WINN FELINE FOUNDATION
For the Health and Well-being of All Cats
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Feline Hypertrophic Cardiomyopathy: Advice for Breeders

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What is hypertrophic cardiomyopathy?

Hypertrophic cardiomyopathy (HCM) is the most common heart disease of cats, whether they are random bred or pedigreed. It is a primary heart muscle disease in which the papillary muscles (the muscles in the left ventricle that anchor the mitral valve) and the walls of the left ventricle become abnormally thickened. HCM may be a progressive disease (it gets worse over time) or it may remain stable. Those cats that progress to having severe HCM often develop heart failure when the muscle thickening and subsequent scarring of the heart muscle significantly affects heart function (makes the left ventricle stiffer than normal, akin to turning it to stone). Cats with the disease may die suddenly and may develop a blood clot in the chamber above the left ventricle (i.e., the left atrium) that often then gets carried into the systemic arterial system, most commonly lodging in the terminal aorta, stopping blood flow to the rear legs.
For more general information on HCM, see: http://mysite.verizon.net/jachinitz/hcm/

What causes HCM in cats?

This is currently unknown in most cats although familial (hereditary) HCM has been observed in several breeds, such as the Maine Coon and Ragdoll. Anecdotal information suggests there is "familial" HCM in many other breeds. Heart muscle hypertrophy (i.e., thickening) in cats can be caused by other diseases, such as systemic hypertension (high blood pressure), aortic stenosis and hyperthyroidism. HCM is a primary disease of the heart muscle. Systemic hypertension, aortic stenosis and hyperthyroidism cause secondary thickening of the left ventricle and so are not causes of HCM (although it is probable that hypertension and hyperthyroidism exacerbate the disease if they become present in a cat with mild to moderate HCM when the cat is older). HCM is diagnosed when the left ventricle is too thick and these other causes are ruled out.

Is HCM genetic?

In Maine Coons and Ragdolls, HCM has been confirmed to be inherited as an autosomal dominant inherited trait and to be caused by a gene mutation (i.e., a change in a gene base pair) in each, as it is in humans where over 1000 mutations in 18 genes have been found to cause the disease. In each breed, a mutation in the gene that produces cardiac myosin binding protein C (cMyBP-C), a protein in the part of the heart muscle cell actually responsible for contraction, has been identified. Although they are present in the same gene, the two mutations are very different, being located in different regions of the gene. In the Maine Coon the location and base pair change is often designated as A31P (the region of the gene is codon 31 and the amino acid alanine is changed to proline). In Ragdolls the designation is R820W. The mutations are very prevalent in both breeds (30-35% of Maine Coon cats,

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for example, that have been tested have the mutation). The majority of the cats with the mutation have one allele mutated (i.e., they are heterozygous). However, a significant percentage have both alleles mutated (i.e., are homozygous) because of inbreeding. In Maine Coon cats that are heterozygous, the percentage of breeding age cats (i.e., cats under 5 years of age or so) that have HCM present on an echocardiogram (cardiac ultrasound) is relatively low (low penetrance). The penetrance in older cats is unknown. In cats that are homozygous for the mutation the penetrance is very high. Most of these get HCM and most of those get severe HCM. Overall the disease is said to have variable expression meaning some cats are severely affected, others are only mildly to moderately affected, and some have no evidence of the disease yet produce affected offspring.
Undoubtedly, other mutations responsible for HCM in cats remain to be discovered. However, since few veterinary cardiologists and geneticists have the expertise to study genes, it may be some time before the responsible gene or genes for each affected breed will be found. So far it appears that the mutations identified as a cause of HCM in Maine Coon and Ragdoll cats are not responsible for HCM in other breeds. Consequently, the genetics of HCM will require investigation of each individual breed.

How is HCM diagnosed?
HCM is diagnosed using ultrasound of the heart – an echocardiogram. Echocardiography is a good way to detect moderate to severely affected cats. However, it may not always detect mildly affected cats where changes in the heart can be minimal. Ideally, an echocardiogram to test cats for HCM should be performed by a board-certified veterinary cardiologist although a board certified veterinary radiologist or internist trained in performing echocardiography may suffice.

In addition to an echocardiogram, other tests may also be useful in assessing cats with HCM. For example, a chest x-ray is necessary to detect heart failure in cats with severe HCM. An electrocardiogram (ECG or EKG) is necessary to diagnose an abnormal heart rhythm. Blood pressure measurement and blood testing for hyperthyroidism are indicated to rule out other diseases that mimic HCM, especially mild to moderate HCM. A blood test to detect a hormone called BNP (NT-proBNP is the specific hormonal product tested for) that is released from stressed or damaged heart muscle can be used to identify cats with severe HCM although false positive and especially false negative results occur with some frequency.

A genetic test is now available for the known cMyBP-C mutations causing HCM in Maine Coon and Ragdoll cats. The test is available from the Veterinary Cardiac Genetics Lab at the College of Veterinary Medicine, Washington State University (http://www.vetmed.wsu.edu/deptsvcgl/) and from the Veterinary Genetics Laboratory at the School of Veterinary Medicine, University of California, Davis (http://www.vgl.ucdavis.edu/services/cat/). The test can identify which cats have the mutation. If a cat is identified as having the mutation, the test can also determine whether the cat carries one copy of the mutation (a heterozygote) or two copies of the mutation (a homozygote).

Should my cats be tested for HCM and how often should they be tested?
In clinical practice, the most common patients tested for HCM with echocardiography are cats with

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suggestive clinical signs of heart disease, such as a heart murmur or heart failure. Testing cats used in a pedigreed breeding program is a more difficult endeavor. Echocardiography is not a perfect tool for the diagnosis of HCM – it is expensive, some mildly affected individuals will escape detection and access to good quality ultrasound services may be difficult for some breeders.

Since HCM can first occur (i.e., develop to a stage where it can be identified) at almost any age, a single normal echocardiogram does not identify a cat as being free of the disease. Breeding cats should probably have an echocardiogram yearly during their breeding years. Examining retired cats periodically is also advantageous as this may allow the identification of affected cats that have offspring in a breeding program. A Maine Coon cat that tests negative for the cMyBP-C mutation is not guaranteed to be free of HCM, for it is known that HCM can be present in Maine Coon cats that do not carry the known mutation. Currently it is not known if there are other causes of HCM in Ragdolls. Ideally, cats that test negative for the cMyBP-C mutation should still undergo echocardiographic screening. Ideally, cats that test positive for a mutation should not be bred. Although a large percentage of cats that carry only one copy of the mutation (heterozygous) do not develop HCM when they are young, the incidence of the disease in these cats when they get older is unknown. In addition, whenever a cat that is heterozygous for the mutation is bred it has the potential to be bred with another heterozygous individual or possibly even a cat that is homozygous for the mutation. Either scenario will usually produce a percentage of kittens that are homozygous for the mutation and so at great risk of developing HCM and of most likely developing severe HCM. However, some cats that carry one copy of an HCM-causing mutation carry breed qualities that could be deemed so exceptional that breeding them would be desirable. In those cases that cat could be bred once and kittens that tested negative for the mutation used for subsequent breedings. A cat that is homozygous for one of these mutations should never be bred.

Some veterinarians are concerned that because these mutations are so prevalent in their respective breeds that if cats that are heterozygous for an HCM-causing mutation are not used for breeding that the breed will run into other genetic problems when recessive traits become magnified. However, cats are already highly selected for genetic traits that amplify their external beauty. Therefore it is hard to imagine that selecting cats to be bred based on their inner beauty (i.e., a beautiful heart) could produce that much further damage to a breed.

At what age should a cat be tested for HCM?

HCM can affect cats at any age. It has been seen in kittens as young as 6 months of age and identified for the first time in cats over the age of 10. It appears that most of the young Maine Coon and Ragdoll cats with HCM are homozygous for the mutation responsible for HCM in that particular breed. Cats that are heterozygous for one of these mutations are most often free of HCM during their breeding years. This may be true for other breeds as well. It is therefore hard to recommend a specific age to start ultrasound testing. It may make sense to screen most breeding cats with an echocardiogram for the first time around the age of 2 years and then yearly after that. Maine Coon and Ragdoll cats may be tested for their cMyBP-C mutations as kittens. A gene mutation is present at birth and never changes throughout life.

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What do I do if my cat is diagnosed with HCM?
The cat should be removed from the breeding program and all offspring should be watched closely for the development of HCM. Statistically, 50% of the cat's offspring would be expected to have the genetic mutation that causes HCM if one parent was a heterozygote. However, the most prudent approach may be not to use any of the offspring in a breeding program. The offspring of Maine Coon and Ragdoll cats with a cMyBP-C mutation should be individually tested to determine their status.

The parents of an affected cat should also be examined with echocardiography (and tested for the cMyBP-C if a Maine Coon or Ragdoll), as one of them likely carries a gene mutation for HCM. In some cases, identification of the affected parent may be difficult, especially if the disease is mild. In these cases, the most prudent approach may be to remove both parents from the breeding program. It is possible for a cat to develop a spontaneous mutation that causes HCM during embryonic development but this is an unlikely cause in a breed known to have the problem.

All breeders that are using cats related to an affected cat should be notified that a cat has been diagnosed with HCM. Similarly, pet owners should be notified that a relative has been diagnosed with the disease. Echocardiographic examination (and genetic testing if a Maine Coon or Ragdoll) of cats related to the affected cat should be performed.

Will we ever eliminate HCM from my breed?

The tools we currently have to diagnose HCM (i.e., echocardiography and necropsy) are not perfect and will not allow us to totally eliminate this disease. However, echocardiographic screening will be able to reduce the incidence of HCM within a breed if enough breeders are involved.

The identification of the cMyBP-C mutations in the Maine Coon and Ragdoll breeds and the development of the genetic tests provide breeders with a new tool to reduce the prevalence of or theoretically eliminate the mutation within this breed by not breeding affected cats. Breeders should use all the information they can gather about HCM in family lines, including pedigree analysis based on accurate identification of affected cats.

Any cat that dies suddenly or dies from HCM should have a necropsy (i.e., post mortem examination). Most cats with HCM will have a heart that weighs more than 20 grams and most cats with severe HCM will have a heart that weighs more than 30 grams. Myocardial fiber disarray, the hallmark microscopic heart muscle abnormality seen in humans with familial HCM, is seen in all Maine Coon cats with HCM. Unfortunately, most veterinary pathologists are not trained to recognize this lesion.

In the long term, a genetic test for HCM in each breed will be needed. A genetic test allows one to identify affected cats before they are bred and do so accurately. Since the disease is inherited as an autosomal dominant trait, once a mutation is identified, if all breeders cooperated by testing their breeding cats for the

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mutation the disease theoretically could be eliminated from the breed within several generations. However, the money and resources necessary to identify the gene or genes and to develop a genetic test for each breed are scarce in veterinary medicine. Breeders and cat fanciers can help by supporting research through organizations such as the Ricky Fund established by the Winn Feline Foundation (http://www.winnfelinefoundation.org/giving/ways-to-give).

Can two normal parents produce a kitten with HCM?

Since HCM is known to be an autosomal dominant trait in the breeds where the inheritance is known, each affected cat must have one affected parent. However, there are possible situations in which an affected cat may come from two apparently normal parents.

The first possibility is that one of the parents has been misdiagnosed. This can happen due to inexperience of the ultrasonographer or poor quality equipment. It can also happen if a cat's status is decided on the basis of only one or two ultrasounds early in life. Since HCM can develop at any age, a cat that is normal on ultrasound one year could still have HCM and show signs later in life.

Since the trait has variable expression, not every affected cat will have echocardiographic evidence of HCM. It is therefore possible for a cat to test negative for HCM on ultrasound, and yet still carry a genetic mutation and pass it to offspring.

Finally, it is possible for spontaneous mutations to occur in cats from normal parents. These cats may then pass on their mutation to offspring. We do not know how often spontaneous mutations causing HCM occur in cats. Statistically, spontaneous mutations are more likely to occur in random bred cats than in pedigreed cats.

What does "HCM free cattery" mean?
There is no universally agreed upon definition of an HCM free cattery. The terminology is currently unclear, as different breeders mean different things when they use this term. Ideally, each breed should develop a specific definition and guidelines for use of this designation for catteries.

Can HCM have a nutritional cause?
There is no evidence in cats, humans or other species of animals that HCM can have a nutritional cause.