

Cystinuria

Disease Description:

Cystine, an amino acid, is one of the building blocks of proteins. Amino acids are part of a normal animal's diet and are absorbed through the intestine. Although they are filtered through the kidney, amino acids are normally reabsorbed (nearly 100%) by special kidney transporters and are not lost in the urine.

In dogs and cats with cystinuria, the kidney transporter for cystine is defective. In acid urine, cystine precipitates to create crystals, which may further precipitate to form calculi (stones) in the kidney and bladder. These calculi can cause serious illness including complete urinary blockage, which is a medical emergency. Because male dogs have a narrower urethra than female dogs, male dogs are more likely to become completely blocked. In this case, the urinary bladder may greatly distend and rupture if not properly managed. Urine may then back up into the kidneys, and the resultant pressure on the kidney may cause cell death and kidney failure. Without appropriate and immediate care, such complications can lead to death. Although cystinuria affects many dog and cat breeds, the most severe form seems to affect Newfoundland dogs.

Cystinuria is inherited as an autosomal recessive trait in the Newfoundland dog. In other words, affected Newfoundland dogs have two mutant genes, one inherited from each parent. Carriers have one mutant gene and do not show clinical signs. We have discovered that one affected Newfoundland stud dog sired over 100 offspring. Thus, all of his offspring are carriers that can, in turn, pass the mutation to their offspring.

Supported by a grant from the NIH and the AKC Canine Health Foundation, the University of Pennsylvania School of Veterinary Medicine discovered the molecular defect in the Newfoundland and Labradors and developed genetic tests for carriers. We are also seeking to determine the molecular defect in other breeds as well. As one example, Mastiff dogs are also known to be cystinuric. However, the gene that is abnormal in the Newfoundland is normal in the Mastiff. Therefore, another, yet undiscovered gene is responsible for the type of cystinuria seen in the Mastiff.

The Section of Medical Genetics at the University of Pennsylvania has several tests to detect affected dogs. We usually test for cystinuric animals of any breed with the nitroprusside urine spot test, which requires a small amount of urine. This test accurately identifies cystinuric dogs (dogs with two mutant genes). In addition, we can also reliably analyze calculi (even when only pinpoint in size) for cystine. Carriers (one mutant and one normal gene) can accurately be detected in the Newfoundland and Labrador Retriever breeds using the breed-specific DNA tests. In order to develop a DNA test in other breeds we need blood (10 to 20 ml blood in EDTA) and urine (2 to 5 ml) from cystinuric dogs and their relatives.

Although any dog can be checked for cystinuria, we recommend testing the following dogs:

Dogs showing suspicious clinical signs.
Relatives of known cystinuric or carrier dogs.
Newfoundland dogs used for breeding.
Other dogs of breeds known to show cystinuria and which are used for breeding.
Puppies that are older than four weeks of any breed known to show cystinuria to prevent the sale of affected puppies.

Clinical Signs:

Cystinuric dogs often show signs of a recurrent urinary tract disorder. Clinical signs may start at almost any age. In Newfoundland dogs, affected animals show clinical signs of illness as early as 6-months of age. Affected dogs may have problems with urination. They may produce blood-tinged urine and pass calculi, or they may be unable to void urine despite numerous attempts.

Affected Breeds:

Any Breed (Canine or Feline), Newfoundland dogs are particularly susceptible. DNA Tests are available for Newfoundlands and Labradors.

Required Samples:

DNA Test (Newfoundland and Labroador ONLY)- EDTA Blood, 1-2 mL
Nitroprusside Urine Spot Test - Urine in a Plastic Vial, 2-5 mL

Cost:

See PennGen Cost Price Sheet for current pricing of both DNA and Urine Tests

*To submit for a Cystinuria DNA test please use our **DNA Submission Form***

*To submit a sample for Urine Cystinuria (Nitroprusside) please use **our Metabolic Submission Form***