

**Differentiating Renal Dysplasia (Juvenile Renal Disease) from Protein-Losing Nephropathy (PLN) in our Wheatens**

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We have a genetic predisposition for two types of kidney disease in our Wheaten community, namely Protein-Losing Nephropathy (PLN) and renal dysplasia (Juvenile Renal Disease, JRD). Phenotypic expression can be mild to severe. Some individuals and families may be affected by both of the diseases. Based on the reporting of documented cases for the Open Registry, PLN is much more commonly seen.

Please let us know of cases of PLN and/or JRD (if you haven't already), not only for the Open Registry, but also for our DNA bank and future genetic studies.

**JRD:** The most severely affected animals with JRD usually die before 2 to 3 years of age, however mild cases may live much longer. The typical cases have clinical signs of renal failure due to decreased renal mass/reserve that affects the entire nephron (the functional unit of the kidney). In this scenario, dogs start to show increased thirst and make lots of watery urine (due to the loss of the ability to concentrate the urine to conserve body water) even before blood values of toxic waste substances (normally excreted by the kidney) become abnormally high. In other words, with decreased renal reserve, polyuria and polydypsia (PU/PD) with low Urine Specific Gravity (USG) precedes azotaemia (high BUN and serum creatinine values). There may be some proteinuria as well, and this may be confused with early PLN.

As renal failure progresses, other signs of uraemia can be seen, such as vomiting, decreased appetite, weight loss, anaemia, bone loss, hypertension, etc. Ultrasound examination of the kidneys may show small, irregular, hyperechoic kidneys with a thin cortex, dilated pelvis, and possibly cortical cysts. Histopathologic findings of a renal wedge biopsy (taken after 16 weeks of age, when the kidneys should be mature), shows abnormal architecture, maldevelopment/disorganization, with immature fetal glomeruli and fetal mesenchyme. Sometimes, other changes of chronic renal disease are seen, e.g., fibrosis, dilated tubules/cysts, and inflammation.

Dogs with JRD may be predisposed to pyelonephritis (kidney infection). Many breeds have been found to have JRD; but since a concert of functioning genes probably are needed for normal maturation of the kidney, a variety of genetic abnormalities may cause this same phenotype. Thus, genetic markers found for one breed may or may not be usefully applied to another breed. Lhasa apsos and Shih tzus, having a similar genetic evolution, may have their own genetic defect(s) causing JRD, while Wheatens may have another.

Geneticist Dr. Urs Giger at Penn (215-898-8830, [penngen@vet.upenn.edu](mailto:penngen@vet.upenn.edu)) is requesting DNA samples from Wheatens with documented JRD.

**PLN:** Most dogs sick with PLN have been diagnosed between the ages of 4-8 years (mean 6.5 yrs.); however, there is no age limit for diagnosis.

The cause of their PLN appears to be an immune dysregulation with immune-mediated disease affecting the glomerulus of the kidney nephron. The tubules are OK in the beginning (that's why they can still concentrate their urine); but eventually, the tubules and interstitium also suffer. Ultrasound of the kidneys may not be helpful. Histopathologically, immune-mediated glomerulonephritis and/or focal segmental glomerulosclerosis are predominant, sometimes with secondary interstitial inflammation. Amyloidosis (another cause of PLN) is rarely seen. Many but not all dogs have concurrent or past history of allergy, inflammatory bowel disease (IBD), and/or protein-losing enteropathy (PLE). Food allergies may play a role, but we do not know for sure what antigens may be involved in this immune complex disorder.

Dogs with PLN usually do not have PU/PD or a low USG until late in the disease process. The earliest warning sign of PLN is protein in the urine (proteinuria), and is often occult. We recommend urine screening for all Wheatens, at least annually, using the ERD (Heska) in-house test for microalbuminuria or screening the Urine Protein/Creatinine ratio (Up/c). Although many labs use 1.0 as their cut-off for a normal Up/c, veterinary nephrologists now consider a Up/c over 0.2 to be abnormal, especially in younger dogs.

Borderline results need to be monitored closely for a trend. Since many things can cause proteinuria (e.g. infection, some medications, hypertension, etc.), interpretation of the findings must include evaluation of the individual case. Later stages of PLN usually include decreased serum albumin (unless masked by dehydration) and increased BUN and serum creatinine. Serum cholesterol is usually high, unless concurrent PLE exists. Clinical signs may include weight loss, thromboembolic events (e.g. pulmonary embolus causing difficulty breathing, saddle thrombus causing difficulty walking), hypertension, edema/effusions, and eventually the other signs of renal failure (vomiting, decreased appetite, PU/PD, etc.).

Dogs with PLN were reported in 2000 to have a median survival of only 3 months, but they have been living much longer now with interventions such as diet changes, ACE inhibitors, low dose aspirin, anti-hypertensives, omega 3 fatty acid supplementation, etc. At Penn, we are collecting DNA samples from dogs with PLE and/or PLN as well as DNA from geriatric dogs without these diseases. (215-898-9288, [merylitt@vet.upenn.edu](mailto:merylitt@vet.upenn.edu)).

Of course, we are especially worried about genetic renal problems in our Wheatens, but renal function may also be impaired by infections (e.g. bacterial infections, Leptospirosis, tick-borne infections), toxins (e.g., antifreeze/ethylene glycol, grapes/raisins, non-steroidal anti-inflammatories, aminoglycoside antibiotics), etc. Sometimes PU/PD and increased BUN and serum creatinine are due to another disease entirely (e.g. Addison's disease, another predisposition in our breed) and not even due to kidney disease. Treatment, monitoring, prognosis, breeding decisions, and our DNA bank (matching up phenotypes/genotypes) depend on making an accurate diagnosis. Consultation with (or referral to) a veterinary specialist may be indicated. You can find one by going to [www.acvim.org](http://www.acvim.org) and clicking on "Find a specialist near you."

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