

Recommendations Concerning Protein-Losing Nephropathy (PLN) in Soft Coated Wheaten Terriers

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1. I recommend having each dog's DNA sample tested for the PLN-associated variant alleles at Dr. Paula Henthorn's lab at Penn Vet. The results will help you know the individual's risk for developing PLN in its lifetime and help you with decisions about breeding partners.
 - a. The information about how to submit DNA samples (cytology brushes for cheek swabs, samples of whole blood or semen) is found at www.scwtca.org/health/dnatest.htm.
 - b. Dogs with homozygous positive genotype (2 copies) have the highest risk of developing PLN, dogs with heterozygous genotype (1 copy) have an intermediate risk, and dogs with homozygous negative genotype (no copies) had the lowest risk of developing PLN during their lifetimes. Any breed dog can develop PLN, which can be due to infectious, inflammatory, neoplastic, toxic, or genetic influences.
 - c. The current effort is to choose mates for dogs so as to avoid producing homozygous positive dogs. Since the allele frequency is high, culling heterozygotes is not recommended since it would lead to loss of genetic diversity in the breed and possible future (other) genetic problems. Thus, healthy dogs that are carriers of one or two copies should have mates that are homozygous negative, so that puppies will be clear or heterozygous at most.
2. Every healthy Wheaten should be screened (blood and urine tests) annually for changes that might suggest the genetic predispositions for the breed (PLN, protein-losing enteropathy (PLE), Addison's disease, renal dysplasia, etc). There are no genetic tests yet for these except for PLN. Dogs that are carrying one or two copies of the PLN-associated variant alleles should be checked for proteinuria more often, perhaps 2-4 times a year, especially after age 3 years. Dogs that are sick should have a thorough work-up.
 - a. Annual recommended screening usually involves urinalysis (SG, dipstick, sediment), either microalbuminuria or urine protein/creatinine ratio (UPC), CBC (complete blood count, to check for cytopenias, eosinophilia), metabolic biochemical screen (Chemscreen, including creatinine, BUN, total protein, albumin, globulin, Na, K, Ca, Phos, glucose, ALT, Alk phos, and cholesterol), and in tickborne or heartworm endemic areas, a SNAP-4DxPlus or AccuPlex4 test. An SDMA test is also helpful to evaluate kidney function. A 'minimal screen' (less expensive) might include a urine SG/dipstick, blood PCV/TS, creatinine, BUN, albumin and globulin. If any tests are abnormal, further work-up is advised.
 - b. If proteinuria is found or suspected, interpretation must be made regarding urine pH, sediment, if the sample were taken post-ejaculation, post-prandial, whether the sample was obtained from home or in the clinic, and whether the dog is hypertensive or on medication that could raise blood pressure measurement (eg, phenylpropanolamine for urinary incontinence).
 - c. If samples are requested for UPC determination, either for screening or to monitor PLN dogs that are on treatments, because of daily variability it is suggested that 3 samples

be brought in from home, collected each day (first morning sample is best) for 3 days, saved in the refrigerator, and brought to the vet so that equal aliquots (1 ml) of each sample can be mixed together and submitted as one sample, to get an averaged UPC determination. Daily variability can be as much as 80% for dogs with UPC of 0.5 and 35% for dogs with UPC of 12.0. Normal UPC is less than 0.2; borderline is 0.2-0.4, and greater than 0.4 is abnormal.

3. When a dog has proteinuria:

- a. It could be due to pre-renal, renal, or post-renal causes. Even if the dog is a carrier of one or two copies of the PLN-associated variant alleles, it should not be assumed to have PLN (renal cause) and will need a work-up, for instance to rule out urinary tract infection, tickborne/heartworm disease, neoplasia, hypertension, and consideration of other causes for PLN such as amyloidosis, lupus, shigatoxin (raw meat diet), etc.
- b. Each dog's diagnosis and management plan must be individualized. For instance, dogs with PLN should be fed a renal diet that is modified to be lower in protein and phosphorus. But if the dog also has had food allergies, inflammatory bowel disease, PLE, pancreatitis, skin or ear issues, then the diet also needs to be lower in fat and also hypoallergenic. There are specific diets that are recommended depending on the needs of the individual. Likewise, medications such as ACE inhibitors, antihypertensives, anti-thrombotics, omega-3 fatty acid supplements, antimicrobials, etc. are individualized depending on the dog's test results and tweaked, based on monitoring over time. I have seen dogs with PLN live quality lives for much longer than in the past because we are screening for occult abnormalities and starting interventions earlier than we used to, when they can really have impact to slow the progression of disease. There are 8 recent IRIS Consensus papers concerning the diagnosis and treatment of PLN that I recommend. They are available on-line at <http://onlinelibrary.wiley.com/doi/10.1111/jvim.2013.27.issue-s1/issuetoc;jsessionid=55A453D9706C2FD288D76133300774F4.f04t01>
- c. Since these cases can be very complicated, I recommend getting a consultation with a specialist near you who is Board Certified and a Diplomate of the American College of Veterinary Internal Medicine, with the initials 'DACVIM' behind their name. Your vet can recommend one or you can find one near you by going to www.acvim.org.
- d. After 41 years of vetting and a wonderful 38-year career at Penn Vet, I retired in July 2016. I am still travelling, speaking, writing, and giving on-line advice. If you want my opinion concerning questions about Wheaten or Airedale genetic diseases (PLN, PLE, inflammatory bowel disease, food allergies, Addison's, renal dysplasia), Lyme and other tick-borne diseases, Leptospirosis, vaccinations, etc., or you want a consultation regarding a sick or healthy dog, you and your vet can still reach me at merylitt@vet.upenn.edu, however, my on-line advice is no longer free. Fees for 'fast' questions are \$25-50 and consultations are \$125-250, depending on complexity. Since I may be travelling, I may not respond to your emails as fast as I used to. I do hope you and your loved ones stay well so you can enjoy each other for a long, long time!
Take care. -Meryl