

Update on Cystinuria in Scottish Deerhounds
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Cystinuria is a renal transport defect of certain amino acids, building blocks of proteins. Instead of having these amino acids resorbed by the kidney, they leak into the urine. The degree of leakage and amino acids involved seems to differ. However, one of the amino acids, cystine, has a tendency to precipitate in acid urine and lead to calculi formation. It is these calculi that can cause severe illness as they irritate the urinary track system and sometimes cause blockage.

Cystinuria has been described in >60 dog breeds, cats, maned wolves, and humans. Much about this disease in dogs has been learned from the study of the cystinuric Newfoundlands. Similar to humans, cystinuria is an autosomal recessive trait caused by a mutation in the renal basic amino acid transporter in Newfoundlands. Nitroprusside testing has been offered and has found to be reliably and consistently to be positive in affected animals and negative in unaffected animals. Now DNA-based testing in the Newfoundland is available and allows the detection of affected, carrier and normal dogs. Urine and DNA studies have clearly helped this breed to deal with the worldwide problem and informed breedings can now assure healthy offspring.

Studies of cystinuria in the Scottish Deerhound and some other breeds indicate that the situation is less clear. Despite extensive and ongoing work at the clinical, biochemical and molecular level, the cystinuria has not been clearly defined and is certainly different from cystinuria in Newfoundland dogs.

Currently we offer the nitroprusside test as a screening test to detect animals that are at risk of developing clinical signs of cystinuria. False positive are very unlikely unless animals are on specific drugs; we do require the animal to be on a normal diet and on no medication except heartworm preventative. Whereas in the Newfoundland breed every, cystinuric dog has a positive nitroprusside test, we have observed in other breeds, dogs that have had cystine calculi but have had negative nitroprusside tests, suggesting that the cystinuria is transient. In order to confirm our results and further understand the expression of the defect, many urine samples that test positive by the nitroprusside test are further analyzed with semi quantitative nitroprusside testing and amino acid quantitation, a lengthy and expensive procedure. At this stage in our investigations, we do not have enough information to accurately predict how likely it is for a dog that has excessive cystine in the urine to develop cystine stones or other clinical manifestations.

Dietary interventions in the form of cystine restriction are difficult to achieve and have not appeared to be helpful in cystinuric people and dogs. Alkalinization, diuresis, drug therapy, and surgical management may be considered by the veterinarian to prevent recurrence of cystine stone formation.

Whereas in Newfoundland dogs and humans, cystinuria is seen in both males and females, it appears that mostly males are affected in many breeds, including Scottish Deerhounds. At this time we do not definitively understand the mode of inheritance, but consider X-linked recessive and sex-limited autosomal recessive modes as possibilities, in addition to more complex patterns. We are adjusting our reporting forms to further reflect our lack of knowledge of cystinuria in Scottish Deerhounds.

Thus, after our initial enthusiasm based on the progress made in the Newfoundland, we now have data indicating that the situation in the Scottish Deerhound and some other breeds is more complicated and different from the situation in Newfoundlands and in humans. We are poised to continue the research to further define the clinical course, the mode of inheritance, and molecular basis of the cystine defect in Scottish Deerhounds and other canine breeds. Our goal is to develop a comprehensive understanding of the disease that will allow us to develop DNA-based tests that can be used to make rational breeding decisions that will allow breeders to eliminate the risk of cystinuria while preserving desirable traits in their breed. Much more work is needed.