

# Evaluation of Hypoalbuminemia

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## Introduction

Albumin comprises 35 to 50% of total serum protein in animals. Synthesized by the liver, albumin solubilizes and transports many substances, is a storage reservoir of protein, and is the major particle that determines plasma oncotic pressure, as it does not freely travel between the intra- and extravascular compartments. Oncotic pressure is the main factor responsible for holding fluid within the walls of the blood vessels.

Decreased concentration of serum albumin develops by two main pathways: albumin is either lost from the body in excessive amounts (hemorrhage, renal, gastrointestinal, severe skin exudation), or there is decreased albumin production (hepatic insufficiency, malnutrition). Other causes of low albumin include hypoadrenocorticism and hyperglobulinemia (due to multiple myeloma). Although reference ranges vary, in general, a serum albumin of less than 2.5mg/dl is considered abnormal, and a concentration less than 1.5 mg/dl may cause significant clinical signs, such as ascites and edema formation. In most cases, significant hypoalbuminemia is due to three main causes: hepatic insufficiency, renal loss (protein-losing nephropathy), and gastrointestinal loss (protein-losing enteropathy). The challenging process of assessing a hypoalbuminemic patient is made easier if these causes are kept in mind.

## Hepatic Insufficiency

Generally, liver disease must be severe and/or chronic to cause reduced albumin production. Differentials for hepatic failure include the following: cirrhosis, neoplasia, portosystemic shunt (PSS), lipidosis, cholangiohepatitis, toxicosis, and chronic hepatitis.

## Protein-losing Nephropathy (PLN)

There are two main causes of renal protein loss: immune complex glomerulonephritis and renal amyloidosis. Immune complex disease, a result of type 3 hypersensitivity reaction, is the most common cause in dogs and cats. Common etiologies include heartworm disease, leptospirosis, feline leukemia virus, and Ehrlichiosis. Familial glomerulonephritis has been reported in Rottweilers and Dobermans, among other breeds. Renal amyloidosis is characterized by inappropriate or excessive stimulation of the immune system and glomerular amyloid deposits. The disease may be familial, such as in Abyssinian cats and Shar-Pei dogs, or due to other inflammatory, infectious, or neoplastic disease. Renal failure is progressive. Renal biopsy provides the definitive diagnosis.

## Protein-losing Enteropathy (PLE)

Albumin is lost into the gastrointestinal (GI) tract as a result of vasculitis; inflammation leads to increased capillary permeability. Common etiologies of PLE include the following: inflammatory bowel disease, lymphangiectasia, GI parasites, and neoplasia. Biopsy provides the definitive diagnosis.

## Diagnostic Approach

*History and physical exam* will often give clues as to the source of the decreased albumin. In a very young patient, consideration should be given to parasitism and congenital disorders. Icterus and abnormalities may prompt evaluation of the hepatobiliary system. Gastrointestinal signs (chronic diarrhea, weight loss, vomiting) may occur with GI albumin losses. Breed predispositions warrant attention (hepatopathies in Dobermans, lymphangiectasia and glomerulonephropathies in Rottweilers, renal amyloidosis in Abyssinian cats and Shar-Pei dogs).

*A complete serum chemistry profile and urinalysis* is the minimum database required in the evaluation of hypoalbuminemia. A *CBC, heartworm test, and fecal examination* complete the database. If effusion is present, evaluation yields a pure transudate: low protein and specific gravity, clear, hypo- or acellular fluid.

- *Evaluate the globulins.* In general, decreased globulin with decreased albumin supports GI loss. Normal globulin supports renal loss, while normal to elevated globulin can be seen with hepatic insufficiency.
- *Next, evaluate the urinalysis.* Proteinuria with normal urine sediment supports glomerular protein loss. A urine protein:creatinine ratio is subsequently indicated to approximate the quantity of protein excreted in the past 24 hours. A UPC ratio greater than 1.0 suggests a protein-losing nephropathy.
- If renal loss has been ruled out, *evaluate the liver.* Hallmarks of hepatic dysfunction include elevated liver enzymes, hypoglycemia, decreased BUN and cholesterol, and hyperbilirubinemia. These tests are not highly sensitive or specific for liver disease; therefore, even in the absence of any abnormalities, perform

liver function testing by means of pre and post-prandial serum bile acids. If liver dysfunction is established, biopsy provides a definitive diagnosis.

At this point, if hypoalbuminemia is not due to kidney or liver disease, protein-losing enteropathy is strongly suspected. Remember that gastrointestinal symptoms may be absent in these patients. Although non-invasive tests such as serum TLI, B12/folate levels, and fecal alpha1-protease inhibitor may provide further evidence of GI disease, intestinal biopsies are performed to confirm a diagnosis so that a specific treatment regimen can be started.

### Treatment Plan

1. Treat the disease. If a definitive diagnosis can be established, many times the disease can be effectively managed or even cured. Examples include immunosuppressive therapy for IBD and some types of hepatitis, hypoallergenic diets for IBD, antimicrobials for infectious disease, and chemotherapy for neoplasia. Diseases causing PLN carry a poorer prognosis, and treatment options are often supportive.
2. Fluid Therapy. Colloids are the first choice to help restore plasma oncotic pressure. Plasma can be useful in hepatic insufficiency, as it provides a source of needed albumin. It is given at 5-10 mL/kg within four hours. Synthetic colloids are preferred for PLE or PLN, as any albumin from transfused plasma would be quickly lost. Hetastarch (hydroxyethyl starch) is given at 10-20 mL/kg/day, usually over several hours. A portion of the dose (such as 5 mL/kg) may be given as a slow bolus if immediate intervention is indicated. If albumin levels are very low, avoid crystalloids unless the patient is very dehydrated or uremic. The added fluid will exacerbate already reduced oncotic pressure by further diluting any albumin present. This may result in severe, possibly fatal, edema and effusions.
3. Drain Effusions. If fluid accumulation is severe or causing dyspnea, centesis can help stabilize and relieve the patient. However, fluid will continue to accumulate unless definitive therapy can be instituted.
4. Nutritional support. High quality protein is indicated as an aid to restore lost protein, as well as specific therapy (i.e. hepatic lipidosis).
5. Avoid furosemide. Unless indicated by a specific disease, furosemide can cause severe hypotension due to volume depletion in hypoalbuminemic patients.

### Summary

Hypoalbuminemia, in the majority of cases, is due to three main causes: liver failure, renal loss, and gastrointestinal loss. Effusions and edema can develop when hypoalbuminemia is severe, usually less than 1.5mg/dL. Use less invasive tests first, including blood and urine analysis, to rule out hepatic and renal causes. Biopsy is indicated for definitive diagnosis and treatment once the disease is localized to a specific organ system. The use of colloids in the hypoalbuminemic patient is an important part of therapy.

**Note:** Veterinary Medicine is an ever-changing field. Standard safety precautions must be followed, but as new research and clinical experience broaden our knowledge, changes in treatment and drug therapy may become necessary or appropriate. Readers are advised to check the most current product information provided by the manufacturer of each drug to be administered to verify the recommended dose, the method and duration of administration, and the contraindications. It is the responsibility of the treating veterinarian, relying on experience and the knowledge of the animal, to determine dosages and the best treatment for the animal. Neither the publisher nor the editor assumes any responsibility for any injury and/or damage to animals or property arising from this publication.

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