Pyruvate Kinase (PK) Deficiency

Description: Pyruvate Kinase deficiency (synonym: erythrocyte pyruvate kinase deficiency) in red blood cells (erythrocytes) causes a severe hemolytic (red cell rupture) anemia as a result of the premature destruction of PK deficient red blood cells. PK is a key regulatory enzyme in a metabolic pathway that generates almost all energy from glucose (sugar) in red blood cells. The clinical signs of anemia are very pale mucous membranes (gums), increased heart rate and pounding pulses, weakness and exercise intolerance. The liver and spleen may be enlarged, and after one year of age, the density of all bones, particularly long bones and skull, appear radiographically increased. Affected dogs that are well confined may not show any obvious signs, but may acutely decompensate and die when severely exercised or stressed.

Age of Onset: The disease is most often recognized between 4 months and 1 year of age, but may not be detected until later in life, if a dog is not very active. Affected dogs develop relatively mild clinical signs during the first year of life, despite severe anemia.

Diagnosis: After excluding the more common causes of hemolytic anemia (autoimmune, toxic and infectious hemolytic anemia), PK deficiency should be considered. A chronic, severe, highly regenerative hemolytic anemia (PCV 15 - 27%) associated with increased radiographic bone density in older animals is highly suggestive of PK deficiency. PK deficiency is diagnosed through DNA analysis. A simple determination of PK activity does not provide a diagnosis of an affected dog, but does allow the detection of carriers. Blood samples must be specially handled and arrangements must be made prior to submitting the sample to a specialized laboratory.

Treatment: There is no simple treatment. Splenectomy and glucorticosteroid therapy are not helpful. Iron chelation may be considered when large iron deposition occurs in tissues. Experimentally, bone marrow transplantation has been shown to cure the disease. Affected dogs usually die at a young age (1 - 4 years) because of progressive anemia or hepatic (liver) failure.

Mode of Inheitance: The disease is inherited as an autosomal recessive trait. Carriers can be detected by measuring PK activity in erythrocytes. Carriers have half-normal PK activity in erythrocytes and are asymptomatic.
The disease occurs in West Highland White and Cairn Terriers, Basenjis, and Beagles.

Thanks to Dr. Urs Giger, University of Pennsylvania, for writing this description of pyruvate kinase deficiency.

PYRUVATE KINASE DEFICIENCY IN DOGS AND CATS

Urs Giger, Yashoda Rajpurohit and Tracy Anne Filler
Josephine Deubler Genetic Disease Testing Laboratory
Section of Medical Genetics
University of Pennsylvania
School of Veterinary Medicine

Pyruvate Kinase (PK) is an enzyme in glycolysis which is essential for the metabolism of glucose into an energy source utilized by cells such as red blood cells. Without this source of energy, red blood cells are unable to function properlyand are consequently destroyed. This process is known as hemolytic anemia.

Various genetic defects cause a PK enzyme deficiency, which causes anemia and is inherited as an autosomal recessive trait. This means that the affected animal must have two mutant PK genes to show clinical signs of the disease. Animals classified as carriers have one mutant gene and one normal PK gene and are clinically asymptomatic. These animals, however, can pass the mutant gene to their offspring.

PK deficient dogs and cats experience anemia, but the clinical signs are different. Affected **dogs** experience exercise intolerance, lethargy, severe chronic anemia, spleenomegaly and osteosclerosis. Affected dogs die because of anemia and hepatic failure and death by five years of age. Clinical signs of anemia in affected **cats** are intermittent with

episodes of pallor and lethargy. They do not develop osteosclerosis and may have a normal life expectancy. The oldest clinically diagnosed cat with PK deficiency was 14 years of age.

Genetic tests have been developed or established at the University of Pennsylvania to accurately diagnose PK deficiency in Basenji, West Highland White and Cairn Terriers, Abyssinians and Somali cats, in order to detect the presence or absence of the mutant gene. These DNA-based screening tests allow for the identification of affected, carrier and clear/normal animals from a small blood sample. These tests, therefore, can assist breeders and pet owners with important health and mating decisions.

We recommend to test animals that
1. display suspicious clinical signs such as chronic anemia,
2. relatives of affected or carrier animals, and
3. are considered to be bred.

Affected animals and carriers can pass the mutated allele on to their offspring and should therefore not be used for breeding. Carrier with exceptional traits may be bred to normal "clear" animals as long as all offspring will be tested before used for further breeding. This approach will decrease and could eventually eliminate the mutant gene from a breed.

Breeders and owners who wish to have their dogs and cats tested should submit 2-3 ml of EDTA anticoagulated whole blood (purple top tube). As affected animals may require a transfusion for treatment of anemia, blood typing (DEA 1.1 in dogs and A and B in cats) is recommended. The same EDTA-whole blood sample submitted for PK screening can also be utilized for the blood typing tests. These tubes placed in a tube mailer can be shipped to the address below. The results will be available three weeks after receipt of the samples. The test will cost $75 for the PK screening and an additional $15 for feline or canine blood typing. Please make checks payable to the Trustees of the University of Pennsylvania/Giger. All results will remain confidential. Please fill out the following on the next page and send all information and samples to:

Dr. Urs Giger/PK Deficiency
Veterinary Hospital, Room 4006
University of Pennsylvania
3850 Spruce Street
Philadelphia, PA 19104-6010

Phone: (215)898-3375
Fax: (215)573-2162
Email: *penngen@vet.upenn.edu*

For additional information and articles, please visit *www.westieclubamerica.com*.

PK Deficiency Information

Owner's Name: _____

Address: _____

City: _____ State: _____ Postal Code: _____

Telephone: _____ Fax: _____

E-mail: _____

Date of Sample Collection: _____

Dog's Name: _____ Sex: ❑ male ❑ female

Date of birth: _____ AKC # _____

Microchip # _____ Spayed/Neutered: ❑ yes ❑ no

Sire's Name: _____ AKC # _____

Dam's Name: _____ AKC # _____

Reason for Testing (select all that apply)

❑ General Genetic Screening ❑ Showing

❑ Suspicious Clinical Signs ❑ Breeding

❑ Puppy (at least four weeks old)

❑ Relative known to be affected (please state who) _____

❑ Other (explain) _____

Tests to be conducted

❑ PK DNA screening only $75

❑ Blood Typing only $15

❑ Both PK DNA screening and Blood Typing $90

Please send the sample, form, and check payable to **"Trustees, Univ. of PA/Giger"** 2-day delivery mail to:

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Philadelphia, PA 19104-6010

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