled out. Organs of interest are therefore liver, pancreas, kidney, and the GI system.

LABORATORY DATA:

Hematology

* HCT (%)	60	H	* WBC (/μl)	4,300	L
* Hb (g/dl)	20.0	H	* Neutrophils (/μl)	1,200	L
* RBC (× 10 ⁶ /μl)	8.0	HN	* Bands (/μl)	500	H
* TP (g/dl)	8.2	HN	* Lymphocytes (/μl)	500	L
Reticulocytes (%)	1.0		* Monocytes (/μl)	2,100	H
* Platelets	Reduced				

Chemistry

* BUN (mg/dl)	45	H	Lipase (IU/L)	1,000	
* Creatinine (mg/dl)	2.5	H	* Sodium (mmol/L)	155	H
Glucose (mg/dl)	80		Potassium (mmol/L)	5.4	
* T. bilirubin (mg/dl)	4.0	H	* Chloride (mmol/L)	130	H
Direct bilirubin (mg/dl)	2.2		Calcium (mg/dl)	11.2	
* TP (g/dl)	7.5	H	Phosphorus (mg/dl)	5.0	
* Albumin (g/dl)	4.6	H	* Cholesterol (mg/dl)	340	H
* ALT (IU/L)	640	H	* Triglycerides (mg/dl)	150	H
* ALP (IU/L)	700	H	* TCO ₂ (mmol/L)	10	L
* GGT (IU/L)	25	H	* Anion gap (mmol/L)	20	H
* Amylase (IU/L)	800				

Urinalysis

Color	amber	Occ. blood	neg.
Turbidity	clear	Urobilinogen (units/dl)	neg.
Sp. gr.	1.045	WBC (/HPF)	neg.
pH	6.0	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	occ. granular
Bilirubin	3+	Crystals	triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Relative polycythemia.* HCT of 60% establishes polycythemia; elevated total protein with a history of vomiting suggests that the polycythemia is most likely secondary to dehydration. MCV and MCHC are normal, as is reticulocyte count.

TP: *Hyperproteinemia.* Consider dehydration or hypergammaglobulinemia. In view of RBC parameters, dehydration is most likely.

WBC: *Severe active inflammatory leukogram.* Neutropenia with a left shift (degenerative left shift) suggests an overwhelming inflammatory process in the dog and implies a guarded prognosis.

Monocytosis suggests tissue necrosis.

Superimposed stress leukogram. The severe lymphopenia is most consistent with endogenous steroid production, ie, stress accompanying the severe inflammation.

Platelets: *Thrombocytopenia.* The combination of thrombocytopenia and overwhelming inflammation suggests the possibility of disseminated intravascular coagulopathy (DIC).

Chemistry and Urinalysis

Hepatic panel (primary and secondary – total bilirubin, direct bilirubin, TP, albumin, ALT, ALP, GGT, cholesterol, triglycerides, glucose, urine bilirubin)

Hepatocellular injury. Ten-fold elevations in ALT imply that large numbers of hepatocytes are injured.

Cholestasis. A 4-fold elevation of alkaline phosphatase is at least suggestive of cholestasis. However, a stress leukogram is present and a steroid-induced elevation of alkaline phosphatase must be at least considered.

Cholestasis is confirmed by the presence of elevated GGT, marked bilirubinuria, and a bilirubinemia.

Altered lipid metabolism. Hypercholesterolemia and mild hypertriglyceridemia in the secondary hepatic panel suggest altered lipid metabolism, common in many liver diseases.

Hyperproteinemia, hyperalbuminemia. Typically, liver disease, particularly chronic liver disease, causes hypoproteinemia and hypoalbuminemia as a result of reduced production. In this case, the reverse changes are most likely the result of dehydration.

Urinary panel (BUN, creatinine, specific gravity)

Prerenal azotemia. Elevated BUN establishes azotemia. High specific gravity implies ability of tubules to concentrate urine and also supports the contention that the azotemia is prerenal (the result of dehydration and reduced renal blood flow) rather than the result of primary renal damage. Occasional casts suggest some tubular destruction, but it is likely secondary to ischemia.

Pancreatic panel (BUN, amylase, lipase, urine specific gravity)

No evidence of pancreatic disease.

Intestinal panel (TP, albumin, sodium, potassium, chloride)

Hypernatremia, hyperchloremia. Elevations of electrolytes reflect concentration due to dehydration. Chloride is increased relative to sodium.

Additional abnormalities:

Metabolic acidosis. Low bicarbonate and elevated anion gap confirm metabolic acidosis. The increased anion gap suggests a titrational acidosis, possibly secondary to decreased tissue perfusion and a build up of lactic acid. The elevated chloride relative to sodium suggests that the acidosis also has a secretory component from loss of sodium bicarbonate.

Summary and outcome:

Data suggest severe inflammatory liver disease with diffuse hepatocellular leakage and cholestasis with the possibility of associated DIC. Metabolic acidosis is present. Other chemistry alterations are secondary to dehydration and hypovolemia. Fine needle aspiration biopsy (done in the face of normal partial thromboplastin time but slightly prolonged prothrombin time) confirmed a diagnosis of ICH.

Case 3

SIGNALMENT: Eight-year-old male Airedale

HISTORY: Chronic weight loss, lethargy, and intermittent diarrhea.

P.E.: Physical reveals an emaciated animal with abdominal distention. The dog is afebrile.

INITIAL ASSESSMENT: History and signs are fairly nonspecific although chronic intermittent diarrhea is most often associated with chronic liver, pancreatic, intestinal, or renal disease. Evaluation of hemogram and organ system data for these organs is certainly warranted.

LABORATORY DATA:

Hematology

* HCT (%)	33	L	* WBC (/ μ l)	32,000	H
* Hb (g/dl)	11.0	L	* Neutrophils (/ μ l)	25,400	H
* RBC ($\times 10^6$ / μ l)	5.0	L	Lymphocytes (/ μ l)	3,200	
* TP (g/dl)	4.8	L	* Monocytes (/ μ l)	3,400	H
Reticulocytes (%)	0.8		Platelets	Adequate	

Chemistry

BUN (mg/dl)	13		Lipase (IU/L)	728	
Creatinine (mg/dl)	0.6		Sodium (mmol/L)	148	
Glucose (mg/dl)	85		Potassium (mmol/L)	5.1	
* T. bilirubin (mg/dl)	1.1	H	* Chloride (mmol/L)	118	
* Direct bilirubin (mg/dl)	0.6		Calcium (mg/dl)	7.0	L
* TP (g/dl)	4.0	L	Phosphorus (mg/dl)	4.1	
* Albumin (g/dl)	1.8	L	Cholesterol (mg/dl)	150	
* ALT (IU/L)	120	H	Triglycerides (mg/dl)	80	
* ALP (IU/L)	800	H	TCO ₂ (mmol/L)	22	
GGT (IU/L)	30		Anion gap (mmol/L)	13.1	
Amylase (IU/L)	542				

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	WBC (/HPF)	neg.
Sp. gr.	1.011	RBC (/HPF)	neg.
pH	6.5	Epithelial (/HPF)	occasional
Protein	neg.	Bacteria	neg.
Glucose	neg.	Casts (/LPF)	neg.
Ketones	neg.	Crystals	triple phosphate
Bilirubin	2+		

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* HCT of 33% establishes anemia. Reticulocyte count of 0.8% confirms that the anemia is non-regenerative. MCV is 66 fl and MCHC is 33 g/dl; the anemia is normocytic and normochromic.

TP: *Hypoproteinemia.* There is a marked hypoproteinemia for a dog of this age. Further investigation and attention to causes of hypoproteinemia are warranted. Possible causes include liver disease (reduced production), renal disease (increased loss), and intestinal disease (increased loss or reduced absorption).

WBC: *Chronic inflammatory leukogram.* A leukocytosis with mature neutrophilia and marked monocytosis is suggestive of a long-standing inflammatory process in which the marrow has expanded to meet tissue demand (therefore, no left shift). A normal lymphocyte count is also suggestive that the inflammatory process is of some duration. The monocytosis is primarily an indicator of increased demand for tissue macrophages.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Mild hepatocellular injury. Mild elevations of ALT imply mild hepatocellular damage or hepatocellular damage involving only a few hepatocytes.

Cholestasis. Marked elevations of alkaline phosphatase indicate either cholestatic liver disease or steroid-induced isozyme formation. Steroid-induced elevations of alkaline phosphatase of this magnitude are highly unlikely in the absence of a stress leukogram (lymphopenia). Other evidence for cholestasis is found in the elevation of GGT and in the secondary hepatic panel as a 2+ bilirubinuria, and a bilirubinemia.

Hypoproteinemia, hypoalbuminemia. Both changes are commonly associated with chronic liver disease but loss through kidney and gut must also be considered. Protein-losing enteropathy is of particular interest here because of a history of chronic diarrhea.

Pancreatic panel (BUN, amylase, lipase, urine specific gravity)

No evidence of primary pancreatic disease.

Urinary panel (BUN, creatinine, specific gravity)

No evidence of primary urinary disease.

Intestinal panel (total bilirubin, TP, sodium, potassium, chloride)

Panhypoproteinemia. As suggested earlier, the hypoproteinemia and albuminemia in this case may be the result of either reduced hepatic protein production or increased enteric loss or both. The fact that both albumin and globulins (TP minus albumin) are reduced suggests that the problem is at least partially enteric. In both liver disease and renal disease, hypoproteinemia is usually due primarily to hypoalbuminemia.

Additional findings:

Hypocalcemia. The hypocalcemia is probably a reflection of the decreased albumin (*see Chapter 7*). No other pancreatic parameters suggest primary pancreatic disease.

Summary and outcome:

Data and clinical signs suggested chronic inflammatory liver disease with cholestasis and hypoproteinemia/hypoalbuminemia. The contribution of protein-losing enteropathy was considered likely. Hepatic and enteric biopsy led to a diagnosis of hepatic and intestinal histoplasmosis.

Case 4

SIGNALMENT: Four-year-old female Beagle

HISTORY: Sudden change of behavior with increased lethargy and irritability; loss of appetite.

P.E.: Extremely pale mucous membranes, slightly yellow.

INITIAL ASSESSMENT: History is nonspecific.

However, physical examination suggests severe anemia and icterus. Hematology and evaluation of liver is warranted.

LABORATORY DATA:

Hematology

* HCT (%)	20	L	* WBC (/ μ l)	17,900	H
* Hb (g/dl)	5.2	L	* Neutrophils (/ μ l)	13,500	H
* RBC ($\times 10^6$ / μ l)	2.43	L	* Bands (/ μ l)	1,100	H
TP (g/dl)	7.0		* Lymphocytes (/ μ l)	1,000	LN
* Reticulocytes (%)	35.0		* Monocytes (/ μ l)	2,300	H
Platelets	Adequate				

Blood film morphology: moderate spherocytes (2+)

Chemistry

BUN (mg/dl)	13		Lipase (IU/L)	225	
Creatinine (mg/dl)	1.0		Sodium (mmol/L)	144	
Glucose (mg/dl)	120		Potassium (mmol/L)	5.2	
* T. bilirubin (mg/dl)	5.0	H	Chloride (mmol/L)	113	
* Direct bilirubin (g/dl)	1.3		Calcium (mg/dl)	11.0	
TP (g/dl)	6.7		Phosphorus (mg/dl)	4.0	
Albumin (g/dl)	3.2		Cholesterol (mg/dl)	100	
* ALT (IU/L)	400	H	Triglycerides (mg/dl)	100	
* ALP (IU/L)	300	H	TCO ₂ (mmol/L)	20	
* GGT (IU/L)	18	H	Anion gap (mmol/L)	16.2	
Amylase (IU/L)	600				

Urinalysis

Color	amber	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.024	WBC	neg.
pH	7.0	RBC	neg.
Protein	neg.	Epithelial	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts	neg.
Bilirubin	2+	Crystals	triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

Comment on blood film morphology: moderate spherocytes (2+)

RBC: *Marked regenerative anemia.* HCT of 20% establishes presence of anemia. Computed absolute reticulocyte count of 850,000 strongly suggests hemolysis. The presence of large numbers of spherocytes on the peripheral blood

smear suggests immune-mediated hemolysis.

A positive Coombs' test would further support this interpretation; a negative Coombs' test result would not rule out this process.

TP: No abnormalities.

WBC: *Inflammatory leukogram.* A leukocytosis with a neutrophilia, left shift, and monocytosis strongly suggests active inflammation. Hemolysis itself may serve as a stimulus for such inflammation.

Stress leukogram. Marginal lymphopenia is highly suggestive of a stress component.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hepatocellular injury. A moderate ALT elevation indicates moderately diffuse hepatocellular injury. Such an elevation may result from primary liver damage or may be secondary to hypoxia caused by severe anemia. Increased cell membrane permeability may or may not be the result of a reversible lesion.

Possible cholestasis. Two-fold elevations of ALP are nonspecific. The stress leukogram suggests that endogenous steroid release may at least be contributory. The minimal increase in GGT also provides some support or cholestasis. In light of ALT levels, intrahepatic cholestasis (due to hepatocellular swelling) is the most likely explanation.

Additional findings:

Prehepatic icterus. Total bilirubin is elevated and over 50% is indirect (unconjugated).

These findings are consistent with hemolytic anemias where increased amounts of unconjugated bilirubin are generated and presented to the liver for processing. Conjugated bilirubin elevates secondarily.

Summary and outcome:

A Coombs' test supported the diagnosis of immune-mediated hemolytic anemia. Liver changes and icterus were con-

sidered secondary to the anemia. The primary disease process was controlled with steroid therapy and ALT activity returned to normal within 7 days.

Case 5

SIGNALMENT: Six-year-old female Doberman

HISTORY: Polydipsia and polyuria of unknown origin. “Bloated” for 2 weeks.

P.E.: Marked ascites. No dehydration. Abdominal palpation impossible because of ascites. Cardiac auscultation normal.

INITIAL ASSESSMENT: Polyuria and polydipsia are associated with abnormalities in a variety of organ systems, including the urogenital system (renal disease and pyometra) and the endocrine system (Cushing’s disease or diabetes mellitus). Ascites may be associated with heart failure (ruled out on physical), or hypoproteinemia, the causes of which include liver disease, protein-losing enteropathy, or protein-losing nephropathy. Endocrine evaluation can only be done very superficially. Panels of primary interest are liver, renal, and GI. Leukogram data, particularly presence or absence of a stress leukogram (steroid-induced, possibly Cushing’s), is also of great interest.

LABORATORY DATA:

Hematology

HCT (%)	44	WBC (/μl)	9,300
Hb (g/dl)	15.9	Neutrophils (/μl)	7,200
RBC (× 10 ⁶ /μl)	6.4	Lymphocytes (/μl)	1,400
* TP (g/dl)	5.3 L	Monocytes (/μl)	600
Platelets	Adequate	Eosinophils (/μl)	100

Chemistry

BUN (mg/dl)	10	Lipase (IU/L)	700
Creatinine (mg/dl)	0.8	Sodium (mmol/L)	148
Glucose (mg/dl)	89	Potassium (mmol/L)	4.4
* T. bilirubin (mg/dl)	1.0 H	Chloride (mmol/L)	118
* Direct bilirubin (g/dl)	0.6	* Calcium (mg/dl)	9.1 L
* TP (g/dl)	5.0 LN	Phosphorus (mg/dl)	3.7
* Albumin (g/dl)	1.8 L	Cholesterol (mg/dl)	166
* ALT (IU/L)	307 H	Triglycerides (mg/dl)	100
* ALP (IU/L)	680 H	TCO ₂ (mmol/L)	22.4
* GGT (IU/L)	25 H	Anion gap (mmol/L)	12
Amylase (IU/L)	552		

Urinalysis

Color	pale	Protein	neg.
Turbidity	clear	Bilirubin	4+
Sp. gr.	1.010	Other chemistries	unremarkable
pH	5.5	Sediment	unremarkable

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: *Hypoproteinemia*. Cause of hypoproteinemia is uncertain and albumin levels should be determined.

Evaluate hypoalbuminemia as a possible cause of ascites.

WBC: No abnormalities.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hepatocellular injury. Elevations in ALT indicate hepatocellular injury. Degree of elevation suggests relatively large number of hepatocytes involved.

Cholestasis. An elevation in alkaline phosphatase of this magnitude (4-fold) suggests either a steroid-induced elevation or cholestasis. Considering the elevation in GGT and the absence of a stress leukogram, cholestasis is the best interpretation.

Hypoproteinemia, hypoalbuminemia. In this case, hypoproteinemia is due strictly to hypoalbuminemia; globulins (TP minus albumin) are normal. Hypoalbuminemia may be the result of protein-losing nephropathy or enteropathy or reduced production by the liver. Urinalysis shows no evidence of protein loss through the kidney. Enteric protein loss usually involves both globulins and albumin; there is no evidence of diarrhea. The likely cause of hypoalbuminemia is reduced hepatic protein production. *Marked bilirubinuria, mild bilirubinemia*. These tests are part of the secondary liver panel and are supportive for the earlier interpretation of cholestasis.

Urinary panel (BUN, creatinine, specific gravity)

Isosthenuric urine. Isosthenuria may indicate inability of tubules to concentrate (*see Chapter 3*); however, it also is expected in cases such as this where polyuria and polydipsia are reported. Without additional tests, and possibly a water deprivation test, the specific gravity is ambiguous. Since BUN and creatinine are both normal, it is likely that diuresis is indeed the cause of isosthenuria.

Intestinal panel (TP, albumin, sodium, potassium, chloride)

Normal, except for hypoproteinemia discussed above.

Additional abnormalities:

Hypocalcemia. The marginal hypocalcemia is associated with hypoalbuminemia.

Summary and outcome: Hepatocellular damage with cholestasis and reduced protein synthesis was established on the basis of signs and laboratory data. Biopsy was recommended and performed for specific diagnosis; chronic active hepatitis was confirmed.

Case 6

SIGNALMENT: Eighteen-month-old male Doberman
HISTORY: Weight loss for 2 months. Depression, occasional diarrhea, and decreased appetite have been observed over the same time period. In recent weeks, the dog has occasionally collapsed and has also seemed blind (ie, walks into walls).

P.E.: T = 101.8°F P = 92 R = 16

Very thin and depressed.

INITIAL ASSESSMENT: Signs are nonspecific.

Diarrhea, weight loss, and anorexia may all result from diseases of a variety of organ systems. Even central nervous system disorders may be primary or secondary. General evaluation of major organ systems (ie, liver, kidney, GI) and hematology are warranted.

LABORATORY DATA:

Hematology

HCT (%)	40	WBC (/μl)	7,100
Hb (g/dl)	13.0	Neutrophils (/μl)	5,600
RBC (× 10 ⁶ /μl)	6.1	* Lymphocytes (/μl)	500 L
TP (g/dl)	6.8	Monocytes (/μl)	400
Platelets	Adequate	Eosinophils (/μl)	600

Chemistry

* BUN (mg/dl)	4 L	Lipase (IU/L)	600
Creatinine (mg/dl)	1.0	Sodium (mmol/L)	144
Glucose (mg/dl)	76	Potassium (mmol/L)	4.4
T. bilirubin (mg/dl)	0.6	Chloride (mmol/L)	116
TP (g/dl)	6.4	Calcium (mg/dl)	10.2
Albumin (g/dl)	3.2	Phosphorus (mg/dl)	3.6
* ALT (IU/L)	110 H	Cholesterol (mg/dl)	260
* ALP (IU/L)	225 H	Triglycerides (mg/dl)	110
* GGT (IU/L)	17 H	TCO ₂ (mmol/L)	15
Amylase (IU/L)	452	Anion gap (mmol/L)	17.4

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.020	WBC	neg.
pH	6.0	RBC	neg.
Protein	1+	Epithelial	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts/(LPF)	2-3 granular
Bilirubin	neg.	Crystals	many ammonium biurate

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: No abnormalities.

WBC: *Lymphopenia.* The most common cause of lymphopenia is stress; however, other features of a stress leukogram are not present. Other causes of lymphopenia that should be considered include reduced lymphocyte production and lymphatic obstruction.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Mild hepatocellular injury. A mild ALT elevation indicates mild hepatocellular leakage, which may be seen with a variety of disease syndromes, including both diseases primary and secondary to the liver.
Nonspecific alkaline phosphatase elevation. A 1.5× elevation in alkaline phosphatase is mild and nonspecific and may be associated with cholestasis and enteritis. Indicators of cholestasis in the secondary hepatic panel (urine bilirubin, serum bilirubin) are not elevated.

Reduced BUN. (Secondary hepatic panel.) In most primary renal diseases BUN is elevated. A reduced BUN is often caused by diuresis and is associated with a urine specific gravity in the isosthenuric range. In this case, specific gravity is slightly above the isosthenuric range. A second possible cause of reduced BUN is failure of the liver to convert ammonia to urea either as a result of a portosystemic shunt bypassing the liver or because of a lack of hepatic urea cycle enzymes. Since there is no evidence of severe primary hepatic disease and the patient is young in age, the presence of a congenital portocaval shunt should be strongly considered. CNS signs secondary to elevated circulating ammonia levels are common in patients with portosystemic shunts.

Urinary panel (BUN, creatinine, specific gravity)

Reduced BUN. See hepatic panel.

Renal tubular degeneration. Granular casts indicate tubular degeneration.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

Intestinal panel (TP, albumin, sodium, potassium, chloride)
No abnormalities.

Additional abnormalities:

Ammonium biurate crystalluria. This finding lends much support to the suspicion of portosystemic shunt. Ammonium biurate crystals are a rare finding in the urine and have usually been associated with severe liver disease, including portosystemic shunts and end-stage liver.

Summary and outcome:

Laboratory data suggested further evaluation for the presence of a portosystemic shunt. Fasting blood ammonia and ammonia challenge tests and contrast venography are considered diagnostic procedures. Circulating ammonia levels were 351 mol/L (normal = up to 125 mol/L) and venography was positive for a portocaval shunt.

Chapter 7: Clinical Pathology of Exocrine Pancreatic Disease

The exocrine pancreas is a digestive glandular organ that empties its secretions into the duodenum via the pancreatic ducts. Pancreatic exocrine secretions contain electrolytes and enzymes, including the lipolytic enzyme lipase, the proteolytic enzymes trypsin and chymotrypsin, and the amylolytic enzyme amylase. Low activity levels of these enzymes are normally present in the serum.

Diseases of the pancreas are either acute and necrotizing or more chronic and smoldering with eventual functional insufficiency. The acute necrotizing conditions are associated with leakage of digestive enzymes into serum. Chronic conditions may have acute exacerbations with typical features of acute disease; however, these conditions often feature no serum enzymic alterations and depend heavily on fecal examination and special tests for diagnosis. For the purpose of this text, we will concentrate on the diagnosis of acute, or at least active, pancreatic disease. The primary pancreatic panel is designed to establish the diagnosis of acute pancreatic disease; the secondary pancreatic panel consists of tests that allow the assessment of the severity of secondary involvement of other organ systems.

Primary Pancreatic Panel Amylase, lipase, and BUN

For dogs, elevations in circulating activities of the 2 digestive enzymes amylase and/or lipase are the most important chemical indicators of acute exocrine pancreatic disease. Interpretation of serum amylase activity is difficult at best for several reasons. First, the reference range for amylase is quite broad and the standard deviation is large, suggesting that elevations should be substantial before they are considered significant. Additionally, amylase has a relatively short half-life so that elevated activities often will return to normal shortly after a disease episode. Because amylase is excreted or degraded by the kidney, increased serum activities may be seen whenever renal function is compromised. Finally, mild to moderate serum amylase activity may be related to disease in other organ systems containing amylase, such as the small intestine.

Of these 2 enzymes, lipase has been reported by some to be a better diagnostic test for acute pancreatitis in dogs. In the authors' clinical experience, this has not proven to be the case. In different cases of pancreatitis in dogs we have

seen simultaneous elevations of amylase and lipase activity, elevations of amylase activity only, and elevations of lipase activity only. Furthermore, renal disease has the same effect on serum lipase as it has on serum amylase. In addition, dexamethasone has been shown to cause a 5-fold increase in serum lipase activity (in the absence of pancreatic lesions) while causing no change in serum amylase activity. Based on these features of amylase and lipase, collectively, it is recommended that amylase, lipase, and BUN constitute the primary diagnostic panel for canine pancreatitis. A greater than 2-fold increase in either lipase or amylase activity in the absence of elevated BUN (and assuming no corticosteroid therapy) is suggestive of pancreatitis.

Pancreatitis in cats is less common than in dogs. In addition, amylase activity is not elevated in reported feline cases of pancreatitis. As in canine cases, lipase elevations have been reported to be more accurate indicators of disease than amylase elevations.

Secondary Pancreatic Panel Calcium, albumin

In nearly 50% of cases of pancreatitis, hypocalcemia develops either as a sequela to saponification of peripancreatic fat and local deposition of calcium salts or the release of glucagon from the pancreas. Glucagon in turn stimulates

Exocrine Pancreatic Disease Panel

- Primary pancreatic panel
 - Amylase
 - Lipase
 - Blood urea nitrogen (BUN)
- Secondary pancreatic panel
 - Calcium, albumin
 - Glucose
 - Alanine aminotransferase (ALT)
 - Alkaline phosphatase (ALP)
 - Cholesterol, triglycerides
- Additional tests
 - Trypsin-like immunoreactivity (TLI)

increased production of calcitonin, which causes hypoglycemia. Therefore, hypocalcemia in conjunction with elevated amylase and/or lipase levels is highly supportive evidence of pancreatitis, and calcium levels should always be evaluated. However, serum calcium can only be evaluated in light of albumin. Measured serum calcium represents total calcium composed of both functional ionized calcium and albumin-bound, biologically inert calcium. With reduced serum albumin, the total calcium levels will therefore always be reduced, even though functional ionized calcium levels may be normal. Hypocalcemia is supportive evidence for pancreatitis only when albumin levels are normal.

Glucose

The most common important sequela to pancreatitis is diabetes, and for this reason blood glucose levels should always be evaluated. Elevations are expected during acute pancreatitis but may be transient and should be monitored after acute disease has resolved.

ALT, ALP

Pancreatitis is almost always associated with localized peritonitis and edema of peripancreatic tissues. Because of their proximity to the pancreas, the liver and duodenum are often involved. Edema of the pancreas and duodenum may cause partial obstruction of the common bile duct. ALT and ALP levels are evaluated to monitor the extent of hepatic involvement.

Cholesterol and triglycerides

The pancreas, like the liver, is involved with lipid metabolism. For example, lipase is involved with the absorption of fat through the intestine, and in pancreatitis this function

may be disturbed. Secondary or even transient diabetes may lead to ketoacidosis and increased mobilization of lipid from body stores. Secondary liver involvement may result in altered lipid metabolism. For these reasons, cholesterol and triglycerides are often elevated in pancreatitis. In fact, lipemia in pancreatitis may cause interference with determination of many chemistries in the large profile.

Additional tests

Because of the difficulties of diagnosing pancreatitis on the basis of amylase and/or lipase elevations, there has been ongoing research to develop alternative diagnostic tests. One such test is trypsin-like immunoreactivity (TLI). The principle reason that TLI has not been identified as a part of the primary diagnostic panel is that it is not usually included in large chemistry profiles.

In contrast to amylase and lipase, the origin of TLI is specific to the pancreas. In experimental canine models, TLI tends to elevate earlier but decrease sooner than either amylase or lipase. Also, in contrast to amylase and lipase, normal TLI is higher in cats than in dogs. In a very limited number of experimental pancreatitis cases in cats, affected animals exhibited significant increases in TLI. However, TLI is excreted by the kidneys and may therefore show the same limitation as amylase and lipase during renal disease.

TLI is also valuable in the diagnosis of end stage canine pancreatitis (exocrine pancreatic insufficiency (EPI)). In EPI, amylase and lipase activities are usually normal. However, TLI concentrations in EPI are consistently markedly reduced. In fact, reduction in TLI may occur before clinical signs of EPI are recognized.

Case 1

SIGNALMENT: Three-year-old female Boston Terrier

HISTORY: Vomiting and bloody diarrhea for 1 day.

P.E.: T = 103°F P = 100 R = panting

INITIAL ASSESSMENT: Painful abdomen, vomiting, and bloody diarrhea are most commonly associated with either acute gastroenteritis or acute pancreatitis. Acute hepatic disease and acute renal disease may also be causes of acute abdominal pain.

LABORATORY DATA:

Hematology

HCT (%)	55	* WBC (/μl)	30,000	H
* Hb (g/dl)	18.2	* Neutrophils (/μl)	25,000	H
RBC (× 10 ⁶ /μl)	7.99	* Bands (/μl)	1,200	H
TP (g/dl)	7.0	Lymphocytes (/μl)	1,800	
Platelets	Adequate	* Monocytes (/μl)	1,800	H

Chemistry

BUN (mg/dl)	15	* Lipase (IU/L)	5,400	H
Creatinine (mg/dl)	1.2	Sodium (mmol/L)	148	
Glucose (mg/dl)	110	Potassium (mmol/L)	4.6	
T. bilirubin (mg/dl)	0.4	* Chloride (mmol/L)	122	H
TP (g/dl)	6.6	Calcium (mg/dl)	10.7	
Albumin (g/dl)	3.2	Phosphorus (mg/dl)	4.5	
ALT (IU/L)	26	Cholesterol (mg/dl)	130	
ALP (IU/L)	51	Triglycerides (mg/dl)	60	
GGT (IU/L)	12	* TCO ₂ (mmol/L)	9	L
* Amylase (IU/L)	6,200	* Anion gap (mmol/L)	21.6	H

Urinalysis

Sp. gr. 1.024

All other findings unremarkable.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Relative polycythemia.* RBC parameters are borderline high normal to elevated but computation of MCV and MCHC yields normal red cell indices. (MCV 69 fl, MCHC approximately 33 g/dl). Total protein is within the normal range, but with the history of vomiting, the likely explanation of the elevated HCT is mild dehydration and hemoconcentration.

TP: No abnormalities.

WBC: *Active inflammatory leukogram.*

White cell parameters indicate leukocytosis with neutrophilia, left shift, and monocytosis. This is the classic active inflammatory leukogram in dogs. Lymphocytes are in the normal range; there is no evidence of superimposed stress.

Platelets: No abnormalities.

Chemistry and Urinalysis

Primary exocrine pancreatic panel (BUN, amylase, lipase)

Acute pancreatic disease. A marked elevation of amylase and lipase in the presence of an inflammatory leukogram and clinical evidence of an acute abdomen and vomiting, in the absence of evidence of impaired glomerular filtration (normal BUN) is highly suggestive of acute pancreatitis.

Hepatic panel (TP, albumin, ALT, ALP, GGT)

No abnormalities.

Urinary panel (BUN, creatinine, specific gravity)

No abnormalities.

Intestinal panel (BUN, TP, albumin, sodium, potassium, chloride)

Hyperchloremia. High chloride relative to sodium suggests a secretory acidosis.

Additional findings:

Mild metabolic acidosis. The low bicarbonate and the elevated anion gap support the interpretation of metabolic acidosis. The acidosis is most likely primarily secretory, resulting from sodium bicarbonate loss through duodenal emesis and diarrhea. This is supported by the high chloride relative to sodium. The specific mechanism for the mild increase in anion gap is not clear. The clinical signs and evidence for mild hemoconcentration may support mild lactic acidosis.

Summary and outcome:

The animal was successfully treated but suffered several recurring bouts in ensuing years.

Case 2

SIGNALMENT: Six-year-old female Miniature Poodle

HISTORY: Dog began vomiting 1 day after Thanksgiving and has continued intermittently for 3 days. Owner is concerned that the dog swallowed a turkey bone.

P.E.: T = 103.2°F P = 106 R = panting

INITIAL ASSESSMENT: Vomiting, abdominal pain, and fever suggest acute abdominal disease. Evaluate pancreas, intestine, liver, and kidney.

LABORATORY DATA:

Hematology

* HCT (%)	55	HN	* WBC (/μl)	41,200	H
* Hb (g/dl)	18	HN	* Neutrophils (/μl)	34,000	H
* RBC (× 10 ⁶ /μl)	8.0	HN	* Bands (/μl)	2,500	H
* TP (g/dl)	8.2	H	* Lymphocytes (/μl)	800	L
Platelets	Adequate		* Monocytes (/μl)	3,900	H

Chemistry

* BUN (mg/dl)	75	H	* Lipase (IU/L)	4,800	H
* Creatinine (mg/dl)	3.1	H	* Sodium (mmol/L)	162	H
* Glucose (mg/dl)	260	H	* Potassium (mmol/L)	7.0	H
T. bilirubin (mg/dl)	0.4		* Chloride (mmol/L)	130	H
* TP (g/dl)	8.0	H	* Calcium (mg/dl)	7.9	L
Albumin (g/dl)	3.6		Phosphorus (mg/dl)	4.8	
* ALT (IU/L)	90	H	Cholesterol (mg/dl)	240	
* ALP (IU/L)	180	H	* Triglycerides (mg/dl)	280	H
* GGT (IU/L)	22	H	TCO ₂ (mmol/L)	22	
Amylase (IU/L)	600		Anion gap (mmol/L)	17	

Urinalysis

Color	dark yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.040	WBC (/HPF)	neg.
pH	6.0	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	2+	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	neg.
Bilirubin	neg.	Crystals	triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Relative polycythemia.* Marginally elevated HCT establishes polycythemia. Computation of indices reveals normocytosis and normochromasia (MCV 69 fl, MCHC 33 g/dl). The most common cause of polycythemia in animals is dehydration. Indeed, in this case, TP is elevated, and with a history of vomiting, dehydration is a strong possibility. Other parameters affected by dehydration, such as BUN, creatinine, electrolytes, and urine specific gravity, must be evaluated cautiously.

TP: *Hyperproteinemia.* The likelihood of dehydration is discussed above. The possibility of hyperglobulinemia should also be considered.

WBC: *Active inflammatory leukogram.*

There is a marked leukocytosis with neutrophilia, a left shift, and monocytosis. This is a regenerative left shift that implies active inflammation.

Stress leukogram. The marked lymphopenia implies superimposed stress and suggests that steroid-induced changes may be present.

Platelets: No abnormalities.

Chemistry and Urinalysis

Pancreatic panel (BUN, amylase, lipase)

Possible acute pancreatitis. Data are inclusive. Amylase is not elevated but lipase is elevated. Interpretation of pancreatic enzymes is clouded by elevated BUN. Nevertheless, hemogram data and a hypocalcemia with a normal albumin are all consistent with a diagnosis of acute pancreatitis. Additional large profile abnormalities seen in this case included hyperglycemia as well as lipid abnormalities reflected by hypertriglyceridemia. All of these abnormalities are commonly seen in pancreatitis as well as in other conditions. Fluid therapy followed by repeated large chemistry profiles are essential to confirm pancreatitis.

Intestinal panel (TP, albumin, sodium, potassium, chloride)

No evidence of primary enteric disease.

Hyperproteinemia. Change in protein, which indicates intestinal disease, is hypoproteinemia. As suggested, the hyperproteinemia most likely reflects dehydration.

Hypernatremia, hyperkalemia, and hyperchloremia. With dehydration, electrolyte levels as well as protein levels elevate.

Increased electrolyte levels in the face of dehydration suggest that electrolyte balance is probably normal.

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Mild hepatocellular injury. Two-fold elevations in ALT are relatively mild and may occur with either primary or secondary hepatic involvement. For example, such elevations commonly occur in association with mild hepatocellular degeneration caused by processes as divergent as acute pancreatitis and chronic passive congestion secondary to cardiac disease.

Mildly elevated alkaline phosphatase. Two-fold elevations of alkaline phosphatase are nonspecific. In this case, the elevation may reflect mild cholestasis associated with the same disease process causing increased hepatocellular plasma membrane injury. An alternative explanation is found in the stress leukogram. The possibility of a steroid-induced ALP elevation must be considered.

Urinary panel (BUN, creatinine, specific gravity)

Prerenal azotemia. Azotemia is established on the basis of moderate elevations of BUN and creatinine. The prerenal nature of the azotemia is suspected because of strong evidence of dehydration (which implies reduced renal perfusion) and no evidence in the urinalysis of primary renal or postrenal involvement. In fact, the high urine specific gravity is strong evidence that renal tubular function is adequate, with concentration of urine in the face of dehydration.

Glycosuria. Glycosuria is expected when renal threshold levels (180 mg/dl) are exceeded in the peripheral blood. Glycosuria is a reflection of primary renal disease only when unaccompanied by hyperglycemia.

Additional abnormalities:

Hyperglycemia. Persistent fasting hyperglycemia is a strong indication of diabetes mellitus. In dogs, recurring bouts of pancreatic necrosis are a common cause of diabetes mellitus. Transient marked hyperglycemia can be a feature of acute pancreatitis. In all cases of pancreatitis, blood glucose should be monitored throughout treatment and following recovery. Moderate elevations in blood glucose (less than renal threshold levels) may be the result of endogenous steroid levels; in this case, levels are too high and cannot be explained on the basis of stress.

Summary and outcome:

Data, clinical signs, and history all suggest dehydration, primary pancreatitis with possible secondary diabetes, and mild liver disease. Laboratory findings are suggestive but inconclusive because of the absence of elevated amylase and existing dehydration and prerenal azotemia. Fluid therapy was initiated and lipase elevations persisted even after BUN and creatinine returned to normal, thus confirming the diagnosis of pancreatitis. The patient was successfully treated, and hyperglycemia proved to be transient.

Case 3

SIGNALMENT: Two-year-old male German Shepherd-Collie mix

HISTORY: Dog is allowed to roam freely. Returned home vomiting and depressed after being gone several days. Depression and anorexia have worsened during past 48 hours.

P.E.: T = 103.4°F P = 90 R = panting

INITIAL ASSESSMENT: Acute abdomen with vomiting and depression are seen with acute pancreatitis, hepatitis, enteritis, and renal disease. A large chemistry profile and hematology are warranted.

LABORATORY DATA:

Hematology

HCT (%)	48	* WBC (/μl)	28,000	H
Hb (g/dl)	16	* Neutrophils (/μl)	25,000	H
RBC (× 10 ⁶ /μl)	6.90	* Bands (/μl)	500	H
* TP (g/dl)	9.2	* Lymphocytes (/μl)	1,100	LN
* Platelets	Reduced	Monocytes (/μl)	1,000	L
Eosinophils (/μl)	400			

Blood film morphology: toxic neutrophils.

Chemistry

* BUN (mg/dl)	280	H	* Lipase (IU/L)	3,800	H
* Creatinine (mg/dl)	7.0	H	Sodium (mmol/L)	150	
Glucose (mg/dl)	85		* Potassium (mmol/L)	8.0	H
T. bilirubin (mg/dl)	0.2		* Chloride (mmol/L)	120	H
* TP (g/dl)	8.4	H	* Calcium (mg/dl)	8.6	L
* Albumin (g/dl)	4.2	H	* Phosphorus (mg/dl)	11.0	H
ALT (IU/L)	30		Cholesterol (mg/dl)	140	
ALP (IU/L)	55		Triglycerides (mg/dl)	40	
GGT (IU/L)	14		* TCO ₂ (mmol/L)	6	L
* Amylase (IU/L)	4,220	H	* Anion gap (mmol/L)	32	H

Urinalysis

Color	amber	Occ. blood	neg.
Turbidity	slightly turbid	Urobilinogen	neg.
Sp. gr.	1.014	WBC (/HPF)	neg.
pH	6.2	RBC (/HPF)	neg.
Protein	2+	Epithelial (/HPF)	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	large numbers coarse and fine granular
Bilirubin	neg.	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

Blood film morphology: toxic neutrophils.

RBC: No abnormalities.

TP: *Hyperproteinemia*. With the history, elevated TP is most likely due to dehydration.

WBC: *Active inflammatory leukogram*. The mild regenerative left shift indicates active inflammation. The presence of toxic neutrophils in the peripheral blood suggests systemic toxemia.

Possible superimposed stress. The marginal lymphopenia raises the question of steroid-induced changes.

Platelets: *Thrombocytopenia*.

Thrombocytopenia in the face of active inflammation with toxicity suggests the possibility of disseminated intravascular coagulopathy (DIC).

Chemistry and Urinalysis

Pancreatic panel (BUN, amylase, lipase)

Possible acute pancreatitis. Elevated amylase and lipase, and hypocalcemia with normal to elevated albumin, are consistent with pancreatitis. However, extreme caution in interpretation should be exercised here; the markedly elevated BUN makes the significance of the elevated pancreatic enzymes questionable. Amylase and lipase are excreted by the kidney and may be substantially elevated with reduced renal perfusion or primary renal disease. Furthermore, mild hypocalcemia is a common finding in renal failure.

Hepatic panel (TP, albumin, ALT, ALP, GGT, sodium, potassium, chloride)

No evidence of hepatic disease. Protein changes are most likely the result of dehydration.

Intestinal panel (TP, albumin, sodium, potassium, chloride)

No evidence of primary enteric disease. *Hyperkalemia*. Renal acidosis and reduced renal excretion of potassium must be considered the primary factors. Marked hyperkalemia is also seen with tissue necrosis. With the marked inflammatory leukogram, this is a definite possibility in this case.

Mild hypernatremia, hyperchloremia.

Proportional increases most likely reflect dehydration and hemoconcentration.

Urinary panel (BUN, creatinine, specific gravity)

Renal azotemia. BUN and creatinine are too elevated for simple prerenal azotemia. Additionally, in light of dehydration, urine should be concentrated (elevated specific gravity); however, the urine is isosthenuric, implying a lack of tubular concentrating ability.

Tubular necrosis. The presence of large numbers of granular casts implies active necrosis and sloughing of tubular lining epithelium.

Additional abnormalities:

Hyperphosphatemia. Phosphorus is excreted largely by glomerular filtration. When BUN and creatinine are elevated, hyperphosphatemia may be expected.

Metabolic acidosis. Low bicarbonate and high anion gap confirm metabolic acidosis. This is most likely titrational as a

result of increased circulating organic acids from renal failure (phosphates, sulfates). Ethylene glycol (a possible cause of the tubular necrosis) may also be contributing.

Summary and outcome:

Data concerning the pancreas were ambiguous because of azotemia and potential reduced glomerular filtration. The renal panel was interpreted as diagnostic for acute primary renal tubular necrosis. The animal was diuresed but without success and died after 2 days of therapy. At necropsy, ethylene glycol toxicity with oxalate nephrosis was diagnosed. The pancreas was histologically normal.

Comment:

This case clearly demonstrates the importance of considering the effects of disease of one organ system on the interpretation of one laboratory test as it relates to another test. Pancreatic enzymes must always be interpreted in light of primary renal parameters.

Case 4

SIGNALMENT: Six-year-old male Doberman

HISTORY: Chronic weight loss and voluminous pale stools. The animal has a voracious appetite.

P.E.: Physical reveals an emaciated animal. No other abnormalities noted.

INITIAL ASSESSMENT: Emaciation and voluminous stools are associated with chronic liver disease (reduced bile production and maldigestion), chronic pancreatic disease (maldigestion), or chronic intestinal disease (maldigestion and malabsorption).

LABORATORY DATA:

Hematology

* HCT (%)	30	L	* WBC (/μl)	20,500	H
* Hb (g/dl)	9.6	L	* Neutrophils (/μl)	15,200	H
* RBC (× 10 ⁶ /μl)	4.30	L	Lymphocytes (/μl)	3,200	
TP (g/dl)	6.2		* Monocytes (/μl)	2,100	H
Platelets	Adequate				

Chemistry

BUN (mg/dl)	12	Lipase (IU/L)	150
Creatinine (mg/dl)	0.8	Sodium (mmol/L)	142
Glucose (mg/dl)	85	Potassium (mmol/L)	3.8
T. bilirubin (mg/dl)	0.1	Chloride (mmol/L)	109
TP (g/dl)	6.0	Calcium (mg/dl)	9.4
Albumin (g/dl)	2.7	Phosphorus (mg/dl)	4.2
ALT (IU/L)	25	Cholesterol (mg/dl)	145
ALP (IU/L)	30	Triglycerides (mg/dl)	32
GGT (IU/L)	8	TCO ₂ (mmol/L)	20
Amylase (IU/L)	340	Anion gap (mmol/L)	16.8

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.030	WBC (/HPF)	neg.
pH	6.8	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	neg.
Bilirubin	neg.	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* HCT of 30% establishes the mild anemia. Computation of indices (MCV 71 fl, MCHC 33%) indicates normocytosis and normochromasia. With the history of chronic disease, the best explanation is anemia of chronic disease. Further specific interpretation requires bone marrow examination.

TP: No abnormalities.

WBC: *Chronic inflammatory leukogram.* There is a mild leukocytosis with a mature neutrophilia, monocytosis, and normal lymphocyte count. The neutrophilia and monocytosis imply inflammation. The fact that the neutrophilia is mature implies that the marrow has had time to reach a new steady state (suggesting chronicity). The chronic nature of the response is supported by the normal lymphocyte count. Lymphocyte numbers are usually depressed during acute inflammatory processes but often return to normal range during the more chronic stages of inflammation. Platelets: No abnormalities.

Chemistry and Urinalysis

Pancreatic, hepatic, urinary and intestinal panels: all normal.

In chronic disease syndromes, chemistry panels may be normal and special tests are required for accurate diagnosis. In this case, the main problem is chronic weight loss and voluminous stools. Trypsin-like immunoreactivity (TLI) tests on the feces for pancreatic and intestinal enzymes, and tests of absorption (oral xylose and glucose absorption tests) are certainly indicated.

Summary and outcome:

In this case, TLI was low (1.8 g/L), glucose absorption was normal, fecal trypsin was negative by gel dissolution test, and there was abundant fecal fat. Addition of pancreatic enzymes to the diet corrected the abnormalities. All of these findings suggest pancreatic insufficiency. The inflammatory leukogram suggests that the problem may have been the result of chronic pancreatitis. Approximately 12 months after initial admission the animal developed diabetes mellitus and was treated for several months. At necropsy, chronic fibrosing pancreatitis and pancreatic atrophy were diagnosed.

Chapter 8: Clinical Pathology of Gastrointestinal Disease

The tubular digestive tract, which includes the stomach, small intestine, and large intestine, performs a variety of functions essential to normal health and homeostasis. Included among these functions are digestion, absorption, and excretion. In addition, gastrointestinal disease can profoundly affect water, electrolyte, and acid-base balance.

The roles of the small and large intestines to the process of digestion are both direct and indirect. For example, the epithelial cells of the small intestine produce enterokinase, the enzyme necessary for enteroenteric activation of the pancreatic proteolytic enzyme trypsin. Trypsin in turn activates all of the other pancreatic proteases, which are released in inactive form. The intestinal epithelial cells also play an active role in digestion, producing numerous enzymes that reduce large chain molecules to a size that can be absorbed across the intestinal mucosa.

Even if digestion of fats, carbohydrates, and protein is totally normal, damage to intestinal mucosa may preclude normal absorption of nutrients. Mucosal damage may be physical, as is seen with chronic fibrosing or atrophic enteritis, or biochemical, where mucosal transport mechanisms are impaired.

The intestines also are involved in water, electrolyte, and acid-base balance. This relationship is readily apparent when the general effects of diarrhea and/or vomiting are considered. In both conditions, there may be tremendous loss of body fluid with resultant dehydration and often pre-renal azotemia. In diarrhea or emesis there may be tremendous loss of electrolytes and acid or base. Intestinal emesis usually results in the loss of sodium bicarbonate and a potential metabolic acidosis. Diarrhea is characterized by loss of bicarbonate and sodium with resultant metabolic acidosis. In metabolic acidosis, hydrogen is exchanged for intracellular potassium; hyperkalemia may be the observed result. In contrast, with vomiting originating from the stomach there is a loss of gastric HCl and a resultant hypochloridemia and metabolic alkalosis.

Although disease of the digestive system may have profound and even life-threatening effects, diagnosis of primary intestinal disease can almost never be made on the basis of abnormalities in the large chemistry profile alone. Instead primary intestinal disease is usually suspected after

other possibilities (pancreatic disease, liver disease, and renal disease) have been eliminated, and is established only after additional tests have been completed. The reason is obvious; there are no tests in most large chemistry profiles that are specific for intestinal disease. For example, none of the serum enzymes, which are standard in most large chemistry profiles, are specifically associated with either the small or large bowel. Even electrolytes and protein, which are a part of the primary intestinal panel, can be significantly altered in a wide variety of diseases affecting several organ systems. The primary intestinal panel listed here is not used to diagnose primary intestinal or gastric disease but rather is a group of tests that may be of value in assessing the general abnormalities common in patients suffering from possible or apparent gastrointestinal disease.

Primary Intestinal Panel Total protein and albumin

Either hyperproteinemia or hypoproteinemia may be seen with intestinal diseases. When present, hyperproteinemia is usually a reflection of dehydration; the other alterations seen with dehydration (*see Chapter 2*) are to be anticipated concurrently. Hypoproteinemia associated with enteric disease may be a reflection of malabsorption but is more commonly seen with protein loss through the gut (protein-losing enteropathy). In both instances hypoproteinemia is usually a manifestation of a relatively chronic disease process. The hypoproteinemia of enteric disease is usually a panhypoproteinemia; albumin and globulin are equally decreased. This finding is of diagnostic importance;

Gastrointestinal Disease Panel

- Primary gastrointestinal panel
 - Total protein (TP)
 - Albumin
 - Electrolytes
 - Sodium
 - Potassium
 - Chloride

the hypoproteinemias associated with protein-losing glomerulopathy and chronic liver disease are usually principally hypoalbuminemias with normal or (in the case of liver disease) elevated globulins.

Electrolytes

Sodium

Sodium is the principal cation of the extracellular fluid; serum levels combined with an estimate of hydration are therefore a good indication of total body sodium balance. In primary enteric disease, sodium levels may be elevated (hypernatremia), normal, or reduced (hyponatremia). Interpretation of sodium levels must always take into consideration the state of hydration of the patient. For example, hypernatremia is most commonly associated with dehydration and hemoconcentration. Patients with elevated sodium levels in the face of dehydration can have normal total body sodium levels. On the other hand, patients having normal serum sodium levels in association with dehydration (elevated TP, high urine specific gravity, etc.) probably have mild to moderate total body sodium deficits. Similarly, animals with hyponatremia associated with dehydration and vomiting or diarrhea are probably suffering from severe total body sodium deficits.

It should be reemphasized that enteric disease is not the only source of altered sodium balance. For example, hyponatremia is a feature of Addison's disease and hyperaldosteronism may result in a primary hypernatremia (*see Chapter 9*).

Chloride

Chloride is the principal anion of the extracellular space and usually correlates with serum sodium levels. When chloride levels are altered relative to sodium, they are suggestive of disturbed acid-base balance. Altered chloride lev-

els usually vary inversely with altered bicarbonate levels; when chloride levels are elevated, bicarbonate levels are generally reduced, and vice versa. A hyperchloremia (or decreased serum bicarbonate) suggests metabolic acidosis, the most common acid-base abnormality encountered in veterinary practice. Hypochloridemia (increased serum bicarbonate) usually indicates metabolic alkalosis. As mentioned earlier, emesis of gastric origin is usually associated with hypochloridemia and metabolic alkalosis; emesis of intestinal origin is often associated with loss of sodium bicarbonate, hyperchloremia, and metabolic acidosis. Of course, these patterns may not necessarily hold in mixed acid-base disturbances (*see Chapter 4*).

Potassium

Potassium is the principal intracellular cation. Because it is located principally within cells, serum levels do not reflect total body potassium. In fact, total body potassium levels are impossible to evaluate conveniently. Altered serum potassium is most commonly associated with altered acid-base balance. In metabolic acidosis, hydrogen ions are exchanged for potassium ions within cells with a resultant hyperkalemia. In metabolic alkalosis, the reverse occurs to a lesser degree and hypokalemia may be seen. In enteric disease, serum potassium levels are usually normal unless acid-base balance is altered.

Serum potassium levels also are affected by factors other than acid-base balance. For example, hypoadrenocorticism (Addison's disease) is characterized by hyperkalemia (*see Chapter 9*). Insulin drives potassium into cells and in some cases of insulin therapy or spontaneous hyperinsulinism, life threatening hypokalemia may result. This mechanism also helps explain the hyperkalemia of hypoinsulinemia diabetes mellitus although metabolic ketoacidosis may also be a factor.

Chapter 8: Case Studies

Case 1

SIGNALMENT: Female Manx cat

HISTORY: Acute onset vomiting, anorexia, and dark tarry diarrhea of 24-hours duration. Polydipsia is also reported.

P.E.: T = 103.2°F P = 120 R = panting

INITIAL ASSESSMENT: History and P.E. suggest acute pancreatitis, acute hepatitis, or acute gastroenteritis. Acute nephritis is a less likely possibility.

LABORATORY DATA:

Hematology

* HCT (%)	28	L	* WBC (/μl)	27,000	H
* Hb (g/dl)	9.2	LN	* Neutrophils (/μl)	18,100	H
* RBC (× 10 ⁶ /μl)	5.8	LN	* Bands (/μl)	6,500	H
* TP (g/dl)	8.8	H	* Lymphocytes (/μl)	800	L
Platelets	Adequate		* Monocytes (/μl)	1,600	H

Chemistry

* BUN (mg/dl)	45	H	Lipase (IU/L)	868	
Creatinine (mg/dl)	2.2		Sodium (mmol/L)	150	
Glucose (mg/dl)	84		* Potassium (mmol/L)	9.0	H
T. bilirubin (mg/dl)	0.4		Chloride (mmol/L)	128	
* TP (g/dl)	8.6	H	Calcium (mg/dl)	10.6	
* Albumin (g/dl)	4.4	H	Phosphorus (mg/dl)	4.1	
ALT (IU/L)	36		Cholesterol (mg/dl)	120	
* ALP (IU/L)	120	H	Triglycerides (mg/dl)	80	
GGT (IU/L)	8		* TCO ₂ (mmol/L)	7	L
Amylase (IU/L)	600		* Anion gap (mmol/L)	24	H

Urinalysis

Color	dark yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	0.1
Sp. gr.	1.050	WBC (/HPF)	neg.
pH	7.0	RBC (/HPF)	neg.
Protein	1+	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	occ. hyaline
		Crystals	triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Anemia, non-regenerative.* HCT of 28% indicates anemia. The elevated TP implies that the anemia may be more severe than the HCT indicates. Clinical history suggests that the elevated TP is most likely the result of dehydration.

Computation of red cell indices indicates that the anemia is normocytic and normochromic (MCV 48 fl, MCHC 33 g/dl) and is most likely non-regenerative. The history of dark tarry diarrhea suggests that acute blood loss anemia, seen before signs of bone marrow regeneration are apparent in the peripheral blood, should be strongly considered.

TP: *Hyperproteinemia.* History of acute disease with diarrhea strongly suggests dehydration as the underlying cause.

WBC: *Active inflammatory leukogram.* A neutrophilia with a left shift (regenerative left shift) and monocytosis is most consistent with active inflammation.

Stress. The marked lymphopenia is consistent with stress.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

No strong evidence of liver disease.

Elevations of alkaline phosphatase are non-specific. Hyperproteinemia has been explained on the basis of dehydration.

Pancreatic panel (BUN, amylase, lipase)

No evidence of primary pancreatic disease.

Amylase is normal even in the face of elevated BUN.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

Electrolyte imbalance. Electrolytes must be interpreted in light of the state of hydration. There is strong evidence of dehydration in this patient. Therefore, the recorded normonatremia is probably indicative of moderate total body hyponatremia. Hyperkalemia is seen with tissue necrosis or acidosis. Hyperchloremia relative to sodium is strongly suggestive of metabolic acidosis.

Low TCO₂ levels confirm metabolic acidosis. The acidosis is secretory in nature and consistent with bicarbonate loss through diarrhea. The very mild increase in the anion gap is likely due to hyperalbuminemia.

Urinary panel (BUN, creatinine, specific gravity)

Prerenal azotemia. Elevated BUN in conjunction with concentrated urine (high specific gravity) and normal urine sediment suggests normal kidney function with elevated BUN from prerenal factors. A common cause of prerenal azotemia is reduced renal perfusion due to dehydration.

Summary and outcome:

Acute gastroenteritis was diagnosed on the basis of laboratory data and radiologic findings. Evaluation of the feces for occult blood confirmed suspicion of a blood loss anemia. The animal was treated supportively and recovered uneventfully.

CASE 2

SIGNALMENT: Six-month-old male German Shepherd
HISTORY: Acute onset explosive diarrhea. Dog brought to clinic within 6 hours of onset.

P.E.: Examination reveals a young dog in good condition, but depressed. Diarrhea was evident at the time of admission.

INITIAL ASSESSMENT: A history of acute onset diarrhea of this nature strongly suggests primary intestinal disease. Acute pancreatitis might also be considered.

LABORATORY DATA:

Hematology

HCT (%)	42	* WBC (/ μ l)	3,700 L
Hb (g/dl)	14.4	* Neutrophils (/ μ l)	900 L
RBC ($\times 10^6$ / μ l)	6.0	* Lymphocytes (/ μ l)	700 L
TP (g/dl)	6.5	* Monocytes (/ μ l)	2,100 H
Platelets	Adequate		

Chemistry

BUN (mg/dl)	12	Lipase (IU/L)	625
Creatinine (mg/dl)	1.0	Sodium (mmol/L)	142
Glucose (mg/dl)	80	Potassium (mmol/L)	3.8
T. bilirubin (mg/dl)	0.2	Chloride (mmol/L)	110
TP (g/dl)	6.3	Calcium (mg/dl)	10.6
Albumin (g/dl)	3.0	* Phosphorus (mg/dl)	7.8 H
ALT (IU/L)	40	Cholesterol (mg/dl)	150
* ALP (IU/L)	320 H	Triglycerides (mg/dl)	40
GGT (IU/L)	14	TCO ₂ (mmol/L)	20
Amylase (IU/L)	432	Anion gap (mmol/L)	16

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.028	WBC (/HPF)	neg.
pH	6.5	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities. Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat. **H** indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.
TP: No abnormalities.
WBC: *Peracute inflammatory leukogram.* A neutropenia unaccompanied by a left shift is most consistent with peracute inflammation and tissue sequestration of neutrophils. The lack of a left shift implies that the marrow storage pool is not yet exhausted. Such leukograms are rare in dogs, but the history strongly supports this interpretation. The peracute inflammatory leukogram may develop into a degenerative left shift if the inflammation is overwhelming, or a regenerative left shift if the marrow can respond appropriately. *Stress leukogram.* The marked lymphopenia indicates stress. The degree of monocytosis could be consistent with a response to glucocorticoids or inflammation.
Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)
Nonspecific elevation in alkaline phosphatase. A 2-fold increase in ALP is nonspecific, but is probably age-related and associated with growth.
Pancreatic panel (BUN, amylase, lipase)
No abnormalities.
Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)
No abnormalities.

Additional findings:

Hyperphosphatemia. Phosphorus, like alkaline phosphatase, must be interpreted in light of the animal's age and the manner in which the reference values were derived. These parameters are higher in young animals with active bone growth than in adult animals. In this case, the reference values were derived from adult animals only; these "elevated" values are actually normal for this puppy.

Summary and outcome:

Findings presented here are similar to those seen in many enteric conditions. An inflammatory leukogram is present, but no abnormalities are noted in the intestinal panel, thus underlining the fact that large chemistry profiles do not contain tests which are specific for enteric disease. After admission to the hospital, the patient developed uncontrollable emesis and hemorrhagic diarrhea. Parvoviral enteritis was diagnosed by viral isolation and histopathology findings at necropsy.

Case 3

SIGNALMENT: One-year-old female Collie

HISTORY: Intermittent emesis, usually shortly after eating but not after drinking water.

P.E.: Examination reveals a clinically normal, active, 1-year-old dog.

INITIAL ASSESSMENT: History and P.E. suggest a noninflammatory noninfectious disease of the GI tract. The GI panel should be evaluated.

INTERPRETATION:

Hematology

No abnormalities.

Chemistry and Urinalysis

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

Hypochloridemia. In the vomiting dog, hypochloridemia suggests alkalosis as a result of gastric emesis and loss of HCl. Elevated bicarbonate confirms metabolic alkalosis.

LABORATORY DATA:

Hematology

HCT (%)	44	WBC (/μl)	11,800
Hb (g/dl)	15.0	Neutrophils (/μl)	8,200
RBC (× 10 ⁶ /μl)	6.2	Lymphocytes (/μl)	2,400
TP (g/dl)	6.4	Monocytes (/μl)	800
Platelets	Adequate	Eosinophils (/μl)	400

Chemistry

BUN (mg/dl)	12	Lipase (IU/L)	320
Creatinine (mg/dl)	0.7	Sodium (mmol/L)	144
Glucose (mg/dl)	85	Potassium (mmol/L)	4.2
T. bilirubin (mg/dl)	0.4	* Chloride (mmol/L)	102 L
TP (g/dl)	6.0	Calcium (mg/dl)	11.1
Albumin (g/dl)	3.0	Phosphorus (mg/dl)	4.5
ALT (IU/L)	45	Cholesterol (mg/dl)	160
ALP (IU/L)	55	Triglycerides (mg/dl)	60
GGT (IU/L)	7	* TCO ₂ (mmol/L)	32 H
Amylase (IU/L)	420	Anion gap (mmol/L)	16

Urinalysis

Sp. gr. 1.025

All other findings unremarkable.

Summary and outcome:

Radiology suggested the presence of a gastric foreign body. A gastrotomy was performed and a rubber ball removed. The alkalosis was corrected by treatment with Ringer's solution.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

Case 4

SIGNALMENT: Seven-year-old male Cocker Spaniel

HISTORY: Chronic weight loss and diarrhea.

P.E.: At the time of presentation, the dog was emaciated and depressed. Temperature, pulse, and respiration were normal.

INITIAL ASSESSMENT: Chronic weight loss and diarrhea suggest primary chronic hepatic, intestinal, or pancreatic disease. The panels for those organ systems should be evaluated.

LABORATORY DATA:

Hematology

* HCT (%)	32	L	* WBC (/μl)	25,000	H
* Hb (g/dl)	10.2	L	* Neutrophils (/μl)	20,000	H
* RBC (× 10 ⁶ /μl)	5.1	L	Lymphocytes (/μl)	2,400	
* TP (g/dl)	4.0	L	* Monocytes (/μl)	2,400	H
Platelets	Adequate		Eosinophils (/μl)	200	

Blood film morphology: acanthocytosis; rare polychromasia.

Chemistry

BUN (mg/dl)	14		Lipase (IU/L)	280	
Creatinine (mg/dl)	0.8		Sodium (mmol/L)	142	
Glucose (mg/dl)	96		Potassium (mmol/L)	4.4	
T. bilirubin (mg/dl)	0.6		Chloride (mmol/L)	110	
* TP (g/dl)	3.8	L	Calcium (mg/dl)	10.0	
* Albumin (g/dl)	1.8	L	Phosphorus (mg/dl)	3.2	
ALT (IU/L)	45		* Cholesterol (mg/dl)	340	H
* ALP (IU/L)	800	H	Triglycerides (mg/dl)	70	
* GGT (IU/L)	30	H	TCO ₂ (mmol/L)	22	
Amylase (IU/L)	420		Anion gap (mmol/L)	14	

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.025	WBC (/HPF)	neg.
pH	6.6	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	2+	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

Blood film morphology: Acanthocytosis; rare polychromasia.

RBC: *Non-regenerative anemia.* HCT of 32% establishes the anemia. The MCV (62 fl) and the MCHC (32 g/dl) indicate that the anemia is normochromic and normocytic and most likely non-regenerative. This is supported by the lack of polychromasia on the peripheral blood film. The

presence of acanthocytes is noteworthy and suggests a possible plasma lipid abnormality associated with liver disease.⁹⁸ Cholesterol and triglycerides should be assessed in addition to the primary liver panel.

TP: *Marked hypoproteinemia.*

Hypoproteinemia may be the result of reduced production or increased loss.

Albumin and globulin concentrations are required for further definition.

WBC: *Chronic inflammatory leukogram.*

Leukocytosis with neutrophilia and monocytosis strongly suggest inflammation. The absence of a left shift and normal lymphocyte count suggest chronicity because development of an expanded myeloid marrow capable of meeting tissue demand without storage pool depletion requires time.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Cholestasis. A 5-fold elevation in alkaline phosphatase in the absence of any evidence of a steroid effect is strongly suggestive of cholestasis. An elevated GGT and a mild increase in urine bilirubin are also supportive. *Hypoalbuminemia.* Hypoalbuminemia can be a feature of liver disease and is often associated with chronic cholestatic disease. However, albumin to globulin ratio is usually not normal. While liver disease could be contributing to the hypoalbuminemia here, a primary protein-losing enteropathy is probably also present.

Pancreatic panel (BUN, amylase, lipase)

No abnormalities.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

Panhypoproteinemia. Hypoproteinemia with both hypoalbu-

minemia and hypoglobulinemia (panhypoproteinemia) is most commonly a feature of enteric disease with protein loss. A history of diarrhea with chronic weight loss is supportive. Further fecal tests of maldigestion and malabsorption would be helpful (*see Suggested Reading; 32*).

Additional findings:

Hypercholesterolemia. Hypercholesterolemia is a nonspecific finding but is often found in cholestasis. It is also a com-

mon accompaniment of hypoalbuminemia.

Summary and outcome:

Data suggested chronic inflammatory disease with both cholestatic liver disease and protein-losing enteropathy. Hepatic and colonic biopsies were taken and granulomatous hepatitis and enteritis due to *Histoplasma capsulatum* were diagnosed.

Chapter 9: Clinical Pathology of Endocrine Organs

The endocrine system is composed of a variety of glands that influence diverse bodily functions through the secretion of hormones. Hormones are defined as substances produced by a particular tissue that are released into the blood and exert an effect on other distant target tissues. Because of the variety of functions of the endocrine glands, and the variety of clinical endocrinopathies, no single endocrine sub-panel can be identified from the large chemistry profile. Instead, separate sub-panels for each endocrine organ have been developed. It should be emphasized that for the most part specific endocrine disorders cannot be identified with chemistry sub-panels alone; rather these sub-panels provide supportive evidence for a diagnosis of endocrine disease that often can only be established with special tolerance tests or hormone assays. This text will not cover such special procedures. In the case examples at the end of this chapter, additional testing is indicated, where necessary, and results are provided, when available.

Clinical Pathology of the Parathyroid Gland

The principal product of the parathyroid gland is parathyroid hormone (PTH), which regulates serum calcium concentration through its effect on both bone and kidney. Parathyroid hormone mobilizes calcium from bone by stimulating osteocytic and osteoclastic bone resorption. In the kidney, PTH stimulates phosphaturia and calcium retention (resorption) as well as stimulating increased formation of dihydroxycholecalciferol, the active form of vitamin D.^{1,25} Vitamin D enhances both the mobilization of calcium from bone and the absorption of calcium through the intestine. Thus, the actions of PTH serve to elevate serum calcium. The hypercalcemic effects of PTH are counterbalanced by the hypocalcemic effects of the hormone calcitonin, which inhibits bone resorption and is secreted by the parafollicular cells of the thyroid gland.

The principal veterinary disease syndrome involving the parathyroid gland is hyperparathyroidism, which may present clinically with hypercalcemia due to PTH mediated bone resorption. Hyperparathyroidism may be primary due to parathyroid hyperplasia or neoplasia, or secondary due to renal disease or nutritional imbalance. It is important to note that secondary nutritional hyperparathyroidism is

caused by high phosphorus/low calcium diets and presents as a bony disease. Also, a paraneoplastic syndrome called humoral hypercalcemia of malignancy (HHM, also known as pseudohyperparathyroidism) has been described in dogs with a variety of neoplasms, most often lymphosarcoma.

All of these entities as well as the less frequent hypoparathyroidism cause disturbances in calcium and phosphorus metabolism and, either primarily or secondarily, kidney function. Consequently, calcium and albumin, phosphorus, BUN, creatinine, and urinalysis should be included in the parathyroid panel (*see below*). Since PTH-mediated bone resorption can result in elevations in the bone isozyme alkaline phosphatase, this enzyme is also included. The definitive diagnosis of either hyper- or hypoparathyroidism depends upon PTH determination. This is not a standard test in the large chemistry profile.

Primary Parathyroid Panel Calcium, phosphorus, albumin

Hypercalcemia is an important finding and when present the possibility of either primary hyperparathyroidism or HHM should be considered. The two conditions cannot be differentiated on the basis of clinical laboratory data; both will also be accompanied by hypophosphatemia. Early in the disease, BUN and creatinine will be normal but renal failure may occur late secondary to hypercalcemia (hypercalcemic nephropathy). Early lesions in hypercalcemic nephropathy involve mineralization of tubular epithelium such that dogs may present with hypercalcemia, polyuria, polydipsia, and

Parathyroid Disease Panel

- ❑ Primary parathyroid panel
 - Calcium, phosphorus
 - Albumin
 - Alkaline phosphatase (ALP)
- ❑ Secondary parathyroid panel
 - Blood urea nitrogen (BUN)
 - Creatinine
 - Urinalysis

non-concentrated urine but without azotemia. Granular casts may be observed at this stage as well.

Calcium levels in secondary renal hyperparathyroidism are usually normal to low-normal, but phosphate levels are significantly elevated due primarily to the reduced glomerular filtration of renal failure. The slightly reduced calcium concentration is due mainly to impaired calcium absorption via the gut as a result of reduced formation of 1,25 dihydroxycholecalciferol. In response to the hypocalcemic effects of renal disease, the parathyroid gland undergoes hyperplasia with increased release of PTH, bone resorption, and the classic lesions of fibrous osteodystrophy. As expected in secondary renal hyperparathyroidism, renal tests (BUN, creatinine, and urine specific gravity) are consistently abnormal.

Secondary nutritional hyperparathyroidism results mainly from diets low in calcium or diets with excessive phosphorus and normal to decreased calcium. With excessive dietary phosphorus, the expected changes are hyperphosphatemia or normophosphatemia and normo- or mild hypocalcemia. With vitamin D deficiency or low dietary calcium, normo- or hypocalcemia with normo- or hypophosphatemia is anticipated. Nutritional hyperparathyroidism presents with marked bone resorption and fibrous osteodystrophy. However, renal tests are normal.

Hypocalcemia and hyperphosphatemia are anticipated abnormalities with hypoparathyroidism. The clinical features are secondary to the hypocalcemia, which causes neuromuscular hyperexcitability and tetanic convulsions.

Hypocalcemia with normal to reduced phosphate levels may be seen in lactating bitches suffering from eclampsia. There is no parathyroid abnormality in these animals; rather, the abnormalities seen result from rapid turnover of calcium and resultant imbalances.

As has been emphasized in other organ systems, hypocalcemia must always be interpreted in light of serum albumin because approximately 50% of circulating serum calcium is albumin-bound. There are also diseases in other organ systems which cause hypocalcemia without attendant hypoalbuminemia; these include acute pancreatitis and oxalate nephrosis.

ALP

Active bone resorption may cause nonspecific (2-fold) elevations in alkaline phosphatase (ALP). Other causes of

alkaline phosphatase elevations have been discussed elsewhere in this text.

Secondary Parathyroid Panel BUN, creatinine, urinalysis

Inclusion of these parameters in the parathyroid panel is explained above. Interpretation is covered in the urinary section.

Clinical Pathology of the Thyroid

The thyroid gland produces thyroxine, a hormone of importance to virtually all metabolizing cells. The specific mode of action of thyroxine is not completely understood; however, the hormone has profound effects on nearly all tissues. Two circulating forms of thyroid hormone are identified: tetraiodothyronine (T₄) and triiodothyronine (T₃). Circulating levels of T₄, T₃, free-T₄, and thyroid stimulating hormone (TSH) can be measured by immunoassay methods. These are special procedures not included in most standard chemistry profiles but absolutely essential to the diagnosis of thyroid disease.

Two forms of thyroid disease, hypothyroidism and hyperthyroidism, are described. Hypothyroidism occurs commonly in dogs and hyperthyroidism is an important disease of cats.

The clinical features of hypothyroidism include lethargy, obesity, mild anemia, infertility, and alopecia. There are no diagnostic serum chemistry alterations in hypothyroidism. Cholesterol is the only parameter that is fairly consistently elevated and this is the only test in the thyroid panel. It is emphasized that elevated serum cholesterol is not a specific change and may be seen with conditions such as chronic liver disease and nephrotic syndrome. Creatine kinase may also be significantly elevated in advanced cases of hypothyroidism but is not generally part of a large chemistry panel.

When hypercholesterolemia is seen in conjunction with signs suggestive of hypothyroidism, special tests for thyroid function are indicated. These special tests may include a baseline serum T₄, free-T₄, and TSH concentration. For a detailed discussion of the administration and interpretation of these and other thyroid related tests, the reader is referred elsewhere (*See Suggested Reading; 3,20,92*).

Hyperthyroidism in cats was first recognized in the late 1970s and has become an increasingly important syndrome in middle-aged and older animals. Clinically, the syndrome

is most commonly characterized by weight loss, polyphagia, vomiting and polydipsia/polyuria. Approximately 35% of all cases exhibit increased activity or restlessness but the occasional patient may appear depressed.

From a laboratory perspective, the most consistent abnormalities in feline hyperthyroidism include erythrocytosis, a stress leukogram, and elevations in liver enzyme activities (ALT, ALP) in the large chemistry profile. Obviously, these changes are non-specific and laboratory diagnosis resides primarily in the demonstration of high basal T₄ levels. Again, for a more detailed discussion of other thyroid function tests in potentially hyperthyroid cats, the reader is referred elsewhere (*See Suggested Reading; 95*).

Clinical Pathology of the Adrenal Gland

The adrenal gland produces 3 forms of steroid hormones—glucocorticoids, mineralocorticoids, and sex steroids. Only the glucocorticoids and mineralocorticoids are usually of clinical significance in dogs and cats.

Two general disease syndromes involving the adrenal gland are described, hyperadrenocorticism (Cushing's disease or syndrome) and hypoadrenocorticism (Addison's disease). In hyperadrenocorticism, the principal clinical syndrome and laboratory abnormalities are a reflection of increased circulating glucocorticoids; in hypoadrenocorticism, the principal alterations relate to a deficiency of the major circulating mineralocorticoid, aldosterone. The adrenal panel listed below cannot be used specifically to diagnose either hypo or hyperadrenocorticism; rather, these tests are used as supportive evidence for the suspicion of adrenal disease based upon characteristic clinical signs. Specific diagnosis of adrenal disease requires determination of resting serum cortisol levels, cortisol levels following

ACTH challenge, and cortisol levels following dexamethasone suppression. These are all special tests and are not covered in this text.

Primary Adrenal Panel ALP

Alkaline phosphatase (ALP) is discussed in Chapter 6 and will only be briefly considered here. It is well established that elevated circulating levels of glucocorticoids will induce the production of a specific alkaline phosphatase isoenzyme in dogs. Greater than 4-fold elevations of alkaline phosphatase are considered relatively specific for either cholestasis or glucocorticoid isoenzyme induction. Such elevation may be caused by either endogenous or administered glucocorticoids. When elevations in alkaline phosphatase are found in the absence of other signs of liver disease in dogs or in association with a stress leukogram and clinical signs of Cushing's disease (alopecia, pendulous abdomen, etc.), hyperadrenocorticism should be strongly suspected and cortisol determinations are warranted. It should be noted that glucocorticoid levels associated with typical stress leukograms are not sufficient to induce greater than 4-fold elevations in ALP. Glucocorticoid elevations in Cushing's disease are of sufficient magnitude and elevation to maintain a stress leukogram and induce isozyme production.

Sodium, potassium

In man, hyperadrenocorticism is often associated with hypernatremia and a hypokalemia. In dogs, mild changes of this nature have been demonstrated in about 50% of Cushing's dogs, but serum sodium and potassium are often within the normal range. However, in dogs with hypoadrenocorticism, serum electrolytes are often severely altered. The principal adrenal mineralocorticoid, aldosterone, causes the renal tubules to reabsorb sodium and excrete potassium. In the absence of aldosterone (hypoadrenocorticism), tubules excrete sodium while conserving potassium. Hyponatremia and hyperkalemia are therefore expected; often, sodium/potassium ratio may dip below 23:1. The sodium/potassium ratio is often recommended to diagnose Addison's disease. It is emphasized that hyponatremia must be present before the ratio can be validly used for this purpose. Electrolyte changes of this type are suggestive of Addison's disease and cortisol determination and ACTH

Primary Adrenal Panel

- Alkaline phosphatase (ALP)
- Sodium, potassium
- Blood urea nitrogen (BUN)
- Urinalysis
- Glucose

challenge tests are recommended. Such changes may be accompanied by peripheral lymphocytosis and eosinophilia. However, lymphocyte and eosinophil counts are often normal in these patients, in spite of severe disease.

BUN, urine specific gravity

Hyperadrenocorticism usually induces polydipsia and polyuria. The causes of polydipsia/polyuria may be multiple. Glucocorticoids have been shown to bind to antidiuretic hormone (ADH) receptors on renal tubular epithelium thereby blocking the water sparing effects of ADH, but increased glomerular filtration rate (GFR) and interference with ADH release have also been incriminated. Furthermore, if Cushing's disease is complicated by diabetes mellitus, a true osmotic diuresis may occur.

Hypoadrenocorticism (Addison's disease) also commonly affects renal tests. BUN and creatinine are both usually increased and urine specific gravity is often in the ambiguous to isosthenuric range. These results may lead to the misdiagnosis of renal failure, but in the true Addisonian, these changes are often reversible with appropriate therapy. The elevations in BUN and creatinine are primarily a reflection of dehydration while the decrease in concentrating capability reflects the hyponatremia, solute diuresis, and medullary washout. All of these changes are reversible with rehydration with appropriate fluids.

Glucose

Glucocorticoids induce hepatic gluconeogenesis that may lead to mild hyperglycemia. Elevations are usually mild enough that renal threshold (180 mg/dl) is not exceeded and glycosuria is not observed. Cushing's disease and diabetes mellitus may be seen together; if so, serum glucose levels of greater than 180 mg/dl may be observed. Hypoglycemia is seen in up to one third of Addison's disease cases; a moderate number of these may be associated with clinical signs of hypoglycemia (weakness, tremors, etc.).

Clinical Pathology of the Endocrine Pancreas

The islets of the pancreas produce several hormones of major metabolic importance, including insulin and glucagon. From a clinical standpoint, diseases of the endocrine pancreas are related almost exclusively to the presence of excessive or reduced amounts of functional insulin.

Insulin is produced by the beta cells of the pancreatic islets. The hormone is necessary for the movement of glucose, potassium, and some amino acids from the bloodstream into tissue cells. Insulin also enhances phosphorus entry into cells. The hormone exerts an anabolic effect on most target cells, stimulating glycogenesis, lipogenesis, protein synthesis, and nucleic acid synthesis. Somatic cells differ in their sensitivity to insulin; for example, liver, muscle, and adipose tissue are particularly insulin responsive, whereas neurons of the brain do not require insulin for glucose uptake.

Both hypoinsulinism (diabetes mellitus) and hyperinsulinism are relatively common entities in companion animals. Diabetes mellitus may be caused by destruction of islets, secretion of nonfunctional insulin, interference with or down regulation of membrane insulin receptors, or the presence of anti-insulin antibodies in the blood. Hyperinsulinism is almost always the result of functional neoplasia of the beta cells, either adenoma or adenocarcinoma.

Both hypoinsulinism and hyperinsulinism will have profound effects on metabolism in general and on carbohydrate (glucose) metabolism in particular. The endocrine pancreatic panel listed below was developed on the basis of the potential abnormalities that may occur. Insulin determi-

Endocrine Pancreatic Disease Panel

- Primary endocrine pancreatic panel
 - Glucose
 - Urinalysis
- Secondary endocrine pancreatic panel
 - Alanine aminotransferase (ALT)
 - Alkaline phosphatase (ALP)
 - Amylase
 - Blood urea nitrogen (BUN)
 - Triglycerides
 - Electrolytes
 - Potassium
 - Phosphorus
 - Acid-base
 - TCO₂
 - Anion gap

nation by radioimmunoassay is also available as a special procedure from some laboratories.

Primary Endocrine Pancreatic Panel

Glucose

The most important common laboratory test in the diagnosis of either hypo- or hyperinsulinism is fasting blood glucose. In most cases, fasting glucose determinations will be fairly diagnostic; additional though less common special tests, such as glucose tolerance tests or serum insulin concentration, may also be required. Diabetes mellitus (hypoinsulinism) is usually associated with a persistent hyperglycemia. In advanced cases, glucose levels are often in excess of the renal threshold with a resultant glycosuria. Hyperinsulinism associated with beta cell tumors is usually characterized by low-normal to reduced blood glucose levels.

Urinalysis (urine glucose, ketones)

As stated above, glycosuria is present in cases of diabetes mellitus where the renal threshold for glucose is exceeded. Urine glucose may be easily detected with semi-quantitative reagent dip strips. Glycosuria without hyperglycemia is not diagnostic for diabetes. In cats, glycosuria is seen with hematuria and stress. Primary renal glycosuria due to a tubular absorptive defect and associated with normal blood glucose has been described in dogs.

Ketones in the urine signify increased fat metabolism and are seen only in advanced cases of diabetes mellitus where the increased utilization of fat for energy occurs due to the unavailability of glucose for cellular metabolism and the resultant mobilization of fat from body stores.

With rare exception, the combination of ketonuria and glycosuria with hyperglycemia is diagnostic for diabetes mellitus. Because ketones act as organic acids, animals with ketones in the urine are usually in a state of diabetic ketoacidosis.

The effect of diabetes on urine specific gravity is unpredictable. Glucose in the urine causes osmotic diuresis. Diuresis should result in dilute urine. However, glucose affects specific gravity, and in cases with profound glycosuria specific gravity may be concentrated (somewhat greater than 1.030) even if the animal is maintained in a balanced state of hydration.

Secondary Endocrine Pancreatic Panel

ALT, ALP

With the increased mobilization of fat from body stores, one of the principal lesions of diabetes mellitus is diffuse hepatic fatty change. This syndrome causes potentially widespread hepatocellular injury and secondary cholestasis from hepatocellular swelling. It is emphasized that despite marked abnormalities in liver enzymes, hepatic alterations may be totally reversible with insulin therapy.

Amylase, BUN

Well over 30% to 40% of all cases of diabetes in dogs are associated with pancreatitis and, in fact, acute pancreatitis is often accompanied by transient hyperglycemia. For this reason, primary pancreatic parameters should be considered in the evaluation of all potential cases of diabetes mellitus.

Triglycerides

Fat mobilization in diabetes mellitus means a potential increase in circulating triglycerides. Cholesterol may also elevate.

Electrolytes, acid-base

Patients with diabetes mellitus may present with severe electrolyte acid-base disorders. Failure to recognize key patterns and institute appropriate restorative efforts prior to insulin therapy may lead to life threatening crisis.

With hypoinsulinism there is a decreased ability to move both potassium and phosphorus from the blood into the intracellular compartment. Furthermore, with developing acidemia (secondary to ketoacidosis) there is a transcellular shift of potassium from cells to the blood in exchange for hydrogen ions. These mechanisms lead to potassium and phosphorus levels that are high-normal to increased. However, osmotic diuresis and polyuria associated with hyperglycemia cause these (and other) serum electrolytes to be wasted in the urine. The net effect over time is potentially severe total body electrolyte depletion that is easily masked by hemoconcentration and acidemia (for potassium). Total body depletion may be present even when serum electrolyte levels are elevated.

Thus, low-normal to decreased levels of potassium or phosphorus in a diabetic animal, especially when accompanied by acidemia, are critical findings. Administration of

insulin will drive both electrolytes into the intracellular compartments, which may precipitate life-threatening hypokalemia, and/or hypophosphatemia related to neuromuscular and cardiovascular dysfunction or hemolytic anemia due to ATP depletion, respectively. Current veterinary medical texts should be consulted for therapeutic strategies.

Clinical Pathology of the Pituitary Gland

It is emphasized that the diagnosis of many of the endocrine disorders is much like the diagnosis of anemia; many underlying mechanisms can cause the same clinical syndrome. For example, hyperadrenocorticism may be caused by a primary adrenal adenoma, idiopathic adrenal

hyperplasia, or an ACTH-secreting pituitary tumor. Similarly, hypothyroidism may result from primary thyroid injury or secondary to decreased pituitary TSH. Identification of the specific underlying mechanism is often difficult and requires either special tests or biopsy. Obviously the pituitary gland occupies a central position in the endocrine system; however, since the majority of cases with pituitary involvement present as endocrinopathies involving other glands, a specific pituitary panel is not listed. Only diabetes insipidus presents as an uncomplicated pituitary disease phenomenon; the major abnormality is constantly dilute urine and special tests (such as ADH challenge) are required for confirmation.

Chapter 9: Case Studies

Case 1

SIGNALMENT: Nine-year-old female Weimaraner

HISTORY: Weight loss and anorexia of several weeks' duration. Increasing lethargy.

P.E.: T = 102°F P = 100 R = panting

Physical examination revealed a thin, moderately dehydrated dog with no other obvious abnormalities.

INITIAL ASSESSMENT: Signs and physical examination are fairly nonspecific. Wasting diseases are severe processes that can originate in many organ systems, including liver, kidney, and GI. A full large chemistry profile is warranted.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* The HCT of 36% establishes a mild anemia. Normal indices (MCV 65 fl, MCHC 33 g/dl) suggest that the anemia is non-regenerative.

TP: *Hyperproteinemia.* Hyperproteinemia is most commonly the result of dehydration, which was clinically evident in this case. Hyperglobulinemia due to chronic inflammation cannot be totally ruled out without further evaluation. With dehydration being the most likely possibility, the anemia described above is probably more severe than the HCT (36%) indicates.

WBC: No abnormalities

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hyperproteinemia, hyperalbuminemia. These alterations are most likely the result of dehydration as described above. There is no evidence of primary liver disease.

Urinary panel (BUN, creatinine, specific gravity, casts)

Azotemia. Elevated BUN and creatinine establish the presence of azotemia but the origin is somewhat unclear. Dehydration and prerenal azotemia could be totally responsible but other primary renal parameters must be evaluated.

Isosthenuria, granular casts. Isosthenuria in the face of clinical dehydration establishes loss of at least two thirds of renal tubular concentrating function. A contribution of primary renal failure to the azotemia is therefore present. Granular casts are consistent with renal tubular disease.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

No evidence of primary gastroenteric disease.

Additional findings:

Hypercalcemia, normophosphatemia. The changes are unexpected and are among the most striking in the large chemistry profile.

Hypercalcemia and normophosphatemia are not typical of primary renal failure in dogs; rather, hyperphosphatemia and normocal-

LABORATORY DATA:

Hematology

* HCT (%)	36	LN	WBC (/µl)	13,200
* Hb (g/dl)	11.8	L	Neutrophils (/µl)	10,000
* RBC (× 10 ⁶ /µl)	5.5	LN	Lymphocytes (/µl)	2,100
* TP (g/dl)	8.20	H	Monocytes (/µl)	800
Platelets	Adequate		Eosinophils (/µl)	300

Comments: Normal on blood film morphology.

Chemistry

* BUN (mg/dl)	50	H	Lipase (IU/L)	900
* Creatinine (mg/dl)	3.2	H	Sodium (mmol/L)	148
Glucose (mg/dl)	100		Potassium (mmol/L)	4.2
T. bilirubin (mg/dl)	0.2		Chloride (mmol/L)	117
* TP (g/dl)	8.0	H	* Calcium (mg/dl)	17.0
* Albumin (g/dl)	4.2	H	Phosphorus (mg/dl)	4.0
ALT (IU/L)	30		Cholesterol (mg/dl)	200
ALP (IU/L)	48		Triglycerides (mg/dl)	42
GGT (IU/L)	8		TCO ₂ (mmol/L)	20
Amylase (IU/L)	600		Anion gap (mmol/L)	15.2

Urinalysis

Color	light yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.012	WBC (/HPF)	0
pH	7.0	RBC (/HPF)	0
Protein	neg.	Epithelial (/HPF)	occasional
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	3-5 granular
		Crystals	amorphous debris

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

emia are usually expected. Hypercalcemia of the degree seen in this patient is almost always the result of primary hyperparathyroidism or pseudohyperparathyroidism and is accompanied by hypophosphatemia. Renal failure can occur secondarily to hypercalcemia as a result of the deposition of calcium within the kidney (hypercalcemic nephropathy). In renal failure, phosphate is retained and the phosphate levels may then return to normal or elevate. This was the suspected pathogenesis in this case.

Summary and outcome:

Radiology revealed diffuse thickening of the intestinal wall and a large abdominal mass. Laparotomy was performed and lymphomatous involvement of gut, liver, and mesenteric nodes was established histologically. Kidney biopsy revealed diffuse mineralization and tubular necrosis. The diagnosis was pseudohyperparathyroidism.

Case 2

SIGNALMENT: Six-year-old spayed female

Abyssinian cat

HISTORY: Polyuria and polydipsia of several weeks' duration. Voracious appetite but progressive weight loss.

P.E.: T = 102.5°F P = 120 R = panting

Physical examination reveals an emaciated, fractious cat.

INITIAL ASSESSMENT: Polyuria and polydipsia are nonspecific findings observed with a variety of diseases of both endocrine and non-endocrine origin. The additional finding of voracious appetite with weight loss makes diabetes mellitus the most likely possibility. A large chemistry profile is warranted.

LABORATORY DATA:

Hematology

* HCT (%)	50	H	WBC (/μl)	11,700
* Hb (g/dl)	16.2	H	Neutrophils (/μl)	8,400
* RBC (× 10 ⁶ /μl)	10.0	HN	Lymphocytes (/μl)	2,000
* TP (g/dl)	7.8	HN	Monocytes (/μl)	900
Platelets	Adequate		Eosinophils (/μl)	400

Chemistry

* BUN (mg/dl)	60	H	Lipase (IU/L)	525	
* Creatinine (mg/dl)	2.4	H	Sodium (mmol/L)	155	
* Glucose (mg/dl)	400	H	* Potassium (mmol/L)	7.2	H
T. bilirubin (mg/dl)	0.4		Chloride (mmol/L)	127	
TP (g/dl)	7.0		Calcium (mg/dl)	11.0	
Albumin (g/dl)	3.6		Phosphorus (mg/dl)	3.8	
* ALT (IU/L)	700	H	Cholesterol (mg/dl)	80	
* ALP (IU/L)	225	H	* Triglycerides (mg/dl)	260	H
* GGT (IU/L)	12	H	* TCO ₂ (mmol/L)	8.2	L
Amylase (IU/L)	680		* Anion gap (mmol/L)	27	H

Urinalysis

Color	yellow	Occ. blood	2+
Turbidity	cloudy	Urobilinogen	1.0
Sp. gr.	1.040	WBC (/HPF)	TNTC
pH	8.0	RBC (/HPF)	50
Protein	3+	Epithelial (/HPF)	occasional
Glucose	3+	Sperm	neg.
Ketones	3+	Bacteria	3+
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	amorphous crystalline material

TNTC—too numerous to count.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Relative polycythemia.* The HCT is mildly elevated. Indices indicate normochromasia and normocytosis. With clinical signs and elevated TP, alterations are most likely the result of dehydration.

TP: *Hyperproteinemia.* Most likely secondary to dehydration.

WBC: No abnormalities.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hepatocellular injury. A 6-fold ALT elevation implies a diffuse hepatic lesion but indicates nothing about the type of lesion. Necrosis as well as reversible diffuse hepatocellular degeneration (such as fatty change) must be considered.

Cholestasis. A 2-fold ALP coupled with a slight elevation in GGT is fairly strong evidence of cholestasis in the cat. Again, the type of lesion is not indicated; even hepatocellular swelling may block bile flow resulting in such an elevation.

Urinary panel (BUN, creatinine, specific gravity, protein, glucose, ketones, occult blood, WBC, RBC, bacteria)

Prerenal azotemia. A moderately elevated BUN and creatinine in the face of urine concentration (specific gravity greater than 1.035) implies functioning kidneys with azotemia resulting from dehydration. This interpretation is consistent with that of the HCT and TP.

Urinary or genital tract infection. Elevated urine pH, protein, WBCs, RBCs, and bacteria all suggest urinary tract infection but do not localize the lesion. The absence of an inflammatory leukogram is supportive evidence for cystitis without renal involvement. Urogenital tract infection does not explain the presence of glucose and ketones in the urine. On the contrary, glucose in the urine can be a cause of urinary tract infection.

Pancreatic panel (BUN, amylase, lipase)

No evidence of primary exocrine pancreatic disease.

Endocrine Pancreatic panel (glucose, urine glucose, ketones)

Hyperglycemia. A marked fasting hyperglycemia is highly suggestive of diabetes mellitus. In the cat, this needs to be reproduced (to eliminate the possibility of stress hyperglycemia).

Glycosuria and ketonuria. Both findings support the suggestion of diabetes mellitus. Ketones in the urine indicate increased fat metabolism, a common finding in advanced diabetes where the animal has begun to utilize fat stores for energy. Ketonuria in diabetes generally implies that the patient is in a state of ketoacidosis.

Additional findings:

Hyperkalemia. The hyperkalemia is explained as a reflection of the diabetic ketoacidosis. Hyperkalemia results from at least two causes; the presence of acidosis and the fact that

insulin is involved in the transport of potassium from the blood into cells.

Hypertriglyceridemia. Elevated triglycerides are expected in patients that have converted to fat metabolism for energy. Metabolic acidosis. Low bicarbonate, elevated anion gap, and normal chloride relative to sodium are consistent with titration acidosis. In this case, the unmeasured anions are ketoacids.

Summary and outcome:

On the basis of laboratory data and clinical signs, diabetic ketoacidosis was diagnosed as the primary disease with associated secondary diffuse hepatocellular degeneration (fatty change) and bacterial cystitis. The animal was treated with insulin and ALT levels had returned to the normal range 1 week after stabilization.

Case 3

SIGNALMENT: Five-year-old female Poodle

HISTORY: Owner complains of gradual hair loss over the past year. No other presenting problems.

P.E.: T = 101.5°F P = 110 R = panting

Generalized alopecia.

INITIAL ASSESSMENT: Generalized acquired alopecia is a nonspecific sign which could be associated with a variety of disease entities including Cushing's disease, hypothyroidism, and even chronic liver disease. A large chemistry profile is warranted to assess general health status.

LABORATORY DATA:

Hematology

HCT (%)	42	* WBC (/μl)	17,900	H
Hb (g/dl)	13.6	* Neutrophils (/μl)	16,200	H
RBC (× 10 ⁶ /μl)	6.0	* Lymphocytes (/μl)	800	L
TP (g/dl)	6.8	Monocytes (/μl)	900	
Platelets	Adequate			

Chemistry

BUN (mg/dl)	10	Lipase (IU/L)	900	
Creatinine (mg/dl)	0.6	Sodium (mmol/L)	146	
* Glucose (mg/dl)	140	H	Potassium (mmol/L)	3.6
T. bilirubin (mg/dl)	0.2	Chloride (mmol/L)	115	
TP (g/dl)	6.2	Calcium (mg/dl)	10.5	
Albumin (g/dl)	3.0	Phosphorus (mg/dl)	4.2	
* ALT (IU/L)	120	H	Cholesterol (mg/dl)	135
* ALP (IU/L)	600	H	Triglycerides (mg/dl)	60
GGT (IU/L)	14	TCO ₂ (mmol/L)	19.3	
Amylase (IU/L)	1,000	Anion gap (mmol/L)	15.3	

Urinalysis

Color	pale yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.015	WBC (/HPF)	1-3
pH	6.8	RBC (/HPF)	5
Protein	neg.	Epithelial (/HPF)	occasional
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	triple phosphate and amorphous phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: No abnormalities.

WBC: *Stress leukogram.* There is a marginal leukocytosis with a mature neutrophilia, lymphopenia, and eosinopenia. This is a classic stress (steroid-induced) leukogram.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

Hepatocellular injury. Mild hepatocellular injury is indicated by the 2-fold elevation in ALT. Elevations of this degree can be a reflection of hepatocellular injury secondary to primary disease in another organ system. *Possible cholestasis.* The 4-fold elevation in alkaline phosphatase is the result of either cholestasis or production of the steroid-induced isoenzyme of alkaline phosphatase. The obvious stress leukogram makes it impossible to positively differentiate between the two conditions without special tests (isoenzyme separation). However, the lack of other evidence of cholestasis (normal GGT, urine bilirubin, and serum bilirubin) suggests that the increased alkaline phosphatase is most likely a steroid-induced change.

Adrenal panel (BUN, glucose, ALP, sodium, potassium, specific gravity)

Elevated alkaline phosphatase. The evaluation and interpretation of the alkaline phosphatase value are discussed above. Obviously, hyperadrenocorticism would explain both the stress leukogram and increased alkaline phosphatase as well as the clinical presentation. Careful consideration of the secondary adrenal panel (*see Additional findings*) is warranted.

Marginal hyperglycemia. A marginal hyperglycemia is consistent with hyperadrenocorticism and lends support to the theory that all changes in this patient are steroid-induced.

Isosthenuria. Isosthenuria in the face of a normal BUN may be normal but would also be seen with diuresis. Polyuria is a feature of many diseases, including hyperadrenocorticism.

Thyroid panel (cholesterol)

No evidence of thyroid disease.

Summary and outcome:

The laboratory data and clinical presentation were considered to be good presumptive evidence of hyperadrenocorti-

cism (Cushing's disease). Serum cortisol determination revealed an elevated resting cortisol level of 10 µg/dl. This data confirmed the diagnosis of hyperadrenocorticism.

Case 4

SIGNALMENT: Five-year-old female Poodle

HISTORY: Owner complains of gradual hair loss over the past year. No other presenting problems.

P.E.: T = 102°F P = 90 R = 24

Generalized alopecia.

INITIAL ASSESSMENT: Generalized alopecia is a nonspecific sign that could be associated with a variety of disease entities including severe endocrinopathies as well as non-endocrine disorders. A large chemistry profile is warranted to assess general health status.

LABORATORY DATA:

Hematology

* HCT (%)	32	L	WBC (/μl)	9,100
* Hb (g/dl)	10.4	L	Neutrophils (/μl)	6,300
* RBC (× 10 ⁶ /μl)	4.8	L	Lymphocytes (/μl)	2,100
TP (g/dl)	7.2		Monocytes (/μl)	500
Platelets	Adequate		Eosinophils (/μl)	200

Blood film morphology: numerous target cells.

Chemistry

BUN (mg/dl)	12		Lipase (IU/L)	820
Creatinine (mg/dl)	0.6		Sodium (mmol/L)	144
Glucose (mg/dl)	100		Potassium (mmol/L)	3.8
T. bilirubin (mg/dl)	0.4		Chloride (mmol/L)	115
TP (g/dl)	6.8		Calcium (mg/dl)	10.2
Albumin (g/dl)	3.2		Phosphorus (mg/dl)	3.6
ALT (IU/L)	40		* Cholesterol (mg/dl)	620 H
ALP (IU/L)	52		Triglycerides (mg/dl)	60
GGT (IU/L)	8		TCO ₂ (mmol/L)	18.0
Amylase (IU/L)	660		Anion gap (mmol/L)	14.8

Urinalysis

Color	colorless	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.020	WBC (/HPF)	neg.
pH	7.0	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	occasional
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	triple phosphate

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

Comments on blood film morphology: Numerous target cells seen.

RBC: *Non-regenerative anemia.* A mild anemia is indicated by the HCT of 32%. Red cell indices (MCV 67 fl, MCHC 33 g/dl) indicate the anemia is normocytic and normochromic and most likely non-regenerative. Target cells are a nonspecific feature of many chronic diseases.

TP: No abnormalities.

WBC: No abnormalities.

Platelets: No abnormalities.

Chemistry and Urinalysis

Adrenal panel (BUN, glucose, ALP, sodium, potassium, urine specific gravity)

No abnormalities noted.

Hepatic panel (TP, albumin, ALT, ALP, GGT)

No abnormalities noted.

Urinary panel (BUN, creatinine, specific gravity)

No abnormalities noted.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

No abnormalities noted.

Thyroid panel (cholesterol)

Hypercholesterolemia. There is a marked hypercholesterolemia. It has been proposed that cholesterol levels of greater than 600 mg/dl are highly suggestive of hypothyroidism in the dog. Further, most other common causes for hypercholesterolemia (eg, pancreatitis, the nephrotic syndrome, cholestatic liver disease) can be ruled out.

Summary and outcome:

Laboratory abnormalities are limited and nonspecific. However, clinical signs of generalized alopecia, in conjunction with a non-regenerative anemia and hypercholesterolemia are highly suggestive of hypothyroidism. Additional tests (T₃ and T₄ determination and TSH response test) are indicated and were done in this case. Resting T₄ was

1.0 μg/dl (low-normal), T₄ response to TSH challenge was 1.2 μg/dl; normal response is a 2-fold increase, indicating hypothyroidism in the patient.

Case 5

SIGNALMENT: Eight-year-old male German Shepherd

HISTORY: Intermittent diarrhea. The owner has noticed increasing unsteadiness in the dog's gait in the last week.

P.E.: T = 101.5°F P = 98 R = 40

On examination the dog exhibited signs of muscular weakness and fatigue.

INITIAL ASSESSMENT: Chronic diarrhea is a nonspecific sign that may be evoked by liver, kidney, or enteric disease. Weakness is also a nonspecific sign. A full laboratory work-up is warranted.

LABORATORY DATA:

Hematology

HCT (%)	42	WBC (/μl)	16,800
Hb (g/dl)	14.2	Neutrophils (/μl)	11,000
RBC (× 10 ⁶ /μl)	6.0	Lymphocytes (/μl)	3,000
TP (g/dl)	7.0	Monocytes (/μl)	300
Platelets	Adequate	Eosinophils (/μl)	2,500

Blood film morphology: normal.

Chemistry

BUN (mg/dl)	14	Lipase (IU/L)	630
Creatinine (mg/dl)	0.8	* Sodium (mmol/L)	132 L
Glucose (mg/dl)	100	* Potassium (mmol/L)	6.8 H
T. bilirubin (mg/dl)	0.4	Chloride (mmol/L)	110
TP (g/dl)	6.6	Calcium (mg/dl)	11.0
Albumin (g/dl)	3.0	Phosphorus (mg/dl)	4.2
ALT (IU/L)	30	Cholesterol (mg/dl)	120
ALP (IU/L)	60	Triglycerides (mg/dl)	80
GGT (IU/L)	14	TCO ₂ (mmol/L)	15.0
Amylase (IU/L)	420	Anion gap (mmol/L)	13.8

Urinalysis

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.025	WBC (/HPF)	0-2
pH	7.0	RBC (/HPF)	0-2
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities.

TP: No abnormalities.

WBC: *Eosinophilia*. The only significant alteration in the hemogram is a marked eosinophilia. Eosinophilias are non-specific and most often are associated with systemic allergic reactions. Eosinophilia and lymphocytosis may also be seen with Addison's disease, but these are inconsistent findings.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel (TP, albumin, ALT, ALP, GGT)

No abnormalities seen.

Urinary panel (BUN, creatinine, specific gravity)

No abnormalities seen.

Gastrointestinal panel (TP, albumin, sodium, potassium, chloride)

Hyponatremia and hyperkalemia. These are unusual changes with diarrhea, but could be seen in extremely severe cases with loss of abundant sodium bicarbonate and the development of secretion acidosis. In this case, there is no acidosis or decreased bicarbonate. Additionally, with secretion acidosis, some degree of hyperchloremia is also expected; in this case, chloride is normal. A better explanation of the data is primary adrenal insufficiency. Sodium and potassium determinations also comprise the adrenal panel.

With hyponatremia and hyperkalemia, a ratio of less than 23:1 is highly suggestive of hypoadrenocorticism. The sodium potassium ratio is 19:1. Eosinophilia is also supportive evidence.

Summary and outcome:

Serum cortisol and ACTH response were performed to confirm the tentative diagnosis of Addison's disease. Resting cortisol levels were subnormal and there was little response to ACTH challenge; these are typical findings in hypoadrenocorticism.

Chapter 10: Case Studies

Case 1

SIGNALMENT: Ten-year-old spayed female DSH cat

HISTORY: Presented with a history of inappetence, polyuria/polydipsia (PU/PD), and chronic weight loss.

P.E.: Thin, poor hair coat, listless.

INITIAL ASSESSMENT: Signs are nonspecific but suggest relatively chronic disease. The history of PU/PD is also nonspecific but raises concerns about renal, endocrinologic, or hepatic disease.

LABORATORY DATA:

Hematology

* HCT (%)	23.8	L	WBC (/μl)	15,300
Hb (g/dl)	8.4		* Neutrophils (/μl)	14,080
RBC (× 10 ⁶ /μl)	5.8		* Lymphocytes (/μl)	770
TP (g/dl)	6.8		Monocytes (/μl)	150
Platelets	Adequate		Eosinophils (/μl)	310

Blood film morphology: microcytes noted.

Chemistry

BUN (mg/dl)	15		* Lipase (IU/L)	4,931	H
Creatinine (mg/dl)	1.3		* Sodium (mmol/L)	141	L
* Glucose (mg/dl)	271	H	* Potassium (mmol/L)	2.5	L
* T. bilirubin (mg/dl)	5.6	H	* Chloride (mmol/L)	105	L
TP (g/dl)	6.2		Calcium (mg/dl)	9.8	
Albumin (g/dl)	3.2		Phosphorus (mg/dl)	2.9	
* ALT (IU/L)	472	H	Cholesterol (mg/dl)	246	
* ALP (IU/L)	1066	H	Triglycerides (mg/dl)	46	
* GGT (IU/L)	13	H	TCO ₂ (mmol/L)	18	
Amylase (IU/L)	1,113		Anion gap (mmol/L)	20	

Urinalysis

Color	orange	Occ. blood	1+
Turbidity	hazy	Urobilinogen	0.1
Sp. gr.	1.022	WBC (/HPF)	5-9
pH	7.0	RBC (/HPF)	1-2
Protein	2+	Epithelial (/HPF)	5-9
Glucose	3+	Bacteria	1+
Ketones	mod.	Casts (/LPF)	1-2 granular
Bilirubin	3+	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* There is a mild normocytic normochromic anemia with the presence of some microcytes. The decreased hematocrit in the face of hemoglobin and total RBC within reference limits is explained by the presence of microcytes and a low-normal MCV. Although a normal number of RBCs are present, the tendency towards small size results in a low RBC mass (hematocrit).

TP: No abnormalities.

WBC: *Stress leukogram.* There is a normal leukocyte count characterized by a mild mature neutrophilia with lymphopenia. This is most consistent with a stress (glucocorticoid-induced) leukogram.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel

Possible diuresis. BUN, creatinine, and urine specific gravity are within normal limits. The urine specific gravity of 1.022 in a cat is, however, relatively low, and with a history of PU/PD, suggests diuresis. If the impact of glycosuria on specific gravity is considered, the urine specific gravity may otherwise be less than 1.020.

Urinary tract infection. The urinalysis reveals a neutral pH (see acid-base), 2+ proteinuria associated with the presence of 1+ occult blood, mild pyuria, bacteriuria, and granular casts. These changes indicate a urinary tract infection with associated mild hematuria, proteinuria, and renal tubular degeneration.

Diabetic ketoacidosis. The concurrent presence of glucosuria and ketonuria indicates diabetes mellitus with ketoacidosis (see *Endocrine pancreatic panel*). The 3+ bilirubinuria is profound in a cat and is strongly suggestive of cholestasis (see *Hepatic panel*).

Endocrine pancreatic panel

Diabetes mellitus. The concurrent presence of hyperglycemia, glucosuria, and ketonuria is diagnostic for diabetes mellitus (ie, lipids are being metabolized for energy in the face of hyperglycemia). In dogs, diabetes mellitus often occurs secondarily to pancreatitis. In cats, pancreatitis is far less common. However, in this cat, there is marked hyperlipasemia

in the face of normal BUN suggesting that pancreatitis is indeed present.

Hepatic panel

Hepatocellular injury. The moderate elevation of ALT is suggestive of diffuse hepatocellular injury.

Cholestasis. The marked elevation in ALP, the slight elevation in GGT, the marked bilirubinuria, and the marked bilirubinemia collectively suggest cholestasis. In cats, a relatively large increase in ALP compared to GGT, as is seen here, suggests that hepatic lipidosis should be strongly considered.

Electrolytes and acid-base balance

Osmotic diuresis. Decreased sodium, potassium, and chloride in this patient are consistent with osmotic diuresis. The hypokalemia in this unregulated diabetic is a potentially

critical finding since insulin administration will drive potassium intracellularly and may exacerbate the hypokalemia into a life-threatening crisis. The low-normal phosphorus is also of concern as phosphorus is also driven intracellularly by insulin. A resultant hypophosphatemia could precipitate a hemolytic crisis.

Summary and outcome:

Data clearly indicate multisystem involvement. Diabetes mellitus is confirmed, as is hepatic disease, possibly due to hepatic lipidosis. Pancreatitis is suspected. There is evidence of urinary tract infection, probably secondary to the diabetes and glucosuria. General electrolyte depletion due to osmotic diuresis is of concern because of the potential exacerbation of these disturbances by insulin therapy. Hematologic findings indicate superimposed stress and mild anemia.

Case 2

SIGNALMENT: One-year-old male Beagle

HISTORY: Presented with a history of vomiting and anuria for 24 hours.

P.E.: Dog is listless and depressed with some evidence of abdominal discomfort on palpation.

INITIAL ASSESSMENT: Emesis and abdominal discomfort suggest involvement of liver, urinary tract, pancreas, or GI. Anuria suggests that urinary tract obstruction/rupture is at the top of the differential list.

LABORATORY DATA:

Hematology

* HCT (%)	56.2	H	* WBC (/μl)	40,000	H
* Hb (g/dl)	18.4	H	Bands (/μl)	400	
* RBC (× 10 ⁶ /μl)	8.7	H	* Neutrophils (/μl)	35,200	H
* TP (g/dl)	9.9	H	* Lymphocytes (/μl)	800	L
Platelets	Adequate		* Monocytes (/μl)	3,600	H

Chemistry

* BUN (mg/dl)	172	H	Lipase (IU/L)	not available	
* Creatinine (mg/dl)	6.7	H	* Sodium (mmol/L)	105	L
Glucose (mg/dl)	106		* Potassium (mmol/L)	5.3	H
T. bilirubin (mg/dl)	0.4		* Chloride (mmol/L)	56	L
* TP (g/dl)	7.8	H	Calcium (mg/dl)	9.8	
* Albumin (g/dl)	4.3	H	* Phosphorus (mg/dl)	19.9	H
ALT (IU/L)	19		Cholesterol (mg/dl)	271	
* ALP (IU/L)	213	H	Triglycerides (mg/dl)	not available	
GGT (IU/L)	13		* TCO ₂ (mmol/L)	31	H
* Amylase (IU/L)	4,151	H	* Anion gap (mmol/L)	23	H

Urinalysis

Not available

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Hemoconcentration.* HCT, Hb, and total RBC count are elevated, suggesting hemoconcentration.

TP: *Hyperproteinemia.* This is consistent with dehydration.

WBC: *Inflammatory leukogram.* There is leukocytosis characterized by neutrophilia and monocytosis. These changes are consistent with inflammation. The number of bands relative to total neutrophil numbers is too low to be considered a left shift.

Stress leukogram. The lymphopenia is consistent with stress.

Platelets: No abnormalities.

Chemistry and Urinalysis

Urinary panel

Azotemia. BUN and creatinine are both markedly elevated. Given the history of anuria, the most likely cause of azotemia is postrenal. A renal contribution cannot be ruled out.

Hyponatremia, hypochloridemia. Sodium and chloride levels are extremely low, suggesting loss or dilution in an expanded extracellular compartment (third space disease). Again, given the clinical presentation and history, the possibility of urinary tract obstruction, postrenal azotemia, and possible ruptured bladder with developing uroperitoneum seem likely. Chloride is significantly depressed relative to sodium suggesting the possibility of loss or sequestration of HCl (vomiting) and alkalosis.

Hyperkalemia. The high potassium level suggests tissue necrosis and/or acidosis. Given the other electrolyte abnormalities identified above, this animal likely has a mixed metabolic alkalosis/acidosis. Electrolytes, TCO₂, and

anion gap must be considered collectively (*see below*). It should also be noted that the low sodium/high potassium values lead to a Na/K ratio of approximately 19.8:1; however, clinically, this animal does not have typical features of Addison's disease.

Hyperphosphatemia. This follows the BUN and creatinine levels and is a reflection of decreased renal clearance.

Hepatic panel

Elevated alkaline phosphatase. There is a less than 2-fold increase in alkaline phosphatase, which is nonspecific and probably related to stress.

Acid-base balance

Mixed metabolic alkalosis/acidosis. TCO₂ is elevated, confirming the suspicion of metabolic alkalosis. This is supported by the disparity of chloride to sodium mentioned above. Anion gap is also elevated, which confirms metabolic acidosis. The metabolic acidosis is titrational, resulting from increased circulating organic acids of renal origin.

Additional findings:

Hyperamylasemia. There is a 4-fold elevation in amylase,

which is ambiguous in light of the azotemia.

Summary and outcome:

Considering laboratory data collectively, the best interpretation is primary urinary tract obstruction or rupture. Rupture is strongly suspected because of the inflammatory leukogram, which would be consistent with a developing peritonitis in association with uroperitoneum. Radiographs were negative for urinary calculi; exploratory laparotomy confirmed bladder rupture and the dog was euthanized.

Case 3

SIGNALMENT: Four-year-old neutered DSH cat

HISTORY: Owner noticed decreased appetite and “yellow” appearance.

P.E.: The cat is icteric and thin and has a poor hair coat.

INITIAL ASSESSMENT: Icterus suggests that 2 organ systems, hematopoietic and hepatic, are primarily involved. Icterus can also result secondarily from pancreatic and GI disorders.

LABORATORY DATA:

Hematology

HCT (%)	42.4	* WBC (/μl)	19,300	H
Hb (g/dl)	14.3	* Neutrophils (/μl)	14,860	H
RBC (× 10 ⁶ /μl)	8.32	Lymphocytes (/μl)	3,090	
* TP (g/dl)	8.3	* Monocytes (/μl)	1,160	H
Platelets	Adequate	Eosinophils (/μl)	190	

Chemistry

BUN (mg/dl)	18	Lipase (IU/L)	728	
Creatinine (mg/dl)	1.5	Sodium (mmol/L)	153	
Glucose (mg/dl)	100	Potassium (mmol/L)	4.3	
* T. bilirubin (mg/dl)	7.7	Chloride (mmol/L)	116	H
* Conjugated bilirubin (mg/dl)	7.2	Calcium (mg/dl)	9.9	H
* TP (g/dl)	7.8	Phosphorus (mg/dl)	5.9	H
Albumin (g/dl)	3.5	Cholesterol (mg/dl)	194	
* ALT (IU/L)	616	Triglycerides (mg/dl)	42	H
* ALP (IU/L)	356	TCO ₂ (mmol/L)	26	H
* GGT (IU/L)	65	Anion gap (mmol/L)	16	H
* Amylase (IU/L)	1,605			H

Urinalysis (cystocentesis)

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	0.1
Sp. gr.	1.010	WBC (/HPF)	neg.
pH	7.2	RBC (/HPF)	neg.
Protein	neg.	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	3+	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: No abnormalities. No evidence of a hemolytic cause of the icterus.

TP: *Hyperproteinemia.* Elevated plasma protein is a reflection of either dehydration or hypergammaglobulinemia. In this case, given the high-normal RBC mass and the inflammatory leukogram, both may be contributing.

Evaluation of protein pattern on serum chemistry is needed for further evaluation.

WBC: *Inflammation.* There is a leukocytosis characterized by a neutrophilia and monocytosis. These findings are consistent with inflammation.

Platelets: No abnormalities.

Chemistry and Urinalysis

Hepatic panel

Hepatocellular injury. A 5- to 6-fold increase in ALT confirms diffuse hepatocellular injury.

Cholestasis. In the cat, 3-fold elevations of ALP are marked and indicative of significant cholestasis. The elevation in GGT is also quite marked. Further evidence of severe biliary involvement is the 3+ bilirubinuria.

Because of a high renal threshold for bilirubin in cats, bilirubinuria of this degree is only seen with marked cholestasis. Finally, serum bilirubin data, with a marked elevation of predominantly conjugated bilirubin, is strongly suggestive of ongoing severe intrahepatic or post-hepatic cholestasis. Based on the clear indicators of marked hepatobiliary disease in this patient (quite possibly inflammatory based on hemogram data), biopsy is warranted.

Hyperproteinemia, hyperglobulinemia. Serum protein is elevated while albumin is within normal. This pattern suggests that the elevated protein primarily reflects increased circulating immunoglobulins in association with the inflammatory disease.

Electrolytes, acid-base balance

Possible metabolic alkalosis. TCO₂ is mildly elevated, suggesting a possible metabolic alkalosis. This is supported further by the

observation that while both sodium and chloride are within the normal range, chloride is low relative to sodium, suggesting possible sequestration or loss of HCl. It is possible that the cat has been vomiting. While acid-base disturbance

is mild at present, TCO₂ and electrolytes should continue to be monitored.

Additional findings:

Hyperamylasemia. The mild elevation in amylase is of equivocal significance.

Summary and outcome:

Laboratory data suggests inflammatory hepatobiliary disease with mild metabolic alkalosis. Hepatic biopsy (done only after confirming normal clotting function) resulted in a diagnosis of pericholangitis. The cat was negative for feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), and feline infectious peritonitis (FIP).

Case 4

SIGNALMENT: Six-year-old spayed female Dachshund

HISTORY: The dog was referred for abdominal pain with a preliminary diagnosis of pancreatitis.

P.E.: T = 102.5°F R = 100.

The dog exhibited abdominal pain on palpation.

INITIAL ASSESSMENT: Abdominal pain suggests involvement of pancreas, liver, GI, or urinary system.

LABORATORY DATA:

Hematology

* HCT (%)	25.4	L	* WBC (/μl)	30,700	H
* Hb (g/dl)	8.5	L	* Bands (/μl)	1,230	H
* RBC (× 10 ⁶ /μl)	3.78	L	* Neutrophils (/μl)	27,020	H
TP (g/dl)	5.6		Lymphocytes (/μl)	1,840	
Platelets	Adequate		Monocytes (/μl)	610	

Chemistry

* BUN (mg/dl)	34	H	* Lipase (IU/L)	8,593	H
Creatinine (mg/dl)	1.2		* Sodium (mmol/L)	133	L
Glucose (mg/dl)	111		Potassium (mmol/L)	4.5	
T. bilirubin (mg/dl)	0.6		* Chloride (mmol/L)	99	L
* TP (g/dl)	4.0	L	* Calcium (mg/dl)	7.2	L
* Albumin (g/dl)	1.6	L	Phosphorus (mg/dl)	5.3	
ALT (IU/L)	63		* Cholesterol (mg/dl)	540	H
* ALP (IU/L)	2,745	H	* Triglycerides (mg/dl)	250	H
* GGT (IU/L)	155	H	* TCO ₂ (mmol/L)	25	H
* Amylase (IU/L)	2,195	H	Anion gap (mmol/L)	14	

Urinalysis (voided)

Color	yellow	Occ. blood	1+
Turbidity	clear	Urobilinogen	0.1
Sp. gr.	1.014	WBC (/HPF)	neg.
pH	6.0	RBC (/HPF)	neg.
Protein	4+	Epithelial (/HPF)	1-2
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	mod. hyaline and waxy
Bilirubin	1+	Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

INTERPRETATION:

Hematology

RBC: *Non-regenerative anemia.* There is a mild to moderate normocytic, normochromic, non-regenerative anemia. The possibility of the anemia of inflammatory disease should be considered.

TP: *Hypoproteinemia.* Hypoproteinemia is an important finding and suggests the possible involvement of 4 systems: blood loss (unlikely, based on the non-regenerative anemia), protein-losing nephropathy, protein-losing enteropathy, and lack of protein production by the liver. The 3 remaining possibilities will be explored further in the urinalysis and chemistry findings.

WBC: *Active inflammatory leukogram.* There is a leukocytosis characterized by a neutrophilia with a left shift indicative of inflammation.

Platelets: No abnormalities.

Chemistry and Urinalysis

Exocrine pancreatic panel

Possible acute pancreatitis. Amylase and lipase are both significantly elevated, but there is a marginal elevation in BUN, casting some doubt over the interpretation of the pancreatic enzymes. The situation is further confounded by the presence of isosthenuric urine specific gravity (in conjunction with the BUN, this suggests renal failure), but the normal creatinine and phosphorus levels.

Hypocalcemia is present, which could indicate pancreatitis, but its association with hypoalbuminemia makes the significance of the calcium value questionable. Considering the clinical signs, inflammatory leukogram, and pancreatic enzymes, pancreatitis is likely.

Urinary panel

Protein losing nephropathy/nephrotic syndrome. A 4+ proteinuria in conjunction with hyaline cast formation and an absence of significant blood in the urine is highly suggestive of

glomerular leakage of protein (glomerulopathy). The serum protein profile (hypoproteinemia, hypoalbuminemia, and normal globulins) is also highly supportive. Proteinuria, hypoalbuminemia, and hypercholesterolemia are 3 of the cornerstones of the nephrotic syndrome; if the fourth (ie, edema/effusion) is present in this patient, then the diagnosis of the nephrotic syndrome can be confirmed.

Possible renal failure. An elevated BUN in the presence of an isosthenuric urine specific gravity suggests the possibility of renal failure. The isosthenuria is even more convincing because 4+ proteinuria can falsely elevate urine specific gravity into the concentrating range. In addition, the waxy casts are clear evidence of renal tubular degeneration. However, as stated above, the normal creatinine and phosphorus are disconcerting, casting doubt on the interpretation of BUN. It is possible that the BUN elevation is merely a third standard deviation abnormality (and therefore insignificant) or a non-GFR-related alteration (eg, high protein diet). In the same way, it is possible that a true decrease in GFR (renal azotemia) is present with an asynchronously low creatinine (possibly due to extremely decreased muscle mass) and low phosphorus (possibly low intake).

Hepatic panel

Cholestasis. The greater than 4-fold elevation in ALP in the absence of lymphopenia confirms cholestasis. The marked elevation in GGT and the presence of bilirubinuria (albeit slight) also support the presence of cholestasis. The cholestasis could easily be secondary to localized edema and obstruction of the common bile duct in association with pancreatitis.

Electrolytes and acid-base balance

Third space disease. The concordant decrease in sodium and chloride suggests loss or dilution of analytes in an expanded extracellular fluid (ECF) compartment. With the strong

suspicion of the nephrotic syndrome (edema/effusion) and evidence of renal tubular degeneration, both loss and dilution may be contributory.

Possible metabolic alkalosis. The minimal increase in TCO₂ may suggest metabolic alkalosis but it is of questionable significance. It could easily be in the third standard deviation of reference values and the lack of a significant decrease in chloride relative to sodium argues against a biologically important change. However, this should be monitored in light of the relatively acidic urine pH (6.0), which might suggest a developing paradoxical aciduria.

Summary and outcome:

There is a protein losing nephropathy with probable nephrotic syndrome and possible renal azotemia as well as an associated electrolyte disturbance (third space syndrome and/or tubular loss).

Based on laboratory data, there is probable pancreatitis with an associated inflammatory leukogram, mild non-regenerative anemia, and hypocalcemia. Renal disease may be contributing both to the inflammation and the non-regenerative anemia (and even to the pancreatic enzyme elevations). The hypoalbuminemia caused by renal protein loss is at least partially responsible for the low calcium. There is significant cholestasis, which may be secondary to the pancreatitis.

Necropsy findings confirmed pancreatitis, copious third space disease, and severe renal amyloidosis.

Case 5

SIGNALMENT: Three-and-a-half-year-old male

Malamute

HISTORY: The dog was presented with a history of anorexia and weight loss.

P.E.: Physical examination was unremarkable except that the animal was thin and depressed.

INITIAL ASSESSMENT: History and physical are unremarkable. A full laboratory profile is clearly warranted.

LABORATORY DATA:

Hematology

HCT (%)	42	WBC (/μl)	14,000
Hb (g/dl)	13.8	Neutrophils (/μl)	10,200
RBC (× 10 ⁶ /μl)	6.3	Lymphocytes (/μl)	2,400
TP (g/dl)	7.0	Monocytes (/μl)	800
Platelets	Adequate	Eosinophils (/μl)	600

Chemistry

* BUN (mg/dl)	76	H	Lipase (IU/L)	220	
* Creatinine (mg/dl)	3.1	H	* Sodium (mmol/L)	149	H
Glucose (mg/dl)	100		Potassium (mmol/L)	4.3	
T. bilirubin (mg/dl)	0.3		Chloride (mmol/L)	110	
TP (g/dl)	6.3		* Calcium (mg/dl)	15.7	H
Albumin (g/dl)	3.1		Phosphorus (mg/dl)	3.9	
ALT (IU/L)	62		Cholesterol (mg/dl)	280	
ALP (IU/L)	140		Triglycerides (mg/dl)	80	
GGT (IU/L)	13		TCO ₂ (mmol/L)	24	
Amylase (IU/L)	820		* Anion gap (mmol/L)	20	H

Urinalysis (voided)

Color	yellow	Occ. blood	neg.
Turbidity	hazy	Urobilinogen	neg.
Sp. gr.	1.018	WBC (/HPF)	3-4
pH	6.0	RBC (/HPF)	neg.
Protein	trace	Epithelial (/HPF)	1-2
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	1-2 granular
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

No abnormalities.

Clinical chemistry

Urinary panel

Renal azotemia (renal failure). Elevated BUN and creatinine in conjunction with dilute urine (specific gravity < 1.030 in the dog) is diagnostic for renal failure. Granular casts in the urine confirm tubular degeneration.

Electrolytes and acid-base balance

Mixed metabolic acidosis/alkalosis. The anion gap is increased, suggesting the presence of acidosis. This is most likely titrational acidosis associated with the renal disease. Metabolic alkalosis is suggested by the low chloride relative to sodium and the high-normal TCO₂ in the face of acidosis.

Marked hypercalcemia. Hypercalcemia occasionally occurs secondarily in renal disease but the elevation is usually relatively minor. Hypercalcemia here is marked, suggesting that it is probably primary. A normal phosphorus level in the face of reduced glomerular filtration is further supportive evidence for primary hypercalcemia.

Primary hypercalcemia can cause renal failure (hypercalcemic nephropathy), which is the probable pathogenesis in this case. Marked hypercalcemia alone is relatively uncommon. It is most often seen as a paraneoplastic syndrome (HHM or pseudohyperparathyroidism) in association with lymphosarcoma, anal gland adenocarcinoma, or a variety of other tumors. Primary hyperparathyroidism and vitamin D toxicosis are also causes of hypercalcemia, but these are quite rare in dogs.

Summary and outcome:

Radiographs revealed marked enlargement of mesenteric lymph nodes and spleen, and thickening of the wall of the jejunum and ileum. A presumptive diagnosis of lymphosarcoma was made and confirmed at laparotomy. The final interpretation of lymphosarcoma with pseudohyperparathyroidism, hypercalcemia, and secondary renal failure due to hypercalcemic nephropathy was therefore established. Acid-base disturbances were minor.

Case 6

SIGNALMENT: Five-year-old neutered male mixed-breed dog

HISTORY: The dog is presented with a history of vomiting of several days' duration.

P.E.: Other than clinical evidence of dehydration, physical examination is unremarkable.

INITIAL ASSESSMENT: Vomiting is a nonspecific sign that may be associated with disorders of the liver, pancreas, GI tract, and urinary system.

INTERPRETATION:

Hematology

RBC: *Relative polycythemia*. Elevated RBC parameters and TP confirms the clinical impression of hemoconcentration (dehydration).

TP: *Hyperproteinemia*. Consistent with hemoconcentration.

WBC: *Active inflammatory leukogram*. There is leukocytosis characterized by neutrophilia, left shift, and monocytosis. These changes are consistent with inflammation.

Stress leukogram. Lymphopenia is consistent with stress.

Platelets: No abnormalities noted.

LABORATORY DATA:

Hematology

* HCT (%)	61	H	* WBC (/μl)	21,000	H
* Hb (g/dl)	20	H	* Bands (/μl)	500	H
* RBC (× 10 ⁶ /μl)	9.0	H	* Neutrophils (/μl)	17,700	H
* TP (g/dl)	8.7	H	* Lymphocytes (/μl)	1,000	LN
Platelets	Adequate		* Monocytes (/μl)	1,600	H
			Eosinophils (/μl)	200	

Chemistry

* BUN (mg/dl)	109	H	Lipase (IU/L)	600	
* Creatinine (mg/dl)	2.3	H	* Sodium (mmol/L)	121	L
Glucose (mg/dl)	110		Potassium (mmol/L)	4.3	
T. bilirubin (mg/dl)	0.3		* Chloride (mmol/L)	71	L
* TP (g/dl)	7.7	H	Calcium (mg/dl)	10.6	
* Albumin (g/dl)	5.2	H	Phosphorus (mg/dl)	7.2	
ALT (IU/L)	50		Cholesterol (mg/dl)	260	
ALP (IU/L)	140		Triglycerides (mg/dl)	75	
GGT (IU/L)	8		* TCO ₂ (mmol/L)	39	H
Amylase (IU/L)	750		Anion gap (mmol/L)	15	

Urinalysis (cystocentesis)

Color	yellow	Occ. blood	trace
Turbidity	clear	Urobilinogen	0.1
Sp. gr.	1.020	WBC (/HPF)	1-2
pH	6.0	RBC (/HPF)	1-2
Protein	trace	Epithelial (/HPF)	1-2
Glucose	neg.	Bacteria	neg.
Ketones	neg.	Casts (/LPF)	neg.
Bilirubin	neg.	Crystals	mod. amorphous

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. L indicates values below the reference ranges.

Chemistry and Urinalysis

Urinary panel

Azotemia. BUN and creatinine are elevated and urine specific gravity is less than 1.030. This pattern is consistent with the azotemia of renal failure (renal azotemia). However, in this case, the sodium and chloride levels cast some doubt on this interpretation.

Sodium and chloride are very low (lower than would be expected in renal failure). Sodium concentration is low enough to directly cause decreased tubular concentrating ability. Thus, the possibility of pre-renal azotemia with hyponatremia induced isosthenuria must also be considered.

Urinalysis findings are unremarkable with the exception of the urine specific gravity.

Electrolytes and acid-base balance

Hyponatremia, hypochloridemia. Marked decreases in sodium and chloride are either the result of loss (eg, medullary washout, or in Addison's disease where tubular ability to resorb sodium is impaired) or dilution in an expanded extracellular fluid compartment (eg, ascites or edema). Though both sodium and chloride are low, the degree of chloride reduction is much greater than that of sodium reduction. This suggests a greater loss of chloride, quite possibly as a result of gastric vomiting (loss of HCl).

Metabolic alkalosis. The relatively greater decrease in chloride compared to sodium coupled with the elevated TCO₂ confirms the diagnosis of metabolic alkalosis. Anion gap is normal, perhaps supporting the notion that the azotemia is not associated with the organic acids of renal failure.

The urine pH of 6.0, although normal for the dog, is worthy of comment in light of the metabolic alkalosis. This is a case of paradoxical aciduria. If able, the kidneys would be expected to compensate for the metabolic alkalosis by excreting bicarbonate thereby elevating the urine pH. In this case, clearly the electrolyte abnormalities are preventing this compensation from occurring and are exacerbating the problem

Summary and outcome:

Laboratory data do not lead to a specific disease diagnosis but rather to a differential diagnosis. Gastric vomiting/GI foreign body, Addison's disease, and third space disease must all be considered as primary syndromes; the electrolyte changes suggest that renal panel abnormalities are most likely secondary. The actual diagnosis was GI foreign body.

Case 7

SIGNALMENT: Ten-year-old spayed female mixed-breed dog

HISTORY: Dog is presented with a history of vomiting and polydipsia.

P.E.: Unremarkable. At presentation the dog was thin but active and alert.

INITIAL ASSESSMENT: Signs are nonspecific. A full profile is warranted.

LABORATORY DATA:

Hematology

HCT (%)	42	WBC (/µl)	15,000
Hb (g/dl)	14	Neutrophils (/µl)	10,500
RBC (× 10 ⁶ /µl)	6.7	Lymphocytes (/µl)	3,500
TP (g/dl)	6.2	Monocytes (/µl)	500
Platelets	Adequate	Eosinophils (/µl)	500

Chemistry

* BUN (mg/dl)	332	H	Lipase (IU/L)	800	
* Creatinine (mg/dl)	10.3	H	* Sodium (mmol/L)	151	H
Glucose (mg/dl)	110		* Potassium (mmol/L)	5.3	H
T. bilirubin (mg/dl)	0.3		* Chloride (mmol/L)	101	L
TP (g/dl)	5.8		* Calcium (mg/dl)	9.4	L
Albumin (g/dl)	3.4		* Phosphorus (mg/dl)	28.9	H
ALT (IU/L)	44		Cholesterol (mg/dl)	75	
ALP (IU/L)	600		Triglycerides (mg/dl)	80	
GGT (IU/L)	8		TCO ₂ (mmol/L)	19	
Amylase (IU/L)	620		* Anion gap (mmol/L)	37	H

Urinalysis (cystocentesis)

Color	yellow	Occ. blood	neg.
Turbidity	clear	Urobilinogen	neg.
Sp. gr.	1.017	WBC (/HPF)	neg.
pH	7.0	RBC (/HPF)	neg.
Protein	3+	Epithelial (/HPF)	neg.
Glucose	neg.	Sperm	neg.
Ketones	neg.	Bacteria	neg.
Bilirubin	neg.	Casts (/LPF)	neg.
		Crystals	neg.

* Chemistry and hematology values preceded by asterisks indicate abnormalities.

Refer to Part IV, Tables I and II, Reference Ranges for the Dog and Cat.

H indicates values above the reference ranges. **L** indicates values below the reference ranges.

INTERPRETATION:

Hematology

No abnormalities.

Chemistry and Urinalysis

Urinary panel

Renal azotemia (renal failure). Markedly elevated BUN and creatinine in the face of isosthenuric urine specific gravity confirms renal failure.

Proteinuria. The 3+ proteinuria in the absence of any formed urinary sediment indicates significant glomerular injury with protein leaking as a part of the renal disease.

Hyperphosphatemia. The hyperphosphatemia follows the BUN and is further evidence of a marked reduction in glomerular clearance (reduced GFR).

Hypernatremia, hypochloridemia. The hypernatremia is mild and probably reflects some degree of hemoconcentration.

Hemoconcentration is probably not reflected by TP and albumin values because of the proteinuria. The hypochloridemia is fairly marked relative to sodium, suggesting loss of chloride (in the form of HCl via emesis) and probable metabolic alkalosis.

Acid-base balance

Mixed metabolic acidosis/alkalosis. The increased anion gap signals titrational acidosis, probably as a result of increased circulating uremic acids (phosphates and sulfates). However, the normal TCO₂ in conjunction with a markedly increased anion gap indicate the presence of metabolic alkalosis, as supported by chloride changes above.

Additional findings:

Hyperkalemia. The hyperkalemia is most likely a reflection of acidosis.

Hypocalcemia. The hypocalcemia is also probably a reflection of the renal disease. At least 2 mechanisms may be involved. First, the renal tubules may be less able to activate vitamin D, resulting in reduced calcium absorption by the gut. In addition, because of the law of mass action, there may be precipitation of calcium in the damaged kidney and other soft tissues because of the very high phosphorus.

Summary and outcome:

All of the changes can be explained on the basis of severe renal disease with renal failure and mixed metabolic acidosis and alkalosis.

Table I.

Chemistry Reference Ranges for the Dog and Cat

Test	Units	Dog	Cat
BUN	mg/dl	7 - 32	15 - 35
Creatinine	mg/dl	0.5 - 1.5	0.9 - 2.3
Glucose	mg/dl	67 - 132	75 - 134
Total Bilirubin	mg/dl	0.1 - 0.8	0.1 - 0.4
Total Protein (TP)	g/dl	4.8 - 6.9	5.5 - 7.1
Albumin	g/dl	2.3 - 3.9	2.8 - 3.9
ALT	IU/L	3 - 69	20 - 108
ALP	IU/L	20 - 157	23 - 107
GGT	IU/L	5 - 16	0.0 - 10.0
Amylase	IU/L	378 - 1033	440 - 1264
Lipase	IU/L	104 - 1753	148 - 1746
Sodium	mmol/L	138 - 148	148 - 157
Potassium	mmol/L	3.5 - 5.0	3.5 - 5.1
Chloride	mmol/L	105 - 117	115 - 128
Calcium	mg/dl	9.7 - 12.3	9.0 - 11.7
Phosphorus	mg/dl	2.2 - 7.0	2.6 - 8.8
Cholesterol	mg/dl	125 - 301	45 - 274
Triglycerides	mg/dl	21 - 120	21 - 81
Total CO ₂ (TCO ₂)	mmol/L	13 - 24	16 - 25
Anion gap	mmol/L	9 - 18	10 - 23

Table II.

Hematology Reference Ranges for the Dog and Cat

Test	Units	Dog	Cat
HCT	%	37 – 55	30 – 45
Hb	g/dl	12 – 18	8 – 15
RBC	$\times 10^6/\mu\text{l}$	5.5 – 8.5	5.0 – 10.0
Total Protein (TP) [Plasma]	g/dl	6.0 – 8.0	6.0 – 8.0
WBC	$/\mu\text{l}$	6,000 – 17,000	6,000 – 18,000
Bands	$/\mu\text{l}$	0 – 300	0 – 300
Neutrophils	$/\mu\text{l}$	3,000 – 12,000	3,000 – 12,000
Lymphocytes	$/\mu\text{l}$	1,000 – 5,000	1,500 – 7,000
Monocytes	$/\mu\text{l}$	150 – 1,350	50 – 850
Eosinophils	$/\mu\text{l}$	100 – 1,250	100 – 1,500
MCV	fl	60 – 75	40 – 55
MCHC	g/dl	32 – 36	30 – 36
Fibrinogen	mg/dl	200 – 400	150 – 300
Platelets	$\times 10^5/\mu\text{l}$	2 – 9	3 – 7
Prothrombin Time	Seconds	5.5 – 7.9	6.4 – 9.6
Partial Thromboplastin Time (APTT or PTT)	Seconds	11.4 – 16.4	9.3 – 18.7
FSPs (Fibrin/Fibrinogen Split Products)	g/ml	<10	<10

Glossary of Terms

-A-

- acetonuria:** presence of acetone in the urine.
- albuminuria:** presence of excessive amounts of plasma albumin in the urine.
- anuria:** total cessation of urine production and excretion.
- azotemia:** an increase in nitrogenous solutes in the blood, classically urea or creatinine.
- activated lymphocytes:** Antigen-stimulated (blast-transformed, reactive) lymphocytes. These lymphocytes are actively gearing up to produce antibodies or lymphokines. They have morphologic features of active protein producing cells: lacy chromatin (primarily euchromatin) and abundant blue cytoplasm rich in RNA.

-B-

- bacteriuria:** presence of bacteria in the urine.
- bilirubinuria:** presence of bilirubin in the urine; the form of bilirubin appearing in the urine is the conjugated or direct-reacting form.

-C-

- calculus:** general term referring to a solid concretion (stone) occurring in a hollow organ or duct.
- cast:** a cylindric mass of material formed in the distal portion of the nephron and passed in the urine; casts may be cellular, granular (coarse and fine), waxy, or hyaline.
- cylinduria:** presence of casts in the urine.
- cystitis:** inflammation of the urinary bladder.
- cystocentesis:** collection of urine by percutaneous needle puncture of the bladder.

-D-

- D. bilirubin:** direct bilirubin.
- diuresis:** urine excretion in excess of the usual volume produced.
- dysuria:** difficulty or pain upon urination.

-F-

- functional proteinuria:** transient and mild proteinuria consisting mainly of albumin, which occurs in certain situations associated with sympathetic nervous system discharge.

-G-

- glomerular proteinuria:** proteinuria of glomerular origin due to increased filtration of plasma proteins usually through an abnormally permeable glomerular filter; in glomerular proteinuria, albumin predominates.

glomerulonephritis: a variety of nephritis characterized primarily by an inflammatory process in the glomeruli; most cases of glomerulonephritis involve immune-mediated injury.

glomerulonephropathy (glomerulopathy): any disease of the renal glomeruli.

glucosuria: presence of glucose in the urine.

glycosuria: presence of an abnormal amount of glucose in the urine; often used interchangeably with the term glucosuria.

-H-

HHM: humoral hypercalcemia of malignancy

HPF: high power field.

hematuria: presence of erythrocytes in the urine; may be gross (visible) or microscopic (occult).

hemoglobinuria: presence of free hemoglobin in the urine.

hyposthenuria: excretion of dilute urine with a specific gravity less than that of glomerular filtrate (1.001 to 1.007).

-I-

interstitial nephritis: nephritis due to inflammation of the interstitial tissues of the kidney; chronic interstitial nephritis refers to interstitial fibrosis and mononuclear inflammatory cell infiltrate; etiology is not specified.

isosthenuria: excretion of urine with a specific gravity in the range of glomerular filtrate (1.008 to 1.012); often used to describe the urine elaborated by diseased kidneys which have lost their ability to concentrate or dilute the urine.

-K-

ketonuria: presence of ketone bodies in the urine.

-L-

LPF: low power field.

-M-

midstream catch: collection of a urine sample by allowing the animal to void spontaneously and collecting a sample after the initial stream of urine has been voided to reduce the chance of urethral, genital, perineal, or preputial contamination.

-N-

nephritis: inflammation of the kidney; does not specify which area of the kidney is mainly involved (ie, tubules, glomeruli, vessels, interstitium).

nephropathy: any disease of the kidney.

-O-

Occ. blood: occult blood; See urinary occult blood.

oliguria: excretion of a reduced amount of urine in relation to normal (<12 to 24 ml/lb/day).

-P-

P.E.: physical examination.

pollakiuria: unduly frequent passage of urine that implies lower urinary tract distress.

polydipsia: frequent drinking due to excessive thirst; daily water intake in excess of normal (>40 ml/lb/day).

polyuria: passage of a large volume of urine in a given period; passage of urine in amounts in excess of normal (>12 to 24 ml/lb/day).

proteinuria: the presence of an abnormal amount of plasma protein in the urine.

pyelonephritis: inflammation of the renal pelvis and kidney proper beginning in the interstitium and extending to the tubules, glomeruli, and blood vessels; usually bacterial in nature.

pyuria: the presence of excessive numbers of white blood cells in the urine (the presence of "pus" in the urine).

-S-

Sp. gr.: specific gravity.

specific gravity: the weight of a substance (in this context urine) divided by the weight of an equal volume of water as a standard.

stranguria (strangury): passage of urine with pain and straining.

-T-

T. bilirubin: total bilirubin.

TNTC: too numerous to count

tubular proteinuria: proteinuria associated with tubular

dysfunction (reduced reabsorption of protein, secretion of protein or tubular necrosis); in tubular proteinuria globulins predominate.

-U-

uremia: the constellation of clinical and biochemical abnormalities associated with a loss of a critical mass of functioning nephrons; includes the extra-renal manifestations of renal failure and is due to a critical loss of the conservation, excretory, and endocrine functions of the kidneys.

urethritis: inflammation of the urethra.

urinalysis: the systematic examination of a urine specimen which includes physical, chemical, and sediment findings.

urinary occult blood: blood present in the urine in such small (ie, microscopic) quantities that it can be detected only by chemical tests; these tests do not differentiate hemoglobinuria, myoglobinuria, and hematuria.

urolith: a polycrystalline concretion which forms in the urinary tract; also known as calculus.

urolithiasis: the disease condition associated with the formation of calculi in the urinary tract.

uropathy: any disease of the urinary tract.

UTI: urinary tract infection.

-V-

void: to urinate; to micturate; to cast out as waste matter.

-W-

water deprivation test: a test used to assess kidney function; it is conducted by withholding water from a patient then observing and measuring urine output to determine the release of ADH and response of the kidneys (elaboration of concentrated urine).

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