



**ANTECH**  
DIAGNOSTICS

*News*

September • 2000

**Lab Locations**

Atlanta  
Georgia

Chicago  
Illinois

Dallas/  
Fort Worth  
Texas

Denver  
Colorado

Honolulu  
Hawaii

Houston  
Texas

Los Angeles  
California

Memphis  
Tennessee

New York  
New York

Phoenix  
Arizona

Portland  
Oregon

San Francisco  
California

Tampa  
Florida

## GLOMERULONEPHRITIS IN DOGS AND CATS

**Glomerulonephritis (GN)** is the term used to describe glomerular cell proliferation and thickening of the glomerular capillary walls. The usual cause for GN is the presence of immune complexes within the glomerulus. *Proteinuria* is the primary clinicopathologic sign of GN. A definitive diagnosis of GN requires renal biopsy. Use of the urine protein:creatinine ratio to quantitatively estimate proteinuria has facilitated the diagnosis and treatment of GN.

Treatment objectives include: 1) identification and elimination of underlying causative antigens and/or inflammation responsible for glomerular immune complex formation; 2) suppressing the immune response; and 3) reduction of glomerular response to the immune complexes. Without treatment, GN can cause irreversible damage to the glomerulus by way of fibrin deposition and glomerulosclerosis. Irreversible glomerular damage renders the entire nephron nonfunctional and can lead eventually to renal insufficiency and failure.

Several infectious and inflammatory diseases have been associated with glomerular deposition or *in situ* formation of immune complexes in dogs and cats:

In **dogs**, infectious (brucellosis, dirofilariasis, ehrlichiosis, Rocky Mountain spotted fever, borreliosis), neoplasia and inflammatory (pancreatitis, systemic lupus erythematosus, polyarthritis, prostatitis) causes have been associated with GN.

Hereditary nephritis includes a group of genetic disorders of basement membrane collagen that causes progressive glomerular disease. Familial glomerulonephropathy has been reported in Samoyeds, bull terriers, English cocker spaniels, Bernese mountain dogs, Doberman pinschers, Rottweilers, soft-coated Wheaten terriers, Newfoundlands, shar-peis and beagles. As most affected dogs develop proteinuria as puppies, it is important to include urinalysis in their health screening.

In **cats**, infectious causes of GN include feline leukemia virus, feline infectious peritonitis virus,

and mycoplasmal polyarthritis. Neoplasia, inflammatory (pancreatitis, chronic skin disease, immune-mediated disease), and familial causes have also been associated with GN in cats.

In both species, the association of GN with diabetes mellitus and hyperfiltration remains questionable. Also, the antigen source or underlying disease process may not be identified and so the glomerular disease is referred to as idiopathic.

### CLINICAL SIGNS

There are often no clinical signs associated with GN. If there is extensive involvement with 3/4 of the glomeruli nonfunctional, renal failure and resultant azotemia, polydipsia-polyuria, anorexia, nausea and vomiting may be seen. If proteinuria is severe and persistent (serum albumin < 1.5 gm/dL), edema and/or ascites may occur. The presence of significant proteinuria, hypoalbuminemia, hypercholesterolemia, and ascites/edema is defined as the **nephrotic syndrome**. Complications frequently observed are hypertension and hypercoagulability. Signs associated with an underlying infectious, inflammatory or neoplastic disease may be the reason the owners seek veterinary care. Rarely, pets may present with acute dyspnea or severe panting caused by pulmonary thromboembolism. Emboli may occur in other vessels (e.g., femoral arteries with caudal paresis). Acute blindness caused by retinal detachment may occur secondary to systemic hypertension.

*In many cases, asymptomatic proteinuria may be detected on urinalysis during clinical evaluation of another medical problem or with routine medical screening.*

### DIAGNOSIS

**Proteinuria**, significant and persistent, with a non-inflammatory urine sediment is the hallmark of GN. Hematuria and pyuria will interfere with accurate assessment by contributing to the protein measured. In dilute urine, even a *trace* of protein can be signifi-

# GLOMERULONEPHRITIS IN DOGS & CATS (CONT'D.)

cant. Azotemia and isosthenuria may not be seen in the early course of the disease. This reinforces the importance of a urinalysis in evaluating canine and feline patients.

Urine protein:creatinine (P:C) ratio is used to quantitate the magnitude of urine protein loss. A P:C ratio > 0.8 is abnormal in dogs, and > 0.7 is abnormal in cats, although GN is usually associated with ratios of 3.5 or greater.

**Hypoalbuminemia** occurs in many dogs and cats with GN. For example, albumin levels < 2.1 gm/dL were found in 70% of dogs with amyloidosis and 32% of dogs with GN.

Other laboratory findings in dogs and cats with renal failure caused by GN include nonregenerative anemia, lymphopenia, azotemia, hyperphosphatemia, hypercholesterolemia, hypoalbuminemia, mild hyperglycemia (caused by insulin resistance), and metabolic acidosis. When present, azotemia reflects prerenal (dehydration) and/or renal (>75% loss of nephrons) factors. Isosthenuria reflects solute diuresis or concurrent renal tubular dysfunction. Hyaline and granular casts may also be present in the urine sediment.

Medical work-up includes a CBC, chemistry panel, urinalysis, urine P:C ratio, urine culture, blood pressure measurement, abdominal radiographs and ultrasound. Identification of an underlying primary problem needs to be pursued. Definitive diagnosis of GN requires renal biopsy. Performing renal biopsies can result in further deterioration of renal function, and so pros and cons of performing the procedure need to be carefully considered. A coagulation profile and bleeding time should be performed prior to biopsy.

## TREATMENT

Successful treatment/management in GN patients depends on identifying an underlying etiology (if possible), correcting the problem, and medical management.

Medical management of GN may include immunosuppressive therapy (cyclophosphamide, azathioprine, chlorambucil or cyclosporine); anti-inflammatory-hypercoagulability treatment (aspirin); dietary control (sodium restriction); anti-hypertensive medication (enalapril, amlodipine), and diuretics. Ideally, renal biopsies should be obtained before instituting immunosuppressive therapy. One controlled study assessed the effects of cyclosporine treatment in dogs with idiopathic GN, but was found to have no benefit in reducing proteinuria.

Use of corticosteroids is contraindicated in dogs with GN, except if the underlying disease process is steroid-responsive (e.g., systemic lupus). In a retrospective study of dogs with idiopathic GN, corticosteroid treatment appeared to be detrimental, leading to azotemia and worsening of the proteinuria. If immunosuppressive drugs are initiated, the urine P:C ratio should be monitored at least monthly to assess the effects of treatment. If the magnitude of proteinuria increases, immunosuppressive therapy should be changed or discontinued.

There is increasing evidence that platelets and thromboxanes are integrally involved in the pathogenesis of GN. Beneficial responses to antiplatelet therapy with aspirin have been demonstrated in several experimental studies. Dogs with antithrombin III concentrations <70% of normal and fibrinogen concentrations >300 mg/dL are candidates for anticoagulant therapy. Antiplatelet drugs, heparin and coumadin have all been utilized here. Low-dose aspirin (0.25 mg/lb PO twice daily) has been reported to inhibit platelet aggregation in dogs and is the treatment of choice for hypercoagulability. It is unclear whether antiplatelet therapy is needed in cats with GN, because thromboembolism rarely occurs.

Treatment with enalapril decreased proteinuria, improved renal function, and prolonged survival in male Samoyeds with hereditary nephritis. Sodium-restricted diets are also strongly recommended. Protein-restricted diets improve the efficacy of enalapril treatment and are recommended to decrease glomerular hyperfiltration and the nonimmunologic progression of GN. Despite urine protein loss, dietary protein supplementation is not advisable as proteinuria can worsen. Dogs and cats with edema or ascites should be treated with cage rest and dietary sodium restriction. Paracentesis should be reserved for animals experiencing respiratory distress and abdominal discomfort. Overzealous use of diuretics (furosemide) may cause dehydration and acute renal decompensation. Plasma transfusions provide only temporary benefits.

Monitoring urine P:C ratio is important after initiating therapy. If proteinuria increases, treatment should be changed or discontinued. The serum creatinine and urea nitrogen should also be monitored. Also, as renal function deteriorates (decrease in glomerular filtration), proteinuria usually decreases. The prognosis for dogs with GN is generally poor, although early recognition and appropriate therapy can extend the lives of these patients.

*References:* Jergens AE, Compend Contin Educ Pract Vet 16: 102-108, 1994; Current Veterinary Therapy XII, Saunders, Phila, 1995; Current Veterinary Therapy XIII, Saunders, Phila, 1999; Ettinger SJ, Feldman EC, Textbook of Veterinary Internal Medicine, 5th edition; Saunders, Phila, 1999; Lees GF, Helman RG, Kashtan CE, et al. AJVR 60: 373-383, 1999; Rha JY, Labato MA, Ross LA, et al. JAVMA 216: 46-50, 2000.

## LAB TIPS

### Sample Deterioration (aka Heat Wave!)

The unexpected heat wave this summer has caused deterioration of mailed-in samples, especially those arriving over a weekend. The blood cells are destroyed and serum parameters may also be altered. **Please add a cold pack with your samples.** Be sure to wrap the tubes to avoid breakage in transit from movement of the cold pack. For mailed samples, submitting a blood slide along with the sample permits cell morphology to be evaluated in the event of sample deterioration.

### Urine Cultures

#### Dogs –

Our recent evaluation of dog urine cultures indicates that positive cultures become positive by 48 hours. Negative cultures at 48 hours remained negative at 72 hours. Thus, all **negative canine urine cultures will be reported as final at 48 hours.**

#### Cats –

A few (~ 1%) of feline urine cultures become positive at 72 hours after being negative at 48 hours. **Feline urine cultures will therefore continue to be checked for 72 hours.**