

Selected Inherited Diseases of the Cat

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- To date, over 250 genetic diseases have been identified in the cat and more are added every year; about half of these diseases have counterparts in humans
- A feline genome project is now in its third decade and has made significant progress; researchers are lobbying to have the feline genome added to a high priority funding list for whole genome sequencing by the National Human Genome Research Institute in the United States
- Two Feline Genetic Diseases conferences have been held in the United States: the first in 1998 at the University of Pennsylvania, the second in 2000 at the University of California; in May 2002, the first Canine and Feline Genomics conference was held in St. Louis; more conferences are planned for 2003

Polycystic Kidney Disease (PKD)

- Autosomal dominant PKD is the most common genetic disorder of humans, with an incidence of from 1 in 200 to 1 in 1000 people, 3 known genes are associated with the adult onset form of the disease
- PKD has been described in Persian-type cats since the 1960s; now found world-wide
- Most of the important feline research was done in the 1990s
- Feline PKD is now established as a model for the disease in humans
- Some affected cats develop chronic kidney failure, usually in the middle years of their lives
- In the late 1980s, Dr. David Biller of the Ohio State University in the United States established a colony of PKD research cats after he acquired the offspring from a 6 year old Persian female with PKD
- Ultrasounds of the sire and 5 kittens from 2 litters found the sire was not affected, 2 male offspring had PKD, 1 female offspring had PKD, 1 female offspring was not affected
- Dr. Biller then developed a pedigree database of 115 cats by crossing some of the offspring with unrelated, normal DSH cats
- Of the 115 cats in database, 102 were positive for PKD; analysis of the data proved autosomal dominant inheritance of PKD in cats
- Starting in the late 1990s, breeders in the United States and around the world have been testing their cats for PKD
- Breeds most at risk are: Persian and its related breeds, Himalayan and Exotic
- Data from some recently published studies on PKD:
 - In 2000, in the United States: 745 Persian/Himalayan cats ultrasounded for PKD at specially arranged clinics, over 42% of cats were positive for PKD
 - In 2001, in Australia: 45% of a group of 250 Persians were positive for PKD

- In 2001, United Kingdom: almost 50% of a group of 132 Persian cats examined at the University of Bristol were positive for PKD
- In all these studies, the majority of cats did not have signs of kidney failure at the time of their diagnosis
- Age at which kidney failure develops in PKD patients ranges from 3 to 10 years of age, average is 7 years of age
- But the high prevalence of PKD in Persians, Himalayans and Exotic Shorthairs makes this an important cause of kidney failure in cats, especially when we consider that over 40,000 Persians are produced by breeders every year in the United States alone and Persians represent about 80% of the pedigreed cat population in that country
- So far, only very low rates of PKD have been reported in other breeds at risk, which include: Scottish Folds, British Shorthairs, and Birmans. In the past, Persians were allowable outcrosses for these breeds and so the PKD gene may have been introduced into some bloodlines.
- Criteria for diagnosis of PKD:
 - Experienced ultrasonographer with good quality machine, transducers of 7.5 to 10 MHz (7.5 MHz for adults, 10 MHz for kittens)
 - Minimum 9-10 months of age; each kidney scanned carefully in two planes
 - Multiple cysts in both kidneys; presence of cysts in one kidney only, especially in a high risk breed, is strongly suspicious for PKD and the cat should be re-scanned when older
- On an x-ray, it may be possible able to see the enlarged kidneys in some patients
- At post mortem, the kidney can be markedly misshapen, variable in size, and contains multiple cysts; the cysts may not be visible on the surface of the kidney, so examination must be done carefully, the pathologist must make several slices through the kidney to identify milder cases
- Advice for breeders:
 - Scan all breeding stock by 10 months of age; may be wise to re-scan at 2 years of age or older because a few cats with mild PKD will not be detected at 10 months
 - To eliminate PKD from bloodlines, it is best to breed only normal cats
 - Since PKD affects such a large proportion of the breed, it may not be practical or wise to immediately eliminate all PKD positive cats (this would restrict the gene pool); you can breed normal cats to heterozygotes and keep only the normal kittens as replacement breeders. Heterozygotes are identified as affected cats that have one normal parent.
- Ultimately, we need a genetic test to properly identify affected and normal cats; at least 3 different genes are known in humans and researchers will be checking these genes first to see if one of them causes feline PKD; if it is not one of these 3 genes, the search for the feline PKD gene will become much harder
- A good website for PKD information: <http://www.felinepkd.com/>

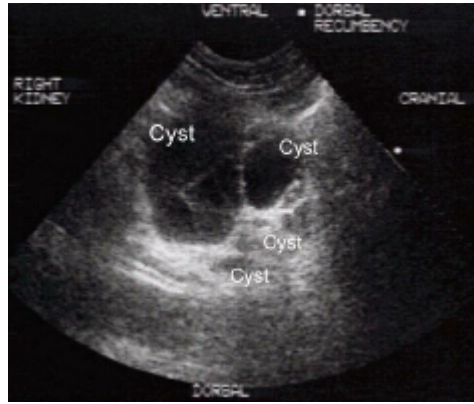


Photo 1: Polycystic kidney disease on ultrasound

Hypertrophic Cardiomyopathy (HCM)

- In humans, HCM often runs in families, with 50% of cases inherited in autosomal dominant fashion
- Several different gene mutations identified in humans
- HCM is the most common heart disease of cats today
- No specific gene mutations have been identified yet in cats
- Male cats are more often affected than females
- The typical HCM patient is male and middle-aged
- Many affected cats have no symptoms of heart disease when they are diagnosed
- Cats in heart failure at diagnosis may have difficulty breathing, lethargy, and a poor appetite
- Cats with blood clots blocking critical arteries may have difficulty walking or paralysis of the hind legs and may be in great pain
- The first breed identified with inherited HCM was the Maine Coon about 10 years ago (Dr. Mark Kittleson, University of California); mode of inheritance identified as autosomal dominant
- Since then, HCM known or strongly suspected to be inherited in several other breeds: American Shorthair, Persian, Rex breeds, Ragdoll, British Shorthair
- Several breeds appear to be at low risk, such as the Siamese and Abyssinian
- Characteristics of HCM vary among breeds:
 - Maine Coons are best studied: usually no disease before 1 year of age; disease present by 2 years old, becomes severe by age 4
 - American Shorthairs appear to have a milder form of HCM
 - Persians appear to have a form involving asymmetrical septal hypertrophy
 - Ragdolls appear to have a severe form with early onset
- HCM is a progressive disease that may progress slowly or quickly
- Characteristics of HCM:
 - Hypertrophy or increase in size of heart muscle, especially of the left ventricle
 - May be associated with enlargement of the left atrium
 - An irregular heart rhythm may be present

- Heart murmurs are usually, but not always present – murmur can be variably present or absent in the same patient. A heart murmur that persists beyond 4-6 months of age in a kitten should be investigated.
- HCM is a common cause of heart failure
- Risk of blood clots that block blood flow to critical arteries
- Sometimes the first and only sign is sudden death
- Diagnosis is most reliable by echocardiogram (ultrasound of the heart)
- Treatment:
 - Some patients are in heart failure and must have their immediate condition stabilized (oxygen, diuretics, treatment of clots if present)
 - Diltiazem (Cardizem®): first line drug therapy
 - Beta blockers (i.e. atenolol): may be best for cats with obstructive form of HCM
 - ACE inhibitors (enalapril – Enacard®, Vasotec®; benazepril – Lotensin®, Fortekor®): may be useful in cats that do not respond to other medications
 - Aspirin: commonly prescribed to prevent blood clots but does not work as well as expected; recent study showed that low dose works as well as higher doses
- Treatment of asymptomatic cats is controversial: some drugs such as diltiazem or ACE inhibitors may be able to reduce the muscle hypertrophy, so it might make sense to treat these cats if they are diagnosed at a young age while the hypertrophy is still developing; some cardiologists do not treat asymptomatic cats unless the left atrium is enlarged
- Prognosis: highly variable; generally worse for cats that are in heart failure or for those with severe enlargement of the left atrium; poorest prognosis is for cats with thromboembolism (blood clots in critical arteries)
 - Some cat family lines have more malignant forms of HCM than others
 - A study published in 2002 on 260 cats with HCM:
 - Well cats: survived up to 10 years
 - Cats with heart failure: survived an average of 18 months
 - Cats with blood clots: survived an average of 6 months, high risk of clot happening again
- Advice for breeders of Maine Coons:
 - Screen breeding stock yearly with ultrasound
 - We can assess males by age 2, females by 3-4 years of age
- Advice for breeders of other breeds:
 - Ragdolls: often have disease before 1 year of age, so can start screening earlier with ultrasound
 - Other breeds: ?? Similar to Maine Coon
- Presents difficulties for breeders because cats have often produced offspring before they can be fully assessed
- A genetic test is needed to identify affected cats earlier, but no gene responsible for feline HCM has yet been identified
- Good website for HCM information: <http://members.aol.com/jchinitz/hcm/index.htm>



Photo 2: chest x-ray of enlarged HCM heart

Feline Hip Dysplasia (HD) and Patellar Luxation (PL)

- Although little information is known about feline HD compared to canine HD, reports of HD in cats date back to at least the 1960s
- Recent research shows feline HD is more common than once thought
- Feline HD is similar to canine HD in some ways:
 - It is a developmental malformation of the hip joint
 - It is not congenital (not apparent at birth)
- Most cats with HD are asymptomatic, and are often diagnosed incidentally when x-rays are taken for other reasons
- One study showed a potential link between HD and patellar luxation (dislocating kneecaps) in cats
- Males and females are equally affected
- Studies done in the United States show some breed predispositions:
 - Devon Rex (about 40% affected)
 - Persian/Himalayan (about 20% affected)
 - Maine Coon (about 23%)
 - Non-pedigreed cats (about 5.8% affected)
- HD is assumed to be an inherited trait in cats, likely polygenic; the role of environmental factors (ie. breed, size, diet, growth rate, etc) is unknown
- Maine Coon breed most studied:
 - Concerns about HD in this breed date to the 1980s
 - Orthopedic Foundation for Animals (<http://www.offa.org>) in United States has data on 617 Maine Coon cats from 1974-2000:
 - 23.3% were dysplastic; only 4.5% scored excellent
 - OFA will give a preliminary report on cats as young as 4 months of age, but will not give a final score until at least 24 months of age
 - May be necessary to x-ray breeding cats yearly since cats rated normal at 2-3 years of age may have HD in later life
- Clinical Signs of hip dysplasia:
 - Decreased activity
 - Abnormal gait (bunny hopping, crouched, wobbly)

- Reluctance to jump or play
- Limping after vigorous exercise
- Pain on urination/defecation or on touching hindquarters
- Some cats develop constipation due to reluctance to defecate
- Most cats have no signs at all!
- Physical findings and x-ray findings do not necessarily correlate: cats with severe HD on x-ray may not have any clinical abnormalities or pain
- Genetic predisposition for patellar luxation (PL) noted historically in Devon Rex, Abyssinian. HD is also prevalent in Devon Rex.
- University of Pennsylvania study (1999), 78 cats (25 cats with HD and 53 cats without HD):
 - 64% of Devon Rex had PL; 32% had HD and PL
 - 80% of Abyssinians had PL; 30% had HD and PL
 - 45% of Maine Coons had PL; 18% had HD and PL
 - 17% of non-pedigreed cats had PL; 29% had HD and PL
 - Overall 58% of cats had PL, most were Grade 1 (mild) and most were affected in both knees; 24% had HD and PL
 - Only 22% of cats had clinical signs referable to either PL or HD
 - The authors concluded that cats were 3 times more likely to have HD and PL together than either condition alone
- Conservative therapy for HD and degenerative joint disease (DJD):
 - Weight reduction if obese
 - Avoidance of activities that worsen pain and lameness
 - NSAIDs: aspirin, ketoprofen, meloxicam; used with caution in cats and only under veterinary supervision
 - Neutraceuticals: (Adequan, Cosequin, Glycoflex) have become popular with pet owners, perceived to have low risk of adverse effects, no controlled trials have evaluated their use for treatment of chronic DJD
 - Corticosteroids: such as prednisone are controversial for treatment of DJD since they have negative effects on cartilage metabolism; may be best to leave to last resort
- Surgical therapy for HD and degenerative joint disease (DJD): considered when conservative management fails, or when owner perceives quality of life is unacceptable
 - Goal is to relieve pain and restore mobility
 - Best surgical technique is femoral head and neck ostectomy (FHO); also called excision arthroplasty
 - Cats do very well post-operatively; experience pain relief and return to normal function
- Good website for feline HD information: <http://www.fhda.com>



Photo 3: severe bilateral hip dysplasia

Amyloidosis

- Amyloidosis is a diverse group of diseases of human and animals, first identified 150 years ago; cause of familial Mediterranean fever in humans
- Familial amyloidosis found in Shar-Pei dogs and in Abyssinian and Oriental/Siamese cats
- Serum amyloid A (SAA) is a protein produced in the liver as part of the immune response
- Amyloidosis occurs when deposits of amyloid protein AA (which is closely related to SAA) are found in body organs such as the liver and kidneys
- Amyloidosis can be due to chronic inflammatory disease, genetic predisposition
- Abyssinian form:
 - First reported in 1982; research funded by Winn Feline Foundation and Aby breeders since 1983; discovered much about the disease and the nature of the amyloid protein
 - Familial, inherited disease but mode of inheritance not yet known; appears to be at least 3 genes involved, each with multiple forms; disease probably due to genetics, stressors, and immune system dysfunction
 - Primarily attacks the kidneys of cats between 2 and 5 years of age; causes kidney failure

- Diagnosed with kidney biopsy and special stain (Congo red)
- Treatment as for any cause of kidney failure
- Need to identify the gene or genes involved to develop a simple test
- Oriental/Siamese form:
 - The liver is main target organ; sometimes kidney involved too
 - Liver becomes enlarged and swollen, fragile and bleeds easily
 - First reported in 1992; affects non-pedigreed cats as well as Siamese and Oriental type cats; also reported in one Devon Rex and one Burmese
 - Affected cats are usually under 5 years old
 - Signs: life-threatening hemorrhage from the liver; queens may be affected at the time of delivery of a litter; sudden death from hemorrhage may occur
 - Genetic sequencing has shown that the amyloid proteins in the Aby form and the Siamese form are not the same, so they are caused by different genes
 - Appears to be a familial predisposition in some Siamese and related breeds
 - The mode of inheritance is not yet known; some cases appear to be spontaneous
 - Diagnosis: suggestive clinical signs, susceptible breed; biopsy of liver
 - Treatment:
 - Supportive: vitamin K for blood clotting, cage rest, antibiotics
 - Drugs used in human forms: colchicine (used to treat Mediterranean fever), cyclophosphamide and chlorambucil (used to treat some forms of kidney amyloidosis in humans), other drugs targeting amyloid formation only used in research settings with mice
 - Prognosis is grave for affected cats
 - We need a genetic test
 - What breeders can do:
 - Request full necropsies on cats that die with symptoms suspicious of amyloidosis
 - Request full necropsies on cats that die unexpectedly
 - Track amyloidosis on your pedigrees, keep good records
 - Be willing to share information with other breeders and with researchers

For more information on many feline diseases and feline research, see the website of the Winn Feline Foundation:

<http://www.winnfelinehealth.org>