

# Nephrotic Syndrome

## Basics

### OVERVIEW

- “Nephrotic” is an adjective that refers to anything that relates to disease of the kidney
- The kidney filters the blood and removes various waste products from the body as it produces urine; the kidney also is involved in maintaining the normal fluid volume of the body; each kidney is composed of thousands of nephrons (the functional units of the kidney, each consisting of the glomerulus [a tuft of blood capillaries—the “blood filter”] and a series of tubes and ducts, through which the filtered fluid flows, as urine is produced)
- “Nephrotic syndrome” is a medical condition in which the pet has significant levels of protein in its urine (known as “proteinuria”); low levels of albumin [a type of protein] in its blood (known as “hypoalbuminemia”); high levels of cholesterol in its blood (known as “hypercholesterolemia”); and fluid accumulation in the abdomen (known as “ascites”), in the space between the chest wall and the lungs (known as “pleural effusion”), and/or under the skin (known as “subcutaneous edema”)
- Nephrotic syndrome occurs secondary to glomerular disease (such as glomerulonephritis, kidney or renal amyloidosis)
- Glomerulonephritis is inflammation and accompanying dysfunction of glomeruli (plural of glomerulus); most commonly due to the presence of immune complexes in the glomerulus
- Renal amyloidosis is a condition in which insoluble proteins (amyloid) are deposited outside the cells of the kidneys, compromising the normal function of kidney



### GENETICS

- No breed appears to be at increased risk of developing the nephrotic syndrome complication with glomerular disease
- Familial glomerular diseases (glomerular disease that runs in certain families of animals) have been reported in several breeds, including Bernese mountain dogs, bull terriers, Dalmatians, Samoyeds, Doberman pinschers, cocker spaniels, Newfoundlands, rottweilers, greyhounds, soft-coated Wheaten terriers, and cats; familial glomerular disease is less likely to result in nephrotic syndrome than non-familial protein-losing kidney diseases (known as “protein-losing nephropathies”)

### SIGNALMENT/DESCRIPTION OF PET

#### Species

- Dogs
- Cats

## **Breed Predilections**

- No breed appears to be at increased risk of developing the nephrotic syndrome complication with glomerular disease

## **Mean Age and Range**

- Likely the same general ages as dogs and cats with glomerular disease
- Mean age of dogs with glomerulonephritis—6.5 to 7.0 years; range, 0.8–17 years
- Cats with glomerulonephritis—mean age at presentation is 4.0 years
- Most dogs and cats with kidney or renal amyloidosis (in which insoluble proteins [amyloid] are deposited outside the cells in the kidney, compromising its normal function) are over 5 years of age

## **SIGNS/OBSERVED CHANGES IN THE PET**

- Fluid buildup under the skin that retains an indentation produced by finger pressure on the tissue (known as “pitting subcutaneous edema”) and/or fluid buildup in the abdomen (ascites) are the most common reasons the owner seeks veterinary care
- Occasionally, signs associated with an underlying infectious or inflammatory disease or cancer may be the primary reason why owners seek veterinary care
- Rarely, dogs may exhibit sudden (acute) difficulty breathing (known as “dyspnea”), severe panting, weakness, or collapse due to fluid buildup in the space between the chest wall and lungs (pleural effusion), fluid buildup within the sac that surrounds the heart (the sac is known as the “pericardium”; and the fluid buildup is known as “pericardial effusion”), fluid buildup in the lungs (known as “pulmonary edema”), or blood clots in the lungs (known as “pulmonary thromboembolism”)
- Complications of high blood pressure (known as “hypertension”): bleeding in the back of the eye (known as “retinal hemorrhage”) or loss of attachment of the retina to the underlying structures of the eye (known as “retinal detachment”); fluid buildup/swelling of the optic disk (known as “papilledema”); irregular heartbeats (known as “arrhythmias”) and/or heart murmurs, secondary to enlargement of the left ventricle (known as “left ventricular hypertrophy”)
- Difficulty breathing (dyspnea) and/or bluish discoloration of the skin and moist tissues (mucous membranes) of the body caused by inadequate oxygen levels in the red blood cells (known as “cyanosis”) in dogs with fluid buildup in the space between the chest wall and lungs (pleural effusion) or blood clots in the lungs (pulmonary thromboembolism)

## **CAUSES**

- Glomerular disease may occur secondary to chronic inflammation (such as caused by infection, cancer, and immune-mediated disease); the “glomerulus” is the tuft of capillaries in the kidney or the “blood filter”
- It is unknown if nephrotic syndrome is a direct consequence of high levels of protein in the urine (known as “severe proteinuria”, regardless of type of glomerular disease, or if additional factors are required to result in fluid buildup in various locations of the body and high levels of cholesterol in the blood (hypercholesterolemia)

# **Treatment**

## **HEALTH CARE**

- Most pets can be treated as outpatients; pets that have very high levels of urea and other nitrogenous waste products in the blood (condition known as “uremia” or “azotemia”) and/or high blood pressure (hypertension); pets with blood-clotting disease (known as “thromboembolic disease”) may require hospitalization
- Tapping the abdomen to drain off excessive fluid (known as “abdominocentesis”) and/or tapping the chest to drain off excessive fluid (known as “thoracocentesis”) are used in pets with severe breathing difficulties (known as “respiratory distress”) and abdominal discomfort caused by fluid buildup in the abdomen (ascites) and/or fluid buildup in the space between the chest wall and the lungs (pleural effusion); in most pets, removal of fluid increases the rate of fluid accumulation and contributes to electrolyte abnormalities via removal of large amounts of sodium from the body
- Plasma transfusion is not indicated for routine treatment of low levels of albumin (a protein) in the blood (hypoalbuminemia); large amounts of plasma are required to significantly increase serum albumin concentrations, and transfused protein does not remain in the circulation for long

- Intravenous human albumin should be considered only in the very rare cases where pets develop life-threatening complications due to fluid accumulation (such as fluid buildup in the lungs [pulmonary edema]; fluid buildup in the space between the chest wall and lungs [pleural effusion])
- Fluid therapy may be necessary

## ACTIVITY

- Unknown whether activity level should be modified in pets with nephrotic syndrome
- Restriction of activity may be beneficial because of the possibility of blood-clotting disease (thromboembolic disease), whereas increased activity may be useful in mobilizing fluid and promoting reabsorption of fluid back into circulation; your pet's veterinarian will discuss activity levels for your pet

## DIET

- Sodium-reduced, high-quality, low-quantity protein diets are recommended currently—commercial “kidney diets” meet these criteria
- Normal or high dietary protein may contribute to the progression of kidney disease, thus dietary therapy should include a reduced (not restricted) amount of high-quality protein

## SURGERY

- Biopsy is required to differentiate between the various types of glomerular disease and to optimize treatment

## Medications

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive

### FLUID BUILDUP (EDEMA AND ASCITES)

- Dietary sodium reduction
- Reserve tapping the abdomen to remove excessive fluid (abdominocentesis) and drugs to increase the amount of urine (fluid) eliminated from the body (known as “diuretics”) for pets with severe breathing difficulties (respiratory distress) and abdominal discomfort
- Overzealous use of diuretics may cause dehydration and sudden (acute) kidney decompensation
- Diuretics include spironolactone and furosemide

### PROTEIN IN THE URINE (PROTEINURIA)

- Angiotensin-converting enzyme (ACE) inhibitors decrease loss of protein into the urine (proteinuria); ACE inhibitors (such as enalapril) should be used to decrease the severity of protein loss into the urine; proteinuria may be toxic to kidney tubules; therefore, ACE-inhibitor therapy should be initiated at the time of diagnosis, unless the pet has very high levels of urea and other nitrogenous waste products in the blood (uremia or azotemia)
- Medications to prevent blood clotting (known as “anticoagulants”), such as aspirin, may be used to decrease the risk of blood clots (thromboembolism); use of aspirin should be under the direction of your pet's veterinarian

## Follow-Up Care

### PATIENT MONITORING

- Urinary protein:creatinine ratio; serum urea nitrogen, creatinine, albumin, and electrolyte concentrations; blood pressure; and body weight; ideally, recheck examinations should be scheduled 1, 3, 6, 9, and 12 months after initiation of treatment

### POSSIBLE COMPLICATIONS

- Long-term (chronic) kidney insufficiency or failure
- Blood clots to the lungs (pulmonary thromboembolism)

### EXPECTED COURSE AND PROGNOSIS

- If the underlying cause cannot be identified and corrected, glomerular diseases usually progress to chronic kidney failure

- Once azotemia (high levels of urea and other nitrogenous waste products in the blood) and kidney failure develop, prognosis is often poor due to rapid progression of the underlying disease(s)

## **Key Points**

- Nephrotic syndrome is a medical condition in which the animal has significant levels of protein in its urine (known as “proteinuria”); low levels of albumin [a type of protein] in its blood (known as “hypoalbuminemia”); high levels of cholesterol in its blood (known as “hypercholesterolemia”); and fluid accumulation in the abdomen (known as “ascites”), in the space between the chest wall and the lungs (known as “pleural effusion”), and/or under the skin (known as “subcutaneous edema”)
- Nephrotic syndrome occurs secondary to glomerular disease (such as glomerulonephritis or kidney amyloidosis); amyloidosis is a condition in which insoluble proteins (amyloid) are deposited outside the cells in the heart and various organs, compromising their normal function
- If the underlying cause cannot be identified and corrected, glomerular diseases usually progress to chronic kidney failure
- Biopsy is required to differentiate between the various types of glomerular disease and to optimize treatment
- Once azotemia (high levels of urea and other nitrogenous waste products in the blood) and kidney failure develop, prognosis is often poor due to rapid progression of the underlying disease(s)