PK Deficiency Q & A

Following international collaboration, a set of questions on pyruvate kinase (PK) deficiency were compiled and co-ordinated by me, then put to Dr Urs Giger, who had earlier kindly agreed to answer them, for publication in the August 2004 issue of The Abyssinian Breeder magazine. Dr Giger is a world-leading scientist in this field, who researched the means of inheritance and established the DNA test that can be used to determine whether a cat is normal, a carrier or affected by PK deficiency. Affected cats may suffer from cyclical anaemia (see below) Dr Giger's CV is given at the end of this Q &A, just after a note on the method of inheritance and its consequences.

The questions are grouped and sequenced; Dr Giger's answers were provided in mid June 2004, and appear below each question, with borders around them for differentiation.

The questions arise because PK deficiency carriers – and even some affected cats – have appeared among Abyssinians and Somalis in the United States, Australia, New Zealand, Denmark, Germany and elsewhere in Europe. Some of us have had all our cats tested. Once carriers (if any) have been identified, steps can be taken to eliminate PK deficiency by keeping normal offspring from carrier-to-normal or (generally inadvertent) carrier-to-carrier matings. In this fashion, all lines and genetic diversity can be preserved. For more information on the implications of PK deficiency and how to test for it, go to http://www.vet.upenn.edu/research/centers/penngen/services/deublerlab/pk.html and follow the links given on that page. Additional, though slightly out of date information is available at http://www.abyssinianbc.org/PKDef_ursgeiger.htm (sorry about the mis-spelling of Dr Giger's name but that's the address).

Finally, those of us who have been through the hoops know to spell out "deficiency" in full, otherwise confusion can arise because the abbreviation "PKD" is customarily used to denote "Polycystic Kidney Disease", totally different from PK deficiency and not known to occur among Abyssinians or Somalis.

George Kennedy

1. PK Deficiency Tests

a. How exactly are results measured? (Is it a simple presence or absence of 'something', a particular 'something' falling within certain percentages of <?> in a scale, a particular spectrograph pattern?)

This is a DNA test that specifically detects the presence or absence of the mutant and normal allele (gene) for PK deficiency. After amplifying the DNA around the known PK mutation we are using a specific digestion procedure to differentiate the mutant and normal allele by size on a gel. A cat can either show only the normal allele (2 copies), or only the mutant allele (2 copies of the mutant, homozygous affected, or can have one normal and one mutant allele. Thus this is a definitive test. One note when submitting cheek swabs: we do need cheek cells rather than saliva, thus you must rub the brush on the inside cheek and follow the instructions carefully.

b. What proportion of test samples comes from outside the United States?
Currently we are the only lab testing for this PK mutation and after initially receiving exclusively samples from within the US, about 30% come from Europe and Australia

c. Do you envisage the tests becoming available at other laboratories, perhaps even outside USA?
Yes; however, shipping cheek swabs is easy, testing is not done frequently, and as long as we are getting the test results we can follow the frequency of the mutant allele

2. PK Deficiency in General

a. Roughly how many Abys and Somalis have been tested, and what proportion of these were found normal, carriers and affected?
About 1000 Abyssinians and Somalis have been tested since 1998, and the mutant allele frequency is very high at about 10 to 20% due to inbreeding practices. In humans diseases with a frequency of 1% are considered common.

b. Any thoughts on why PK deficiency in cats is encountered almost exclusively among Abyssinians and Somalis?
It appears likely that the mutation has a arisen in one of these breeds; they have the same mutation and thus all of these cats are related. High mutation frequencies are recognized in various breeds in cats and dogs as well as ethnic and geographical areas in people. For instance a high frequency for PK has been seen in the Amish population

c. Why have so few cats (zero in Denmark, apparently) been diagnosed with PK deficiency; there must be affected cats in different lines, so why haven't we met them as ill cats?

The number of cats tested in Denmark is small; it is well possible that these cats in Denmark are from a line free of the mutation. If there are carriers, matings between carriers may not have been done. Furthermore, only one quarter of a carrier-to-carrier mating will be affected and indeed not every PK-deficient cat will develop clinical signs or may only show intermittent mild signs or the signs are thought to be caused by something else, like haemobartonellosis or immune-mediated haemolytic anaemia.

3. Affected Cats

a. How likely is it that an affected cat will suffer from anaemia during its life?

This is not known, because many cats have been treated for anaemia before a diagnosis is made and others are screened for because of related cats are anaemic. Thus our sample pool is biased. Following PK deficient cats however indicates that they remain most of the time slightly anaemic. Cats can readily compensate for the anaemia presumably due to their life style.

b. What are the first clinical signs that an affected cat usually shows other than

anaemia; are there other signs as well?

The clinical signs vary and are unspecific, but lethargy, depression and lack of appetite may be observed. The gums may be pale and rarely icteric and the abdomen may be enlarged. Indeed, some PK-deficient cats are incidentally found to have been treated for other potential diseases including haemobartonellosis and immune-mediated haemolytic anaemia. In particular, some of the potent immunosuppressive agents are not helpful and can be harmful.

c. Is it beneficial to give affected cats special diets right from the start, e.g., high doses of iron?

There seems to be no problem with iron absorption and storage or utilization. In fact the body iron stores are adequate (normal) to increased, and further supplementation may cause hepatic and splenic organ failure and thus is not advisable. However, it is advisable to keep the PK-deficient cat on a well balanced diet to avoid any untoward stress and gastrointestinal upset. It is imperative to provide good care, a stress free environment, and routine health check ups.

d. What is the best treatment once the first symptoms start, or the best course of action for my vet to take?

The best treatment has not been scientifically determined. However, the diagnosis of PK deficiency will help the vet to avoid certain unnecessary or even harmful medications. Some cats may require some prednisone or even a splenectomy if the crises become more frequent. In a crisis they may also need a blood type compatible transfusion.

e. What are the prospects of a cat diagnosed as affected, for length and quality of life?

Many cats can live good lives for many years, with the oldest reaching thus far 12 years.

f. If you have bred from an affected cat to say a carrier, or carrier to carrier, and you know you have affected kittens, is it best just to pet these kittens out free, and tell the new owners, or keep them for observation, rather than euthanasing the kittens?

Affected cats should best be not bred. In case this has happened they should be sold and placement should be carefully considered as it can be a hardship for an owner to see the cat suffer and to pay for the medical care of the cat. I have adopted one of the affected cats and have enjoyed her tremendously over the past several years, with TLC as the only treatment albeit she is always anaemic.

g. Just how important is PK deficiency within the two breeds? This question is being asked because there are sceptics out there who don't think it is important??

Just like I discovered the blood type issue in the neonatal Abyssinians and Somalis hopefully have help many breeders to prevent neonatal isoerythrolysis (NI, hemolysis of the newborn), I am convinced that testing for PK and informed breeding away from

PK will improve the health of the breeds affected and prevent further suffering. Based upon our - albeit biased -frequency within the two breed this is an important health issue.

NOTE *No questions were asked on inheritance, since it was established by Dr Giger that pyruvate kinase (PK) deficiency is carried by a recessive gene and hence the usual laws of heredity apply, viz.:*

- *normal X normal matings always produce normal offspring;*
- *normal X carrier matings will on average produce 50% normal and 50% carrier offspring;*
- *carrier X carrier matings will on average produce 25% normal, 50% carrier and 25% affected offspring*
- *affected X normal matings will produce offspring that are all carriers*
- *affected X carrier matings will on average produce 50% carrier and 50% affected offspring*
- *affected X affected matings will always produce affected offspring*
- *only affected cats may get anaemia, not carriers*

Urs Giger received his veterinary degree from the University of Zürich, Switzerland, where he also pursued his initial clinical training in small animal medicine and surgery and a doctoral thesis on the orthopaedic correction of canine hip dysplasia. In 1981, he moved as a postdoctoral fellow to the United States where he subsequently completed a postdoctoral fellowship and residency in small animal medicine at the University of Florida.

He then joined the faculty of the School of Veterinary Medicine at the University of Pennsylvania in Philadelphia and has been over the years a clinician in the Medicine, Oncology, and Pediatrics/Genetics Service. He is currently the Charlotte Newton Sheppard Professor of Medicine and Chief of Medical Genetics and has a secondary professorship at the University of Zürich. He is a diplomate of the American and European College of the Veterinary Internal Medicine and is heading the Pediatrics and Genetics Clinic, the Metabolic Genetics Laboratory, the Josephine Deubler Genetic Disease Testing Laboratory, and the Transfusion Medicine Center at the University of Pennsylvania. His clinical and research expertise and interests are in hereditary and hematologic disorders of small animals and are reflected in over 150 original publications as well as many more reviews, chapters, and scientific abstracts.

He was the recipient of the International Scientific Lifetime Achievement Award in 2002 from the World Small Animal Veterinary Association and the John McCoy award in 2004.

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