

## **Pyruvate kinase (PK) deficiency**

**Andrea Harvey, FAB Clinical Associate, University of Bristol Veterinary School**

### **What is PK deficiency?**

Pyruvate kinase (PK) deficiency is an inherited disease occasionally encountered in Abyssinian and Somali cats, and also reported in the domestic shorthair cat. Pyruvate kinase is an enzyme found within red blood cells which enables them to produce energy to survive. If this enzyme is lacking, the lifespan of the red blood cells is significantly reduced, resulting in a reduction in the number of red blood cells in the circulation (anaemia).

### **What signs does it cause?**

The main consequence of the disease is the development of anaemia. However since the body can quickly manufacture new red blood cells the anaemia is usually only intermittently detectable. Most of the time the anaemia is either only mild, or occurs gradually, enabling the cat to adapt to the anaemia and not show any obvious symptoms. Anaemia often results in only vague signs such as lethargy and inappetance. However, a rapid severe life-threatening anaemia can also develop. Although PK deficiency is hereditary, since the anaemia is usually mild and clinical signs may not be obvious, the anaemia may not be noticed until the cat is quite old.

### **How is PK deficiency inherited?**

The disease is inherited as an autosomal recessive trait (figure 1). This means that a cat can be carrying the defective gene (heterozygous) without having any symptoms of the disease at all. Affected cats (homozygous) arise when 2 carrier cats are mated with each other. Since carrier cats remain healthy, and the anaemia of affected cats may not be detected until they are a few years of age, the potential exists for carrier cats and affected cats to have had significant numbers of offspring before the disease is identified. However, the positive side of this is that it also means if carrier cats are identified they can still be used for breeding as long as we ensure that they are NOT mated with another carrier. Mating a carrier with a non-carrier will not produce any offspring that will suffer from PK deficiency, and 50% of the offspring will be free of the defective gene. As long as the offspring are also tested, even carriers can be bred from again as long as it is ensured that they are only mated with a non-carrier cat. In this way, controlled breeding programmes can be implemented so that important lines can be retained within the gene pool.

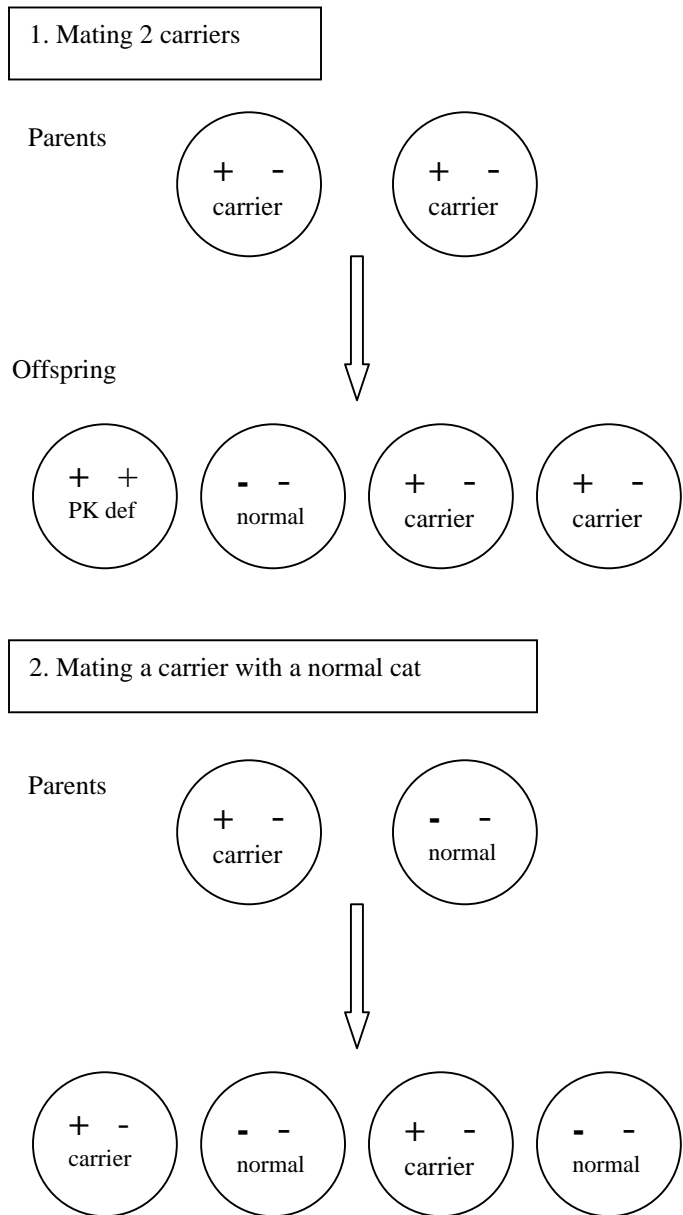
### **What tests are available and can carrier cats be detected?**

Fortunately a reliable test does exist for PK deficiency. It comprises a DNA test that is performed on either a blood sample or cheek swab. Only one laboratory, the Josephine Deubler Genetic Disease Testing Laboratory at University of Pennsylvania in the US, is able to do this test. Affected cats as well as carrier cats can be identified with the test. However the test is expensive (\$75 per cat; approximately £43) and additional costs of taking samples and shipping them to the US further increase the cost.

**Figure 1: Diagram illustrating how PK deficiency is inherited**

**Key:**

- + = chromosome with defective gene
- = chromosome without defective gene



**Why worry about PK deficiency?**

- PK deficiency is inherited and although predominately a problem in the US it is being reported increasingly in cats throughout Australia, New Zealand and Europe, including the UK. Approximately

2500 cats have been tested at Pennsylvania since 1998, and around 15% of those have been found to carry the defective gene (personal communication, Giger U, 2005).

- As described above, the clinical signs that develop can be serious and life threatening
- Because initial clinical signs can be mild or go unnoticed, affected cats may not be identified until after they have had large numbers of offspring
- Carrier cats do not show any clinical signs at all. The disease occurs when 2 carrier cats are mated with each other. This is important because a large number of carrier cats can arise in a population before PK deficiency is even noticed
- With any genetic disease, by the time the disease becomes an obvious problem within a population it is much more difficult to control and involves a lot more expense and heartbreak.

### **THE GOOD NEWS!**

- Although we know that the disease is already present in the UK, affected cats do not yet appear to be very prevalent in the UK. Identifying carrier cats NOW could stop PK deficiency becoming a prevalent disease in the UK
- We can reliably test for affected cats, including identifying asymptomatic carriers
- With help from all Abyssinian and Somali owners, breeders and breed clubs we can identify the prevalence of PK deficiency in the UK (see below project details)
- If carrier cats are identified they can still be used for breeding (and must be still used to retain a diverse gene pool) as long as we ensure that they are NOT mated with another carrier.

### **How can we tackle this disease together before it becomes a problem in the UK?**

- We know that there are some affected cats in the UK already, but we do not know how many cats are affected or are carriers. It is possible that there could be a large number of carriers.
- The first step should be to try and establish the prevalence of the disease within the UK.
- In order to do this we need to test as many Abyssinian and Somali cats (breeding and neuter cats of all ages) as possible.
- Once we know the prevalence of the disease in the UK we can establish effective breeding programmes to prevent carrier cats being mated with each other, in order to eradicate PK deficiency from UK Abyssinian and Somali cats, while maintaining the desired qualities in these breeds.
- It is extremely important that carrier cats ARE still bred from (but in a controlled way) since if they are all neutered, the gene pool will be significantly reduced which will increase the risks of other genetic problems arising.

**NB** It is important that we recognize and tackle this problem now to ensure that PK deficiency does not become a problem in UK cats. However, we do not want to unduly worry owners of Abyssinian and Somali cats, as to date, the disease has been rarely recognized in the UK and many breeders are already testing for the disease.

### **Current project**

We have begun a project to try and determine the prevalence of PK deficiency in UK Abyssinian and Somali cats. This is being done in collaboration with Urs Giger from the Josephine Deubler Genetic Disease Testing Laboratory at University of Pennsylvania, whereby they will perform the testing for a much reduced cost of \$30 (approx £16.50) per cat if we send them large numbers of DNA samples in batches. In addition to performing the actual testing, there are also several other steps involved which further increase the cost of testing including the cost of swabs, taking the cheek swabs from cats, extracting the DNA from the swabs and sending the DNA to the US. We had applied for a grant to enable all of these costs to be covered so that there would not be any costs involved for owners. Unfortunately we were not awarded this grant. However, the University of Bristol has raised funds to cover the costs of the swabs, travel/taking the swabs, DNA extraction (£10 per sample) and postage, which just leaves £16.50 per cat to be raised to enable the project to go forward.

The main problem we are currently encountering is that whilst most breeders are willing to pay this reduced cost to test their own breeding cats, not many people are willing to pay to test neutered or retired breeding

cats as it is of no significance to breeding programmes whether these cats are carriers or not. However, it is very important that we also test neutered pet cats and cats of all ages, in order to obtain enough samples to give us meaningful results regarding the prevalence of the defective gene in the UK. Furthermore since the numbers of breeding cats is relatively small, it is unlikely we will be able to offer the low cost of testing if we are only testing breeding cats.

We therefore are unable to offer this reduced cost to enable testing of specific individual cats, but are instead looking to raise enough funds through donations towards the study to enable us to test at least 150 Abyssinian and Somali cats in the UK, to include breeding and neutered cats of all ages. Although we have already begun sampling some cats, we are unable to process these samples or take further samples until we have raised sufficient funds. We are hoping that owners that were willing to pay for their cat to be tested will still contribute the same amount of money to the project, but please be aware that this will be partly used to help test other neutered and retired breeding cats. We are hoping that the remainder of the required funds will be donated by the breed clubs and other individuals.

Any additional funds raised will be used to test additional cats in the future and/or put into a fund to help with the treatment of any cats suffering from PK deficiency.

**Please note** that samples submitted for this study will be tested in batches once the target number of samples has been taken, as this is the only way that we can cover the costs for the study. We can therefore not guarantee how long it will take before results are obtained, as this will depend on how long it takes us to raise the necessary funds and obtain all the samples. We can only offer this reduced cost for testing for samples submitted for the purposes of this study. Owners who require test results more urgently will need to have their cats tested by the conventional route (ie sending samples directly to University of Pennsylvania, cost \$75 per cat)

If you would like any further information regarding the study, or if you would like to make a donation towards this study please contact **Andrea Harvey at The Feline Centre, University of Bristol Veterinary School, tel. 0117 928 9558, fax 0117 9289559, email: [a.m.harvey@bristol.ac.uk](mailto:a.m.harvey@bristol.ac.uk)**

Please send donations to Andrea at the above address. Cheques should be made payable to The University of Bristol, but please include a note stating that it is a donation for the feline PK deficiency study.