Heart Conditions Affecting the Birman Breed: Where Are We Now?

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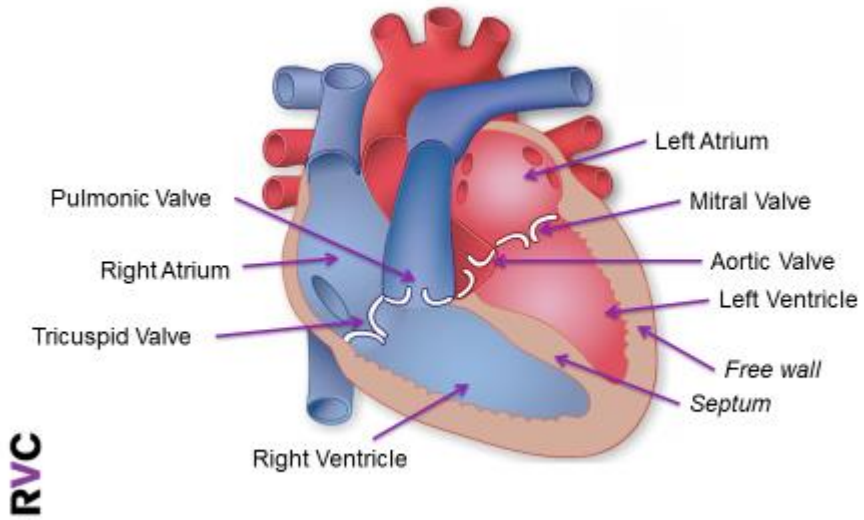
Overview

- The normal heart
- Cardiomyopathy in cats
- Signs and consequences of cardiomyopathy in cats
- Study update

The Heart



The heart is a muscle that pumps blood around the body. It is made up of four chambers, two at the top and two at the bottom. The two top chambers are called the atria, which serve as pre-chambers to collect blood as the heart fills. The two chambers on the bottom are the ventricles, which pump blood out of the heart. Valves prevent blood from flowing backwards. The tricuspid valve and the mitral valve allow blood flow from the atria to the ventricles. The other two are called the pulmonic and aortic valves; these control blood flow leaving the heart.

Deoxygenated blood from the body flows into the right atrium, through the tricuspid valve into the right ventricle. It is then pumped out through the pulmonic valve and via the pulmonary artery to the lungs where oxygen is picked up. Oxygenated blood then flows from the lungs via the pulmonary vein into the left atrium. It then continues through the mitral valve into the left ventricle where it is pumped out through the aortic valve and via the aorta to supply oxygenated blood to the body.

The left ventricle is made up of the septum and the free wall. The septum is a thick wall of muscle that runs down the middle of the heart, separating the right and left sides. You may see these terms written on heart scan reports, both refer to measurements of the left ventricle.

Cardiomyopathies

What is cardiomyopathy?

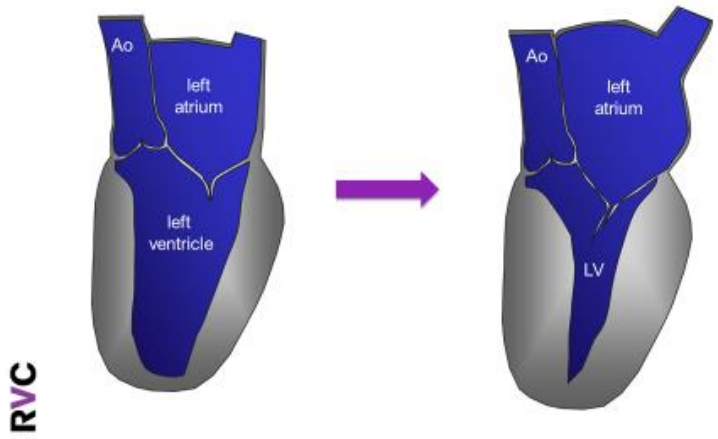
Cardiomyopathy means primary heart muscle disease, it is not caused by anything else going on within the body. This disease starts in the heart. There are several forms of cardiomyopathy and these diseases are similar, if not identical, in humans and cats.

What causes cardiomyopathy?

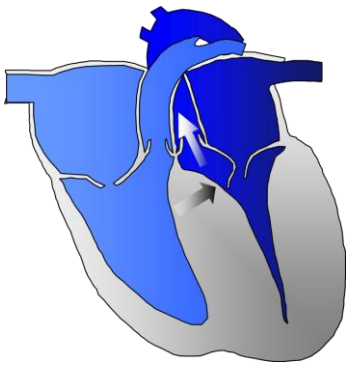
It is thought that cardiomyopathy in cats is a familial, genetically inherited disease caused by a genetic mutation. There are over 1500 genetic mutations that are known to cause cardiomyopathy in humans and, unfortunately, the situation is likely similar in cats.

Hypertrophic cardiomyopathy (HCM)

Hypertrophic Cardiomyopathy (HCM) is the most common form of cardiomyopathy in humans and cats. In HCM, the walls of the left ventricle thicken (hypertrophy). Along with the thickening of the left ventricular walls, the papillary muscles (small muscles within the heart that anchor some of the heart valves) may be enlarged.



There may also be an abnormality called systolic anterior motion (SAM) of the mitral valve that may precede, as well as accompany, the hypertrophy in HCM. This abnormal valve motion can contribute to 'dynamic left ventricular outflow tract obstruction', which may be termed obstructive HCM or HOCM. This happens when the mitral valve leaflet flicks back into the path of blood leaving the left ventricle when the heart contracts, creating a partial obstruction to blood flow. SAM is the usual cause of a heart murmur in a cat with HCM, as it causes a turbulence of blood within the heart.



Can anything else cause the left ventricle to become thick?

Left ventricular walls may also become thick as a result of other diseases. It is important to rule out other disease that can mimic HCM.

High blood pressure (hypertension) is common in older cats, particularly those that have been diagnosed with chronic kidney disease (CKD). High blood pressure within the circulation results in the heart having to work harder to pump blood. This causes a secondary thickening of the heart muscle in response to demand. We measure blood pressure in every cat that has a thick left ventricle on a heart scan, in order to rule out high blood pressure as a cause.

Hyperthyroidism (overactive thyroid gland): This is a common condition of older cats, the most common clinical signs of which include: weight loss despite an increased (often ravenous) appetite, behavioural changes and possibly vomiting & diarrhoea. Excess thyroid hormone causes an increase in metabolic rate, which results in an increase in the work the heart has to do and subsequent enlargement of the heart or heart muscle thickening. Hyperthyroidism can be easily diagnosed with a simple blood test and there are different treatment options available.

Acromegaly (hypersomatotropism): This is caused by excess growth hormone production by a benign tumour of the pituitary gland in the brain. It is usually only seen in diabetic cats, especially if their diabetes is difficult to control with insulin.

Although these diseases cause the walls of the left ventricle to look thick, they are not HCM and are all very simple to rule out as causes of a thick left ventricle in older cats.

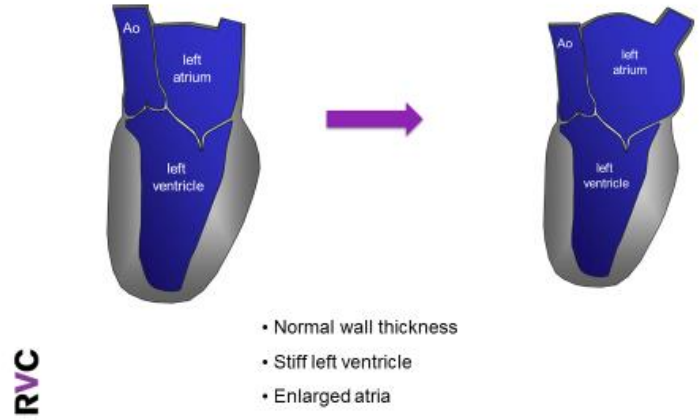
Does HCM just affect certain breeds?

Some breeds are reportedly predisposed, such as the Maine Coon, Ragdoll, Norwegian Forest Cat, Sphynx, British Shorthair and American Shorthair. However, the majority of cats with HCM are mixed breed, non-pedigree cats - ‘moggies’.

How common is HCM?

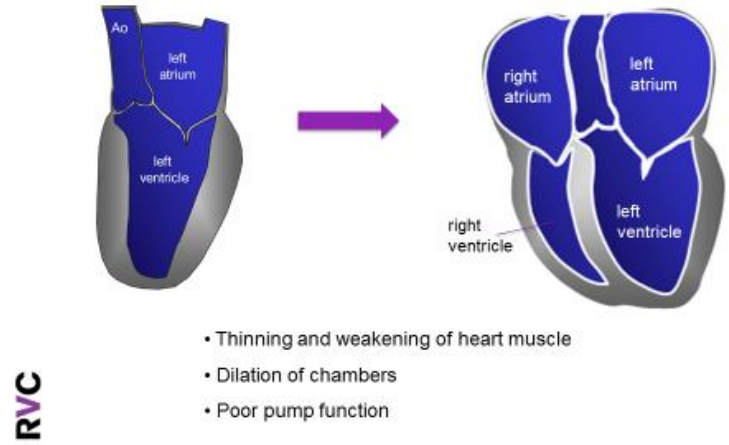
This disease is very common in the general feline population. Dr. Rosie Payne at the Royal Veterinary College looked at the prevalence of HCM in cats in rehoming centres. She went to two different rehoming shelters in the UK and scanned every cat over 6 months of age, over a period of 3 years. She found that approximately 15% of the general feline population in cat shelters have HCM. However, the prevalence of serious consequences of HCM was low – most of these cats will live a normal lifespan and never show any consequences of their heart disease.

Restrictive Cardiomyopathy (RCM)



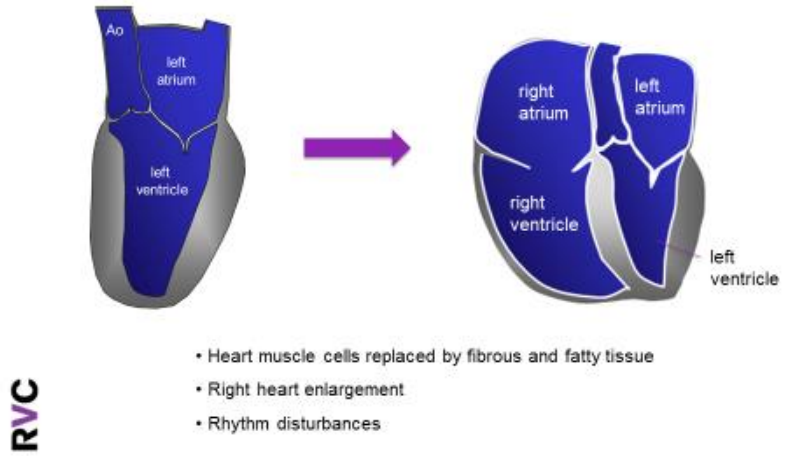
In restrictive cardiomyopathy (RCM) the wall thickness is normal and the left ventricle can look relatively normal, but in fact it is stiffer than normal so the left ventricle still doesn't fill very well and generally there will be an enlarged left atrium. This disease can be very difficult to detect in the early stages, as the left ventricle will look normal and the atrium will not be enlarged, therefore it can look like a normal cat heart on a heart scan!

Dilated Cardiomyopathy (DCM)



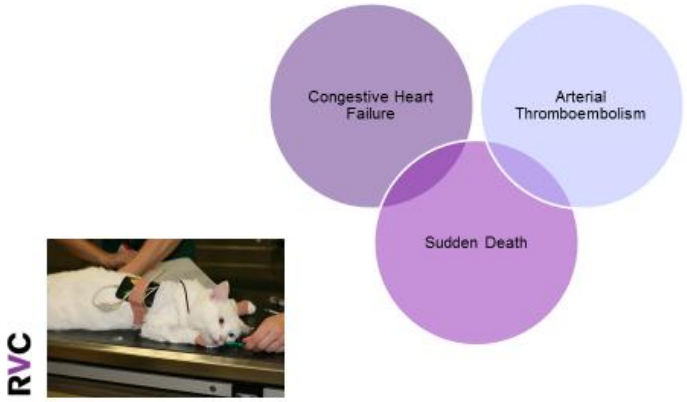
DCM is characterised by thinning and weakening of the heart muscle, leading to dilation of the heart chambers because the heart can no longer pump blood effectively. Historically this disease was associated with a diet deficient in taurine, an essential amino acid. However, since this was discovered in 1987, food manufacturers have adjusted taurine levels such that deficiency is no longer seen in cats eating a commercial diet. DCM is now rare in cats and when seen may represent the 'end-stage' or 'burn-out' phase of another cardiomyopathy, such as HCM. This can happen when the blood flow and oxygenation to the heart muscle itself is compromised and heart muscle cells die off.

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)



ARVC has only recently been recognised in cats and is rare, but there is suggestion that Birmans may be predisposed. In this disease, heart muscle cells of the right ventricle are replaced by fibrous and fatty tissue. This causes weakening and thinning of the muscle in the right side of the heart. It may lead to right-sided heart failure, where the liver enlarges, fluid can build up in the abdomen and fluid can also form around the lungs. Abnormal heart rhythms are also common with this condition.

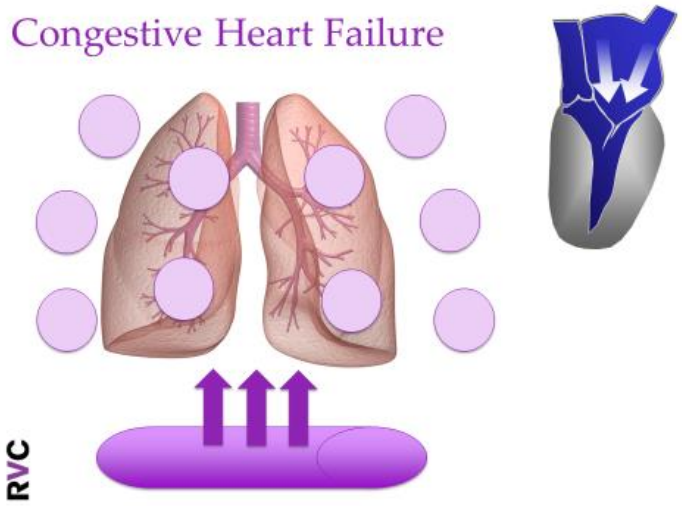
Why it Matters: Consequences of Cardiomyopathy



There can be some very serious consequences of any type of cardiomyopathy, including congestive heart failure, arterial thromboembolism and sudden death.

Congestive Heart Failure

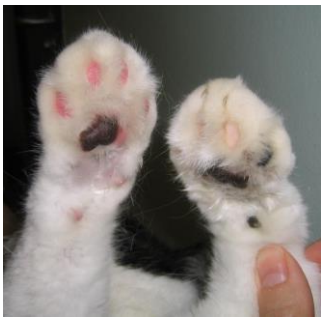
When the left ventricle becomes thick or stiffened, it is unable to fill properly. This can lead to a build-up of pressure in the left atrium. This causes enlargement of the left atrium and high pressure, so the blood draining from the lungs into the pulmonary veins and into the left atrium can't drain very easily. This then causes high pressure within the vessels of the lungs, which can start to leak fluid. This can lead to fluid build-up in the lung tissue (known as pulmonary oedema) or around the lungs (known as pleural effusion).



This can be a life-threatening situation, cats can die if they don't get treatment quickly enough. Signs that would alert you to the possibility of congestive heart failure are fast breathing or difficulty breathing. Some cats will open-mouth breathe (pant like a dog).

Arterial Thromboembolism

This devastating complication of cardiomyopathy occurs when a blood clot (thrombus) forms within the left atrium. As the left atrium becomes enlarged it loses function, blood swirls around within it and does not move into the left ventricle properly; so you can start to develop a clot within this chamber of the heart. If a small piece (embolus) breaks off, moves into the left ventricle and is pumped out into the circulation, it can block the blood supply to major arteries. In cats, the most common place for this clot to lodge is where the main artery of the body (aorta) divides to supply the back legs. Smaller clots can go to many places within the body and cause damage.



This causes sudden paralysis of the legs, which are usually cold because the blood supply has been cut off and the paw pads may turn pale or blue. This is incredibly painful and cats will usually be vocalising in pain; it is a very distressing situation.

Sudden Death

Sadly there are cats that die suddenly, sometimes with no warning at all. This may be associated with abnormal excitability of the heart muscle cells, leading to fatal heart rhythm disturbances. This is an important consequence of cardiomyopathy that we are currently looking at identifying risk factors for. You may not even know your cat had cardiomyopathy, and the first sign of problems may be when they are just found dead. In this upsetting circumstance, although very difficult to think about, *post-mortem* examination is very valuable.

Does My Cat have Cardiomyopathy?

Signs of heart disease

It is very difficult to detect early signs of heart disease in cats. In dogs you might notice reduced exercise tolerance, but cats might just spend more time resting or sleeping (when the average is 22 hours a day, that's difficult to notice!). Cats are very good at hiding signs of disease. Remember, approximately 15% of apparently healthy cats have HCM.

Occasionally, cats will faint as a result of their heart disease. Even fainting in a cat can be very difficult to spot!

In some cases, signs include panting (open-mouth breathing) particularly after exercise. In humans, we know that HCM causes angina (chest pain), so we think this may be what causes cats to suddenly stop and pant after exertion.

My cat is coughing

Coughing is rarely seen in cats with heart disease. In cats, coughing is much more likely to be caused by airway disease such as asthma or bronchitis.

My vet heard a heart murmur

Heart murmurs are common in cats. Around 15-40% of the healthy feline population have a heart murmur. Of the cats with a heart murmur, approximately half of them will have a murmur as a result of heart disease, and the other half will have a normal heart and the murmur is 'innocent' or 'physiological'. It is also worthy of note that cats can have cardiomyopathy and not have a murmur. Therefore a heart murmur is not a reliable indicator of heart disease in cats.

Heart murmurs in cats may also be dynamic in nature, meaning they can be heard at one vet visit and not at the next (this is not a case of one vet being better at detecting murmurs than the other, or whether or not your vet spent all night at a heavy metal concert the night before – they really can come and go!). If your vet hears a 'gallop sound' or arrhythmia, these are much more indicative of heart disease.

Can cardiomyopathy be diagnosed on chest X-rays?

Chest x-rays can show changes in the overall shape and size of the heart. They do not allow precise determination of the type of cardiomyopathy present, nor do they tell you anything about heart function. They are most useful for diagnosing congestive heart failure, by detecting a build-up of fluid in or around the lungs (pulmonary oedema or pleural effusion). Repeating x-rays might be useful for monitoring the effectiveness of treatment in cats with heart failure, to document resolution with treatment.

What about a blood test for cardiac biomarkers?

Biomarkers are hormones released by the heart into the blood stream. NT-proBNP is released in response to heart stretch and stress. Troponin I is released by heart muscle cells when they are damaged. This means that we can take a blood sample and measure the level of these biomarkers to get some idea of how much stress the heart is under, and whether the heart muscle cells are being damaged.

It will not give you a definite diagnosis of cardiomyopathy, but a cat with high results would be one which you would want to scan. We are currently looking at whether these tests are able to detect mild heart disease earlier than we can see changes on a heart scan. This would be particularly important in cats with RCM, where we don't see changes on a scan until late in the disease course.

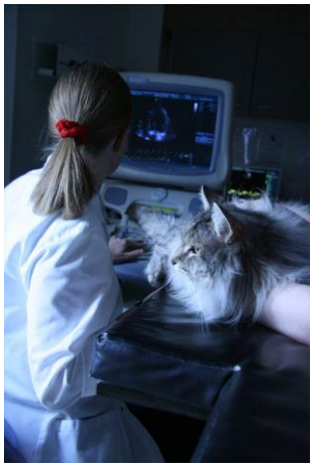
It should be remembered that biomarkers are not a test for breeding soundness, nor are they a test for HCM. In cats with suspicious findings on examination, such as a murmur, 'gallop sound' or abnormal heart rhythm, they can be a relatively cheap test to give an indication of the likelihood of heart disease.

In cats with respiratory signs (fast breathing, laboured breathing), biomarkers can give an indication of whether heart disease is likely to be the cause of these signs, or whether lung or airway disease is more likely.

They can also be useful for monitoring a cat that has been diagnosed with cardiomyopathy on a heart scan. If a biomarkers are measured at the time of a heart scan, this means that a baseline can be established regarding biomarker levels compared with what the heart looks like on a scan. Rather than having to travel to a specialist cardiologist for heart scans every 6 months, you could have biomarkers routinely tested at your local vet practice. If there is an upward trend in biomarker measurements, or a sudden increase, this would indicate the need for a re-check heart scan.

Echocardiography (ultrasound scan of the heart)

At the moment, this is the best test for we have diagnosing cardiomyopathy. It allows definitive diagnosis of the specific cardiomyopathy in most cases as well as assessment of heart size and function. It may be able to give an indication of prognosis, for example a large left atrium would indicate that blood is starting to back up and the cat is at risk of going in to congestive heart failure. It may be possible to visualise clots or slowing of blood within the heart, which would indicate the cat is at greater risk of ATE. However, it may not detect mildly affected cats where changes in the heart are minimal.



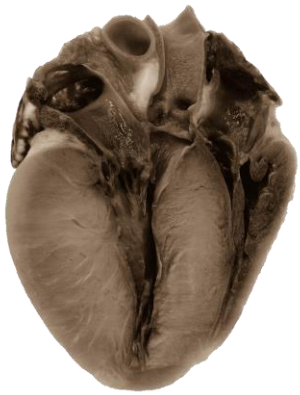
This test should be performed by a specialist cardiologist. Even for experienced cardiologists, screening cats for cardiomyopathy is very difficult. Experience is very important for detecting subtle disease and taking very precise measurements. To find a board –certified cardiologist, look for ACVIM or ECVIM diplomates, you can search for local specialists via these websites:

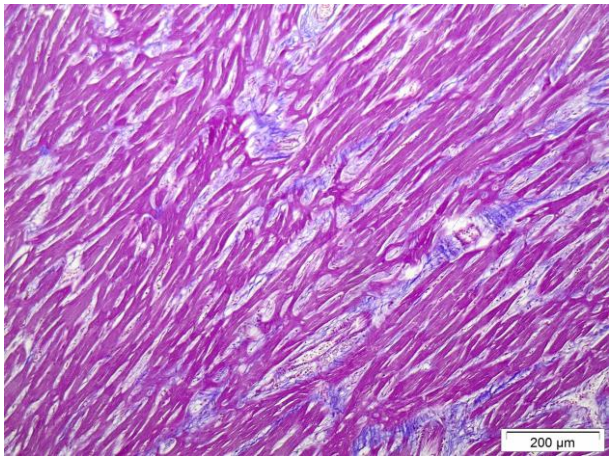
http://www.ecvim-ca.org/diplomate-list

http://www.acvim.org/Home.aspx

Pathology

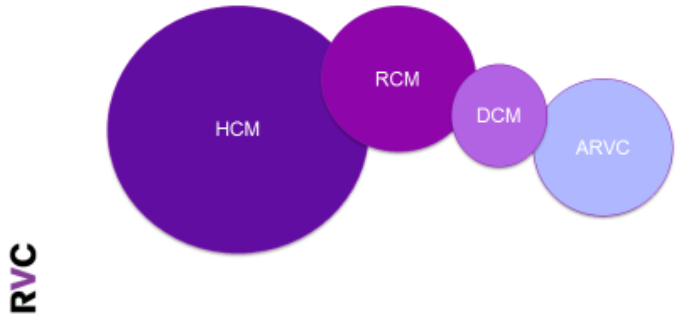
The other thing that is difficult to discuss, but really important to our understanding of this condition, is to get information on *post-mortem* (autopsy). Unless we can look at the hearts from cats that have died from this disease, we won't know some of the really important characteristics. We look at the whole heart and also do microscopic analysis (histopathology) to identify the arrangement of the heart muscle cells and to look at fibrosis and scarring of areas within the heart.





Cardiomyopathy in Birmans: Study Update

In contrast to most other cats with cardiomyopathy, which have a low prevalence of bad disease and many of them will go on to live a normal lifespan, Birmans seem to get very bad disease and are more likely to suffer the serious consequences.



Initial analysis of family trees indicated that cardiomyopathy in Birmans is likely a genetically inherited disease. The majority of cardiomyopathy in Birmans has been HCM, however RCM and DCM is also seen. Birman cats have been reported to develop arrhythmogenic right ventricular cardiomyopathy (ARVC) more frequently than other breeds. This disease is known to be inherited in certain breeds of dog, but there have been no genetic studies in cats.

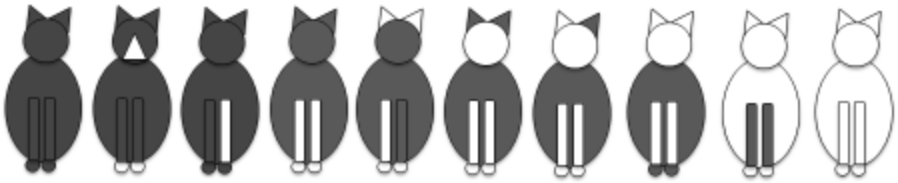
A crucial question that must be answered before a genetic mutation can be identified is whether HCM, RCM, DCM and ARVC are different diseases with different causes, or whether they are part of a spectrum of one disease with one genetic cause. We are studying Birmans using a combination of heart scans (echocardiography), blood tests, pathology and pedigree analysis to determine the key features of these heart muscle diseases. If there is substantial overlap in their ultrasound and pathology characteristics, or we find families of Birmans with multiple members affected by more than one type of cardiomyopathy, we can be more confident that we are dealing with one disease, and so can proceed to genetic research.

Genetics in Birman Cardiomyopathy

We think that the genetic inheritance pattern is autosomal dominant. In plain terms, this means that the following rules apply:

- Only one parent needs to have the mutation for the offspring to be affected
- There are cats with HCM in every generation from that parent

The situation is complicated by the fact that some cats can carry the mutation but never show signs of the disease themselves (silent carriers). This is known as incomplete penetrance and creates problems because it means that we cannot pick up affected cats by looking at the heart with a scan. Therefore they continue breeding and can pass on the mutation to their kittens, which may show the disease.



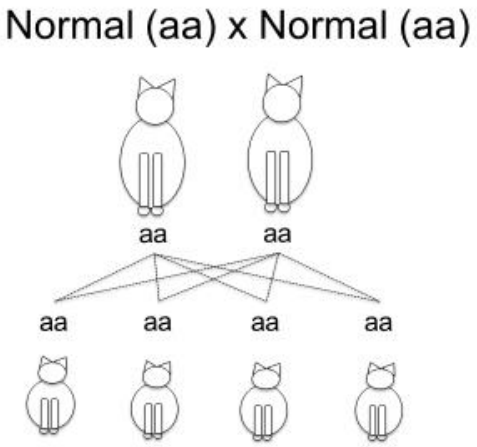
A simple example of this is coat colour. In the above example, only the completely black cat on the left does not have the gene. All the other cats are affected, and have the same gene. However, variable penetrance results in them being more or less white. In cardiomyopathy, some can carry the gene and not be affected while others with the same gene can be severely affected.

A further complicating factor is age-dependent penetrance. This means that even though the mutation or 'bad' gene is inherited and present from birth, the disease that we see develops over time and cats do not usually show detectable disease until they are an adult. We don't yet know what is the latest age cardiomyopathy can develop. Personally, I have seen it develop as late as 12 years old in a cat that was screened annually, but I think this is the exception rather than the rule. We think it usually develops at less than 10 years old if it is going to.

Male and females are both affected, although males seem predisposed to developing the disease and develop the disease younger than females. Females appear more likely to be 'silent carriers'.

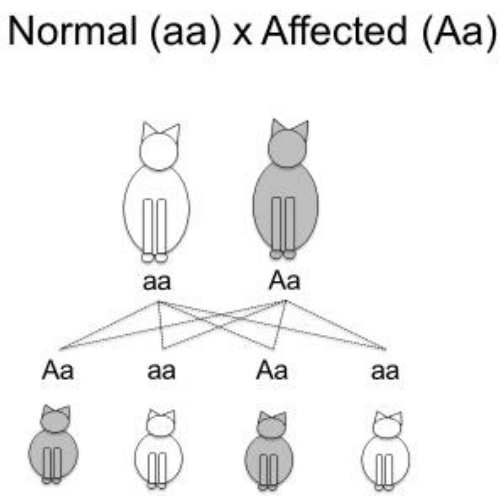
The cat inherits two copies of a gene, one from each parent. There are three possible genotypes:

- *Homozygous wild-type (aa)*: Two copies of the normal gene with no mutation. The cat is negative for this particular genetic predisposition to cardiomyopathy.
- *Heterozygous mutation (Aa)*: One copy of the normal gene and one copy of the mutated gene. The cat has the particular genetic predisposition to cardiomyopathy.
- *Homozygous mutation (AA)*: Two copies of the mutated gene. The cat may be more likely to develop moderate to severe cardiomyopathy earlier in life than a heterozygous cat.



RVC

In this example, both parents are normal and do not carry the mutation responsible for cardiomyopathy. The offspring have a normal genotype and are not affected by cardiomyopathy.

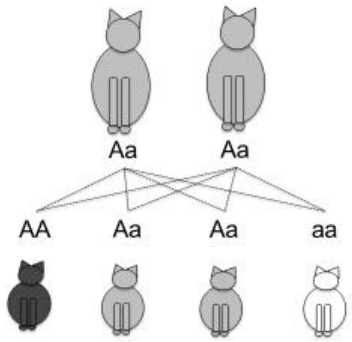


RVC

In this example, one parent is normal (aa) and the other is heterozygous for the mutation that causes cardiomyopathy (Aa).

- 50% of their offspring inherit one copy of the mutated gene and one normal copy (heterozygous). They have the particular genetic predisposition to cardiomyopathy.
- 50% of their offspring inherit two copies of the normal gene and are unaffected.

Affected (Aa) x Affected (Aa)

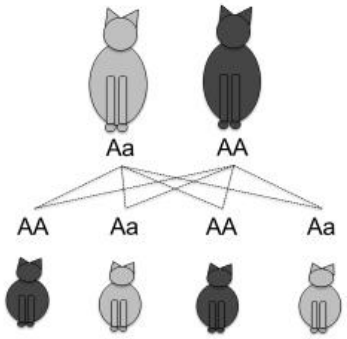


RVC

In this example, both parents are heterozygous for the mutation that causes cardiomyopathy (Aa).

- 50% of their offspring inherit one copy of the mutated gene and one normal copy (heterozygous). They have the particular genetic predisposition to cardiomyopathy.
- 25% of their offspring inherit two copies of the mutated gene with no normal copy (homozygous). They may be more likely to develop moderate to severe cardiomyopathy earlier in life than a heterozygous cat.
- 25% inherit two copies of the normal gene and are unaffected.

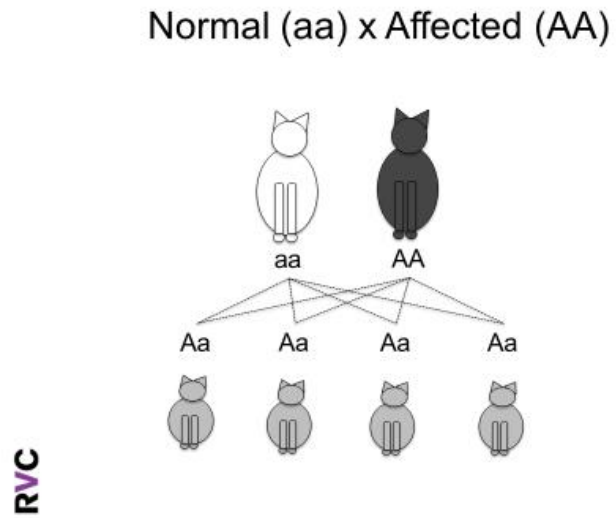
Affected (Aa) x Affected (AA)



RVC

In this example, one parent is heterozygous for the mutation that causes cardiomyopathy (Aa) and the other parent is homozygous for the mutation (AA).

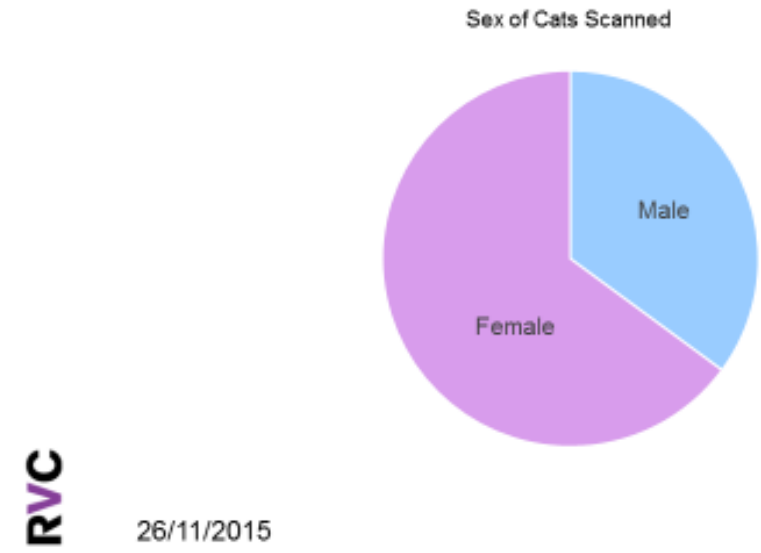
- 50% of their offspring inherit one copy of the mutated gene and one normal copy (heterozygous). They have the particular genetic predisposition to cardiomyopathy.
- 50% of their offspring inherit two copies of the mutated gene with no normal copy (homozygous). They may be more likely to develop moderate to severe cardiomyopathy earlier in life than a heterozygous cat.
- All of their offspring are affected



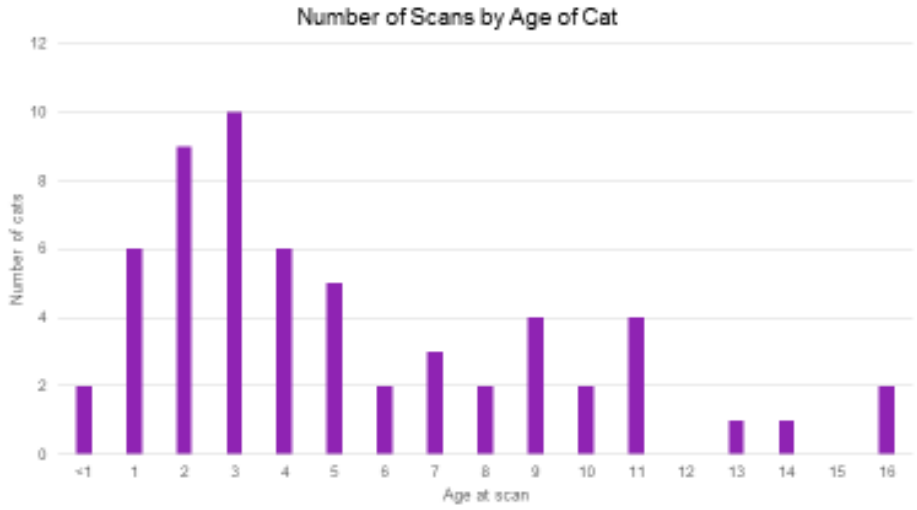
In this example, one parent is homozygous for the mutation (AA) and the other parent is normal.

- 100% of their offspring inherit one copy of the mutated gene and one normal copy (heterozygous). They have the particular genetic predisposition to cardiomyopathy.
- All of their offspring are affected

Progress so far



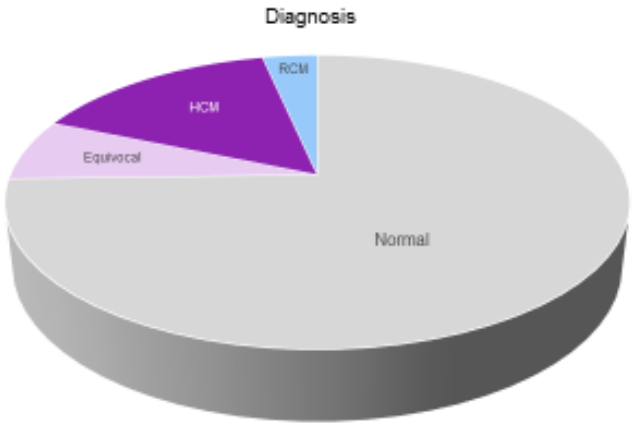
The cats we have scanned so far have been predominantly female. It would be nice to see more male cats, as they contribute significantly to the genetic pool.



RVC

26/11/2015

The age group we are most commonly seeing is young cats, with a median age of just 3 years old. However, the age group where we have the best chance of detecting cardiomyopathy, if it is going to develop, is older.



RVC

26/11/2015

- Post-mortem data on 5 cats
  - HCM: 2
  - HCM/RCM: 1
  - DCM: 1
  - HCM/ARVC: 1

So going back to our original question, it seems that we do see several forms of cardiomyopathy in Birmans and that features of these diseases overlap. We are also seeing different cardiomyopathies within the same lines, suggesting we are looking at a spectrum of disease with a single genetic cause, as opposed to several different diseases.

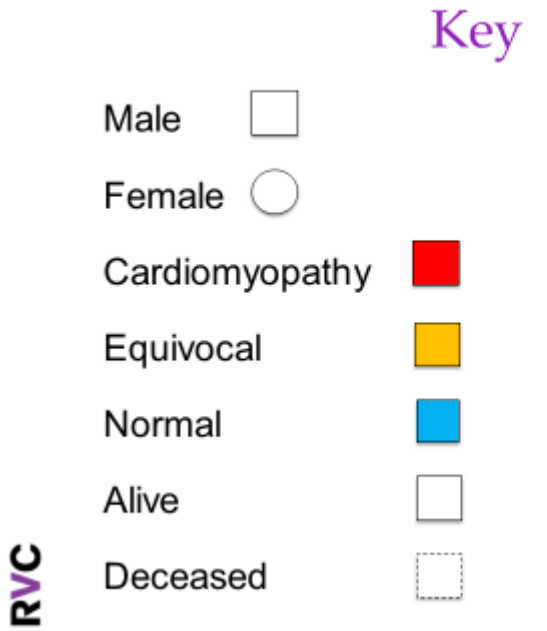
Why Scan?

Heart scans will allow you to assess risk for the individual cat. It will also help to identify carriers of the genetic mutation in breeding programs, therefore allowing you to think about removing cardiomyopathy genetic mutations from future lines.

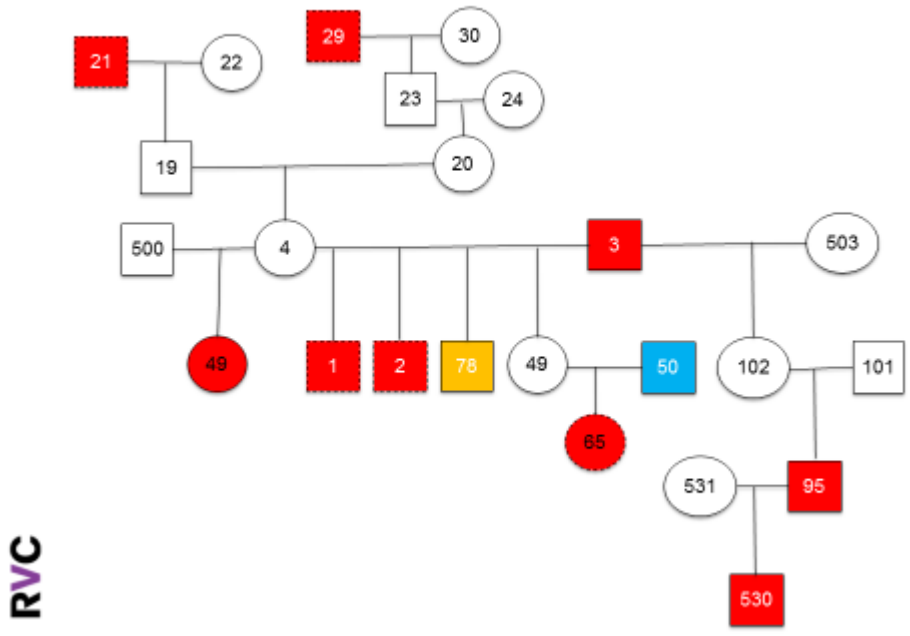
The best way to demonstrate this is with a case example:

Cat 1 is a 5 year old male, neutered Birman. He had a heart murmur detected by his vet at a routine vaccination visit. Upon further questioning, the owners recalled that he had been less active for the past 6 months and had fast breathing on exertion. The owners also knew that his sibling had died suddenly and HCM had been confirmed as the cause of death at *post-mortem*. The vet decided to do a blood test for biomarkers as an initial screen, which revealed levels of NT-proBNP were high.

He was referred to the Royal Veterinary College for echocardiography (heart scan), where he was diagnosed with cardiomyopathy that had features of both HCM and RCM. He was considered at high risk for thromboembolism (clot) and congestive heart failure, so was started on treatment. A repeat heart scan 2 months later revealed progression of his disease, and new medications were added to his treatment. He battled with heart failure for 4 months before he was put to sleep. A *post-mortem* at the Royal Veterinary College confirmed cardiomyopathy (HCM/RCM).



This cat is number 1 on the following pedigree tree. We already knew that he had one brother that died suddenly from HCM (cat 2). We tried to screen as many of his relatives as possible, and here is a snapshot of what we uncovered:



He has another brother which we screened equivocal (cat 78). We have no information on his sister (cat 49), but she mated a normal male (cat 50) to produce a daughter that had an ATE (clot to the back legs) secondary to HCM and died (cat 65).

His father (cat 3) has HCM and when mated with a different female (cat 503) also produced HCM-affected kittens in 2 generations (cats 95 and 530).

His mother mated with a different male (cat 500), whom we have no information on, to produce an affected daughter (cat 49). Tracing her lines, we uncovered males on both sides that died suddenly from HCM (cats 21 and 29).

Therefore cat 1 could have inherited two copies of the mutated gene, from both his sire (cat 3) and dam (cat 4); making him homozygous for the mutation. This may explain the severity of disease in this litter.

So, why scan? Cat 3 is a 16 year old, healthy male. He was diagnosed with mild HCM and a normal sized left atrium on a heart scan, putting him at low risk for heart failure or developing a clot. No treatment was necessary. If only this cat was scanned, it would be very easy to think that he is old and healthy with only mild HCM, therefore it is of no consequence to breeding. I hope I have demonstrated that this is not the case. Cats with mild HCM can pass the mutation to their offspring and they can be severely affected. Cat 3 is still alive and healthy at 16 with mild HCM, but many of his offspring are sadly deceased as a result of the mutation he passed on.

Screening at the Royal Veterinary College

Screening is free of charge for all Birmans. During the visit we weigh the cat and take their blood pressure, listen to their heart and then perform an ultrasound scan of their heart. For the scan, they do not require an anaesthetic or sedation. The complete heart scan takes approximately 10-20 minutes per cat and you are very welcome to remain with your cat throughout the visit. We take a small blood sample (the equivalent to half a teaspoon) which we use to measure cardiac biomarkers and store any remaining blood as DNA for future genetic analysis. A full report of our findings will be sent to both you and your vet, but will otherwise remain strictly confidential.

Suggested screening protocol

- Echocardiography in cats ≥ 1 year
  - Earlier if known cardiomyopathy in the line
  - Earlier if history of sudden cardiac death in relative
- A single normal echo does not guarantee HCM-free
  - Repeat scanning
- Any cat that dies should have a *post mortem*

We do not know the age of onset for cardiomyopathy, so a single normal echocardiogram does not guarantee that the cat will not develop the disease in the future, or that it will not pass the disease on to its offspring. It is recommended for cats to be scanned yearly. We also do not know at what age a normal scan means the cat is truly cardiomyopathy free, but suggest that 10 years old may be appropriate.

Why screen old cats?

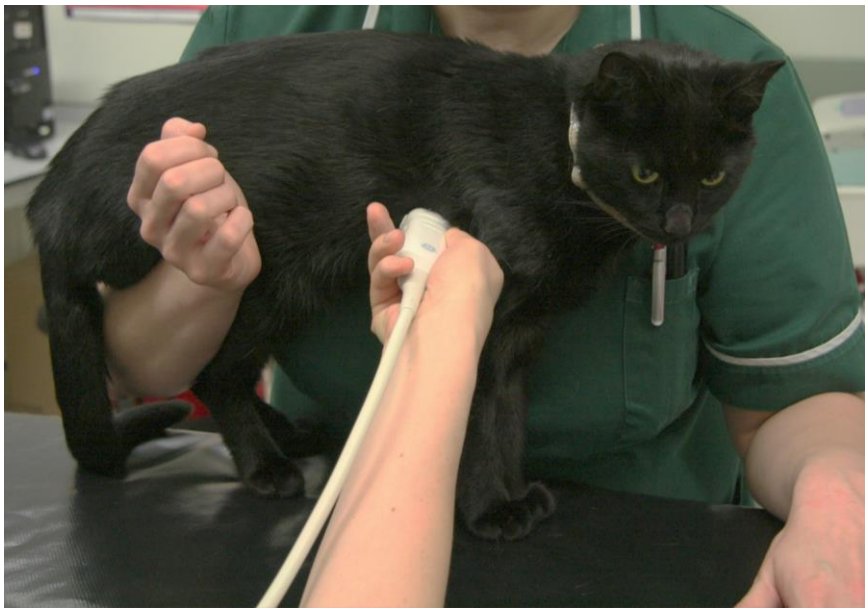
- If old and screened normal, much more likely to be normal
- Screening older generations related to your breeding stock will tell you much more about cardiomyopathy risk than screening young cats prior to first mating
- Old, normal cats as controls for developing genetic test

RVC

Thank you Trina Balharrie and Simone Ensor!

I don't want to stress my old cat!

We are used to working with cats and the last thing we want to do is cause them stress. We can work WITH your cat. For cats with arthritis that do not tolerate lying down, we can acquire a basic set of images from a standing position. You are more than welcome to stay with your cat for the entire visit.



Why is identifying a genetic mutation advantageous?

Once you know which mutation you are looking for, you don't need very much DNA and can look for it using mouth swabs; as is possible for Maine Coons and Ragdolls. This is quick and practical and means you can then make more informed decisions about breeding. It will also allow you to monitor particularly closely those cats with a responsible mutation predisposing them to cardiomyopathy.

What do we still require for the first phase of the study?

- *Post-mortem* data on cats dying of heart disease
- Screen cats related to Birmans dying of cardiomyopathy
- Screen cats in Birman families FREE of a history of heart disease (especially older cats)

When is *post-mortem* appropriate and what happens?

Post-mortem is free of charge for any Birman, not just those with known heart disease or that died suddenly with suspicion that cardiomyopathy may be responsible. It is very important that we understand the specific features of the normal Birman heart, therefore we will perform a post-mortem exam on Birmans that have died or been euthanized for other reasons.

If you send your cat for a complete post-mortem, they can still go for individual cremation with the ashes returned, if desired. You can also send any blankets/toys etc. with them, and be assured that they will be treated with respect.

Alternatively, you can ask your vet to send only the heart and an accompanying blood or tissue sample for DNA.

A full report will be send to yourself and your vet, but will otherwise remain confidential.

If you find yourself in this terrible situation, please contact Lois on 07983044485, or lwilkie@rvc.ac.uk who can advise you further or liaise with your vet if necessary.

If you wish to send a formalin-fixed HEART ONLY sample, more detailed instructions can be found as a separate document.

What is the next phase of the study?

- Range of cats for screening and sampling
- Outcome data – what happens to screened cats?
- Information from heart scans, biomarkers, outcome and *post-mortem* will be used to determine which cats have cardiomyopathy
- Genetic testing can be performed on DNA samples from clearly affected cats compared with clearly normal (older) cats

The deadline for the next round of applications to WINN is 14th December, and we can confirm that we will be applying for the next phase of this study.

What is the ultimate goal of this research?

To reduce the prevalence and consequences of cardiomyopathy in Birmans.

Acknowledgements

I extend my sincere gratitude to the following:

- Beata Garncarz, who first invited me to speak on cardiomyopathy in 2013 and prompted our investigation into cardiomyopathy in Birmans.
- Alwyn Hill, without whom pedigree mapping to trace the origin and inheritance pattern of cardiomyopathy in Birmans would have been very difficult.
- Birman Breed Clubs and individual fundraisers: without the combined effort of all of you, we would not have obtained the WINN Feline Foundation grant to enable this research. It is thanks to your hard work that we are able to offer screening and *post-mortems* free of charge, and are making progress towards establishing the responsible genetic mutation.
- Breeders and owners that have brought cats for screening – some of you have travelled great distances and showed tremendous dedication. My personal thanks and heartfelt condolences go to those who have sent me their beloved Birmans (or their hearts) for *post-mortem* examinations – I know how difficult this is. Thank you also to those who have sent DNA samples in circumstances where your cat has died of severe cardiomyopathy.
- The cats: we appreciate their patience and tolerance greatly (even if we have heard the 'Birman huff' on several occasions).
- Owen Burt for technical support
- Jose Novo Matos: A board-certified cardiologist who joined our team in May as a PhD student, supervised by Virginia Luis Fuentes. He has undertaken the majority of Birman heart scans to date and has been a brilliant addition to our research group.
- Professor Virginia Luis Fuentes