

Understanding Renal Disease

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According to Dr. Urs Giger, Dipl. ACVIM and Dipl. ECVIM, at the University of Pennsylvania, hereditary diseases involving the renal system are being diagnosed with increasing frequency in dogs. This trend may be the result of advances in clinical laboratory techniques and comparative genetics studies. Hereditary kidney disease commonly begins when the dog is young, but may not show symptoms until middle age when serious damage has already taken place. Diagnoses may reveal kidney defects or other forms of organ failure as well as anemia. In most cases, the clinical signs are chronic and progressive.

Overview of the Renal/Urinary System

The canine renal system consists of two kidneys, two ureters (each linking a kidney to the urinary bladder) and the urethra located at the base of the bladder through which urine leaves the body. Within the kidney are a multitude of tiny filtration units called nephrons. Dogs (and humans) are born with a finite number of nephrons to last their entire lives; once disease destroys a nephron, it is lost forever and cannot be replaced. Fortunately, a dog is born with nearly 800,000 nephrons. Not all nephrons are working at the same time; some are held in reserve until they are recruited to replace failed nephrons. Although larger breeds have larger kidneys, they have the same number of nephrons as smaller breeds. Generally, overall kidney function does not show failure until a dog has lost around 80-85% of his nephrons. Nephrons may fail quickly or slowly. At this stage therapy involves easing the workload of the kidney by using medication, specially-formulated foods and/or supplements and, if possible, retarding disease progression.

Located within the nephron is the main filter called the glomerulus. The filter resembles a twisted mass of capillaries through which unfiltered blood passes. As blood is conveyed through the semi-permeable capillaries of the glomerulus, water and soluble wastes pass out through the capillary walls and are ultimately excreted as urine. The filtered blood, containing proteins and other valuable substances, is retained by the body.

While most of us associate the kidney with the removal of waste and the production of urine, the renal system performs many other important functions. For example, the kidneys aid in water conservation, red blood cell production, blood pressure regulation, salt balance and activation of Vitamin D, just to name a few. Hence, when a dog's kidneys fail, these other functions may also fail, putting the dog at additional risk.

What Happens in Renal Failure?

Renal failure occurs when abnormally high levels of nitrogen-type toxins accumulate in the blood. Toxins such as creatinine and urea build up in the body, creating a condition called azotemia. These toxins damage tissues and reduce organ function. Although lab tests are abnormal, the dog may or may not show the effects of the toxins at this stage. Typically an animal with kidney failure produces urine in excessive quantities because the kidneys are not conserving water properly. As a result the urine is dilute. Normal kidneys produce highly concentrated urine in which large amounts of toxins are excreted in small amounts of water. When kidneys fail, they are no longer able to concentrate urine and as a result require more water to excrete the same amount of toxins. A dog will begin to drink excessively to compensate for the increased water loss. Sooner or later, the dog cannot drink enough water, and the toxin levels increase. At this point, the dog may suffer from uremic poisoning (uremia). The dog's lab tests are not only abnormal, but now he is feeling the effects of the toxins. Typically, the filtration rate drops, and serum urea (usually expressed as Blood Urea Nitrogen/BUN) and creatinine rise to very high levels. However,

BUN and creatinine measurements are only roughly correlated with the clinical signs of uremia. Other nitrogenous compounds present in small amounts may produce most of the toxic effects. Uremia is a syndrome that occurs at the end-stage in renal insufficiency/failure.

Major Renal Diseases Affecting BMDs

Hereditary kidney diseases in dogs are classified as belonging to one of four categories: developmental anomalies (e.g., renal dysplasia); inflammatory processes (e.g., glomerulopathy); familial renal cancer (e.g., renal cystadenocarcinoma); and metabolic renal transport defect (e.g., cystinuria). This section focuses on two renal diseases

affecting Bernese Mountain Dogs: renal dysplasia and glomerulonephritis.

Renal dysplasia (see article in this issue by L. Gerson) is considered a disease of developmental anomaly. Renal dysplasia, also called juvenile renal dysplasia or progressive nephropathy (PNP), results when a puppy's kidney fails to grow and develop properly, either because the cells do not develop or they develop abnormally. It is primarily a disease

Symptoms of Renal Dysplasia

Frequent Urination (polyuria)
& Drinking (polydypsia)
Weight Loss/Anorexia/Wasting
Vomiting or Diarrhea.
Lethargy
High Blood Pressure
(systemic hypertension)
Failure to Come in Season
Stunted Growth
Bone Pain (renal osteodystrophy)
Blood in the Urine (hematuria)
Poor wound healing

Note: Often there are no symptoms.

When a number of BMDs were diagnosed with renal dysplasia in the mid 1990s, concerned Swedish BMD breeders petitioned the Swedish Kennel Club (SKK) for Central Registration status for renal dysplasia. This was granted in 1998 and now, when a case of renal dysplasia is diagnosed by a veterinarian in a Swedish BMD, it must be reported to the SKK for registration in an open database (SKK Hunddata). Hips and elbows have similar status for BMDs. For more information on the Swedish control program for renal dysplasia, see "Renal Dysplasia," by Lisbeth Plant, at http://www.bmdca.org/health/Miscellaneous/Renal_Dysplasia.php

of young dogs, developing symptoms usually before two years. It is also considered to be familial (occurring in families), but some disease is non-familial (e.g., the result of in utero viral infection).

Associated conditions include chronic renal failure (CRF), stunted growth, softening and fibrous degeneration of the bone (renal osteodystrophy) and high blood pressure (systemic hypertension).

An affected dog may show no symptoms, but if symptoms are present they may include failure to come in season, anorexia/wasting, bone pain, lethargy, blood in the urine (hematuria), excessive urination and water consumption (polyuria/polydipsia), poor wound healing, stunted growth, vomiting or diarrhea. Early diagnosis is important because it has implications for the dog's prognosis. Once diagnosed, the goals of treatment are to maintain normal hydration, electrolyte and acid-base balance, to delay the progression of renal failure and its complications, to address the dog's uremia and to minimize loss of protein in the urine. The dog's prognosis depends on the extent of the dysplasia, the age, the severity of dysfunction at diagnosis and subsequent treatment. Renal dysplasia is irreversible, and long-term prognosis is poor. At a minimum, owners are advised not to breed affected dogs. Certainly, data on such dogs should be recorded in the Berner-Garde database.

Glomerulonephropathy, classified as an inflammatory process disease, is associated with abnormality in the glomeruli, the tiny tufts of capillaries used in filtration referred to previously. It is primarily a problem of filtration in which the glomeruli "leak" large molecules such as proteins that are then urinated away rather than retained in the body. This condition is called proteinuria (protein in the urine). Retention of proteins is important to the body for several reasons. One of these proteins, albumin, keeps water in the bloodstream. In addition, many substances needed by the body are not water-soluble and so they will not dissolve in the blood stream. Fortunately, non-water soluble substances bind to the albumin enabling transport where they are needed to other parts of the dog's body. Because the albumin molecule is relatively small, it is often among the first proteins to enter the urine after glomeruli are damaged, serving as an early warning system for even minor kidney dysfunction. As the level of albumin in the blood declines, fluid in the body is retained. In more critical cases, the chest and abdomen fill with fluid causing other problems.

Glomerulonephritis is believed to be the most commonly occurring glomerular disease in dogs. Bernese Mountain Dogs are known to have familial glomerular disease. Glomerulonephritis is the result of immune-mediated injury to the glomeruli. Immune complexes develop or are deposited on the membranes of the tiny capillaries of the glomerulus. Once this happens a cascade of events takes place that further damages the glomerulus. In lay terms, antibody complexes stick to the walls of the glomeruli



photography by: Carol Maurin

and summon other inflammatory cells. These work to create holes in the glomerular membrane that are large enough for proteins to pass through and be lost. Often some other underlying disease (e.g., infection, inflammation or cancer) stimulates this immune-mediated process.

Glomerulonephritis is often difficult to diagnose, and diagnosis is complicated. The classic sign of glomerular disease is protein excreted in the urine (proteinuria), measured as a urine protein: creatinine ratio of less than one in a urine sample containing no blood or inflammation. Unfortunately, even this is not definitive. Dogs with glomerulonephritis can have creatinine ratios as low as 1 or in excess of 40. Kidney biopsy provides a definitive diagnosis of glomerular disease, but if the dog is already azotemic (has high levels of serum creatinine), its value in diagnosis may be reduced. One common clinical finding in dogs with glomerular disease is hypertension; in one study 93% of dogs with chronic kidney failure also had hypertension. As in humans, control of blood pressure is critical to prevent further damage to the kidney. What is perhaps most important for the BMD owner to take away from this article is that many glomerular diseases develop secondarily to a systemic infectious (e.g., bacterial, brucellosis, pyometra), inflammatory (e.g., chronic dermatitis, IBD, polyarthritis), or neoplastic (e.g., lymphosarcoma, mast cell sarcoma, carcinoma) disease process. Hence, diagnosis and treatment of the predisposing underlying disease is normally the first step in the management of dogs with glomerulopathies. Once this is done, treatment is focused on reducing proteinuria and addressing uremia. Typical approaches include low-protein, low-sodium, low-phosphorus diets, medication (ACE inhibitors such as Enalapril), aspirin and Omega 3 fatty acid supplementation. Adequate exercise may help to reduce fluid retention (edema and ascites). All therapy programs require careful monitoring of the dog, and making an accurate prognosis prediction is difficult.

Suspected Modes of Inheritance for Renal Dysplasia and Glomerulonephropathy in BMDs

While there are exceptions (e.g., Samoyed), most canine kidney disorders are inherited by an autosomal recessive trait. It is believed that kidney dysplasia is inherited this way. That means that if an affected puppy is produced, then both the sire and the dam are carriers of kidney dysplasia, although



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they are most likely unaffected.

Like other diseases that are passed on this autosomal recessive way (e.g., vWD or IHPSS in Bernese), normal-looking carriers are also produced when one or both parents have carrier status. These carrier puppies, if bred, will pass on this defective gene to some of their puppies as their parents did to them. If they are bred with another normal-looking carrier, on average 25% of their puppies will be born with kidney dysplasia and on average half the litter will be normal-looking carriers. If they are bred with a genetically normal dog, on average 50% of their puppies also will be carriers.

In the face of an autosomal recessive mode of inheritance, the ease with which a silent epidemic can be born in a breed

One need only look at Dobermans and vWD for an example of what can happen – in a screening of over 15,000 Dobermans, over 70% were found to carry the vWD gene, either as carriers or affecteds.

is astonishing.

Despite the absence of a genetic test, there are things that conscientious breeders can do to reduce the spread of this disease among the BMD population. Remove breeding stock that has produced an affected puppy from further breeding, and record their data in the Berner-Garde database.

Unlike renal dysplasia, the mode of inheritance for glomer-

ulonephropathy, found in Bernese Mountain Dogs, is unknown. This makes developing breeding strategies more difficult. Obviously, affected dogs should not be bred. Data on affected dogs should be entered into the Berner-Garde database.

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AMERICAN KENNEL CLUB
CANINE HEALTH FOUNDATION

BMDCA Members Awarded 2008 AKC-CHF President's Award

Congratulations to the members of the Bernese Mountain Dog Club of America, Inc. on winning the prestigious AKC Canine Health Foundation's 2008 President's Award. This honor is bestowed annually on an individual or club making an extraordinary contribution to the mission of the AKC Canine Health Foundation.

Announcing the winner of the Award on August 26th, Cindy Vogels, President of the the AKC-CHF, said, "The BMDCA has been a model in demonstrating a commitment to conquering the diseases which threaten our dogs." She added, "Always generous contributors, the Berner community has made an enormous effort already this year, raising more than \$60,000 for the BMDCA Donor Advised Fund."

Formal presentation of the President's Award will be made at the AKC Gala By the Bay in Long Beach, California, on December 12, 2008. Thank you to everyone whose generosity made this honor possible.