THE CAT FANCIERS' ASSOCIATION

BASIC GENETICS
FOR THE CAT BREEDER

Basic Genetics for the Cat Breeder

Introduction

The genes that control coat, color and pattern in cats are now being identified and studied. This has been made possible by the mapping of the feline genome, along with the genes that control diseases and structural abnormalities. The resulting information, as it becomes available, allows breeders and others interested in the subject plan what colors will result from a particular mating. In addition, it is now possible to learn more about how diseases and abnormalities can be deselected or eliminated before they become an integral part of a breed. An in depth discussion of colors and patterns can be found at “Understanding the Basic Genetics of Cat Colors” at http://catgenes.org/pdf/understanding-cat-colors.pdf.

The following material is a discussion of basic genetics that breeders of pedigreed animals need to know in order to understand some of the issues facing those who work with pedigreed animals. Those breeders who have been successful have in some way intuitively mastered these basics over time. We see this in all species that are selectively bred. Some groups, such as food animals (cows, pigs, chickens, etc), have been easier to study due to the massive scale in which offspring are produced. We can learn from these large groups because their breeders keep careful tabulations of the positive - as well as negative - influences.

We, as breeders of pedigreed cats, also have learned from the work that has been done in the past. Have you ever heard the expression “Don’t double up on that line” when talking to another breeder? Or conversely, “I have had success line breeding these cats”? Both of these statements contain information about the genetics of a given breeding program.

Selective Breeding

Coats, colors and patterns are passed down from parents to offspring, i.e., inherited. But so are aspects of temperament, size, susceptibility to disease, and even diseases themselves. Particular pedigreed breeds may have issues that have arisen through selective breeding (the selection of a particular trait such as a short nose or fine boning), or issues that have been there all along because of the foundation breeding stock for the breed. If a kitten was suddenly born with 5 legs (clearly an “interesting” mutation) and those who were breeding that breed decided that this was a desirable trait, then more kittens would be born with 5 legs because matings would be done to “select” for this “desirable” trait. If the addition of the leg was not thought to be desirable, then no more matings would be done to “select” for that trait. “Selective breeding” is the heart of any successful breeding program, be it fish, mice, hamsters, or cats.

There is a written set of descriptions that discusses the ideal specimen of a breed, as well as the colors that are accepted for a particular breed. This is called a “Breed Standard” or “Standard of Points”. The standard for a given breed may differ from registering organization to registering organization around the world, and the colors that are accepted may differ as well. However, the ideal example of the breed is what is being discussed. The trick, if you will, is to come very close to the description of the ideal example in as bright and clear a color and pattern as you can, while still maintaining the “genetic strength” of the animal and the breeding program. Thus, if you have the prettiest animal in the world, it will be to no avail if it is genetically weak, (that is, produces a lot of undesirable or unhealthy traits when it is bred). Conversely, it will do no good to have the most genetically sound animal in the world if it is not remotely close to the standard for the breed.

For those individuals who have been selecting for specific traits or characteristics within a breed, careful attention needs to be given to changing the breed. For example, increasing the length of the head may have other effects such as a change in eye aperture or a change in the slope of the forehead of the animals produced. The “breed standard” may be affected by the decisions of a group of individuals who think that they have enhanced the breed where, in actuality, they have changed the breed standard.

Genetics and the Environment

The occurrence of any particular characteristic depends on two factors: “genetics” and the "environment". "Genetics" refers to the encoded information (instructions) that are carried within the cells of all living organisms and which control traits. These encoded instructions are responsible not only for maintaining the continuity of a species (or breed) but also for many of the differences between individuals within a species or breed. Thus, if you are a breeder and like a particular “look” in your cats, you could influence the breed positively or negatively depending upon what that “look” involves. A good example can be found in the Persian. The Persian breed group has many colors and patterns in the different divisions. However, some years ago, breeders began to select for much shorter noses and faces that were more flat. This was thought to be a desirable set of visual traits until the resulting offspring had difficulty breathing with eyes watering because the apparatus that controlled these activities was not structurally sound. Today, successful breeders have balanced that pleasant short-faced look with space in the head in which the nose, eyes and tear ducts, jaw, and other structures have room to perform their functions properly. By selecting away from Persians whose tear ducts do not function correctly, or whose eye aperture is not the correct size for the eye, a healthier group of Persians is produced. This does not mean that the resulting offspring will be less close to ideal, but they combine the pleasant “open” expression with the health that perpetuates the breed.

The “environment” that a given animal lives in contributes to the differences between individuals as well. The relative contribution of genetics and environment is not the same for every trait. Some traits such as ear shape or size are influenced very little by the environment. For others, such as temperament, the effect of the environment is much greater. Geneticists use the term heritability to indicate the proportion of the total possible variability in a trait that is genetic. However, except for the cases where genetics is the main source of variability, the **heritability** of a trait is difficult to establish, and may not be the same for different breeds. Therefore, it is not possible today to say that the heritability of size, for example, is 70% genetic (or whatever it may be), so aside from understanding the basic concept, the notion of heritability has little to offer the breeder at this time. It is possible that, as more is understood about the feline genome and the inheritance of some of the genes, it will be possible to have more information on heritability. What do we mean by environment? For a kitten, the first environment it encounters is that of the mother's womb. Is the mother well nourished, healthy, and free from stress or parasites? How old is she? Is this her first litter? How big is the litter? Once the kitten is born, it experiences a new environment where it has to compete for food and attention. Litter size is still a factor. How much food does the kitten get? How much attention does it get from the mother, the breeder, and the eventual owner? Does it have a safe and healthy environment? Does it have other cats to associate with?

Epigenetics, the study of multifactorial issues that cause variability while not changing the actual DNA in a gene is a new concept for scientists. As these researchers have looked at the feline genome (and other genomes including the human genome) they have begun to understand that the simplified model of one gene, one trait is not adequate to explain all diseases, abnormalities or variability. Muscular dystrophy is a simplified model where one gene is responsible for the disease in humans (and perhaps cats). However, most diseases are multifactorial – that is, influenced by many genes interacting with one another and by a huge array of signals within the cellular environment (including nutrient supply, hormones, and electrical signals from other cells). In addition, many diseases are altered when the conditions of life are altered, especially in early life. For diseases involving many genes, the effect of each gene is small, and loss of function for one may be compensated by gene interaction and by environmental conditions.

What are Genes Anyway?

The gene is often called the basic unit or building block of inheritance. A gene carries the information for a single step in a biological process, but most biological processes -- even the ones that may appear to be simple -- are made up of more than one step. Thus, it is false to assume that a trait is determined by a single gene, but rather that many genes often control a single trait. A good example is color. In some breeds there are a great variety of colors, so it should come as no surprise that this is the result of the action of a variety of genes. There are not only genes for making the different colored pigments, but also genes that control the distribution of the pigments both within the individual hairs, and over the entire body. Other breeds may come in only one color. These breeds have the same genes, but only one version (allele) of them is present. For more information about colors and patterns, see "Understanding the Basic Genetics of Cat Colors" at http://catgenes.org/pdf/understanding-cat-colors.pdf.

All animals have 20-25,000 genes, but they do not float around loose in the cells. To make cell division and reproduction more manageable, genes are physically connected to other genes to form long strands called chromosomes. Animals have two sets of chromosomes- one from the mother and the other from the father. These are contained in the egg and the sperm. When the two (egg and sperm) unite, the resulting offspring contain two sets of chromosomes. However, the mechanisms that determine this are not able to tell which chromosomes came from the mother and those that came from the father. Therefore, the set that is passed on in a particular egg or sperm is a mixed set. The number of possibilities depends on the number of chromosomes.

All pedigreed cats (like all random-bred cats) belong to the same species. This means that they all have the same amount of chromosome material and the genes line up basically the same way on those chromosomes. So, any of these could be bred together and produce viable offspring. This is the way cat breeds have been produced – by selecting for specific traits that are desirable and mating cats until the offspring are uniform for that trait. If one tried to breed a cat to a member of another species, there would be no resulting offspring. Assuming that the physical act of mating could take place, the number of chromosomes differ from those in the cat. Therefore, no line up of chromosomes would occur and no resulting offspring would be produced.

In any species, one of the chromosomes carries genes that determine sex. In mammals (including humans) the chromosomes carrying the "female" genes is designated X and the one carrying the "male" genes is designated Y. If you looked at the X and the Y chromosomes under the microscope, the X chromosome resembles the letter X, and the Y chromosome resembles the letter X without one of the arms – therefore, like the letter Y. An animal with two X chromosomes will be a female, while one with an X and a Y will be a male. Genes other than those determining sex can also be located on these chromosomes. These genes are said to be sex-linked. A good example of this is the tortoiseshell color. The genes that control the color black and that control the color red in the cat are located on the X chromosomes (one color on each chromosome). Furthermore, these genes are located on the arm of the X chromosome only, and are not present on the Y chromosome. So in a male offspring (with only one X chromosome) only one color is represented (either black or red) but in the female who has two X chromosomes, it is possible that both black and red can be expressed – tortoiseshell.

What are Mutations?

Most genes carry out their functions correctly. Sometimes, however, a gene or multiple genes can be altered by exposure to radiation (natural or man-made), certain chemicals, or accidentally through random chance when a cell divides. A gene may be thought of as a small computer program. There are many possible places in the program where an error (**mutation**) might be introduced. Many of these errors will have the same effect; the program will not function. Others may modify the action of the program. Some may appear not to affect the program at all. All mutations, regardless of their effect, change the information carried in the program. Each is, therefore, a different version of that program. In genetics we call each version an "**allele**". Different versions, even if they produce the same effect, are different alleles. Generally, we are only concerned about the alleles that produce different effects; we treat alleles that produce identical effects as though they were the same.

Though there are potentially a large number of alleles for each gene, by far the most common are those that entirely prevent function. Therefore, for many genes we only find the normal allele, often called the wild type and "no-function" (null) alleles. For some genes, we also get alleles that function partially or abnormally. However, no matter how many alleles there are in a population, an individual can carry only two -- one from the sire and one from the dam. When the two alleles are the same, the individual is said to be **homozygous** for that gene. When the alleles are different, the individual is **heterozygous**.

Dominance

If, for a particular gene, the two alleles carried by an individual are not the same, will one predominate? Because mutant alleles often result in a loss of function (null alleles), an individual carrying only one such allele will generally also have a normal (wild-type) allele for the same gene, and that single normal copy will often be sufficient to maintain normal function. The gene is said then to be dominant.

When someone speaks of a genetic “abnormality” being "carried" by an individual or line, they mean that a mutant allele is present, but it is not apparent. Unless we have a sophisticated test for the allele itself, we cannot tell just by looking at the animal that carries that allele (the carrier) that it is any different from an individual with two normal copies of the gene. An example of this is the black cat that carries dilute. From looking at this cat, it is impossible to tell if the cat genetically carries two genes for black or one gene for black and one for blue. When mated to a dilute cat, a black cat carrying dilute will produce a larger percentage of dilute offspring over time, while one homozygous for black will produce only non-dilute offspring.

Lacking a genetic test for carrier states, the carrier will go undetected and inevitably pass the mutant allele to approximately half of its progeny. Every individual, be it man, mouse or cat, carries a package of those undetected mutant alleles. Since we all have thousands of different genes with many different functions, and as long as these abnormalities are rare, the probability that two unrelated individuals carrying the same abnormality will meet (and mate) is low. Breeders, however, “select” the mate for their cats, rather than allowing them to breed randomly. Thus, we increase the degree to which our cats are related to one another and increase the probability that cats will be mated that have the same mutant allele inherited from shared ancestors. In other words,these hidden alleles will become visual. A good example of this is the weakening of the knee joints (called patella luxation). When the knee joint is not correctly formed, the muscle structure that holds the knee together is often not able to function correctly and the knee joint wobbles. This effect can be seen when the animal runs, and can be pronounced or just hinted at. However, if two animals with weakened knee joints are bred together, the effect can be really pronounced with knee joints not able to withstand even small weight.

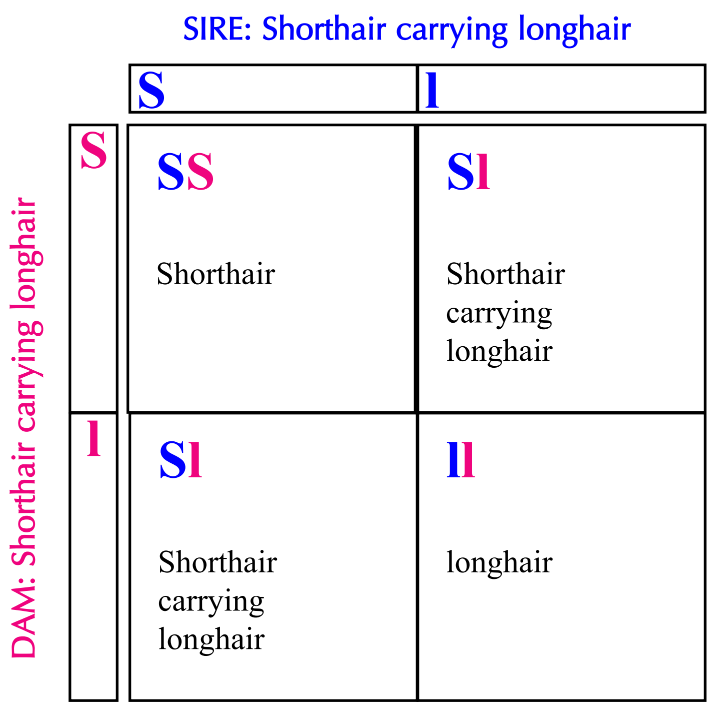
Sometimes individuals with only a single normal allele will have an "intermediate" phenotype. Mendel, a monk who lived in the 19th century, illustrated this principle dramatically with pea plants. He had red peas and white peas. When he “mated” them together, the resulting crosses were pink peas (they contained one red gene and one white gene). When these pink flowers were “mated” together, there was a resulting batch of peas with some flowers that were red, some that were white and some that were pink. The resulting theory posed by Mendel based on the observations with these peas still hold to this day and percentages of offspring can be theoretically derived based on the results of these experiments.

Penetrance and **expressivity** are terms that describe the ability of the allele to affect the offspring. If the gene under study is not expressed each time it is inherited, the penetrance may not be full (partial penetrance). If the gene is expressed every time, but the expression is different, it is called **variable expressivity**.

Recessive Traits

If a trait is carried, but not expressed, it is often because it is "recessive". Two like alleles are needed for the recessive trait to be seen. For example, long hair is recessive. Take a normal domestic cat that is genetically homozygous for short hair (it has two shorthair genes). Should this cat be bred to a long haired cat with two "not shorthair" genes, the resulting offspring will be short-haired, but carry the longhair gene. There may be a way to discern that these cats carry that longhair gene because the hairs are softer and stand away from the body rather than having hard hairs (called guard hairs) of the short hair variety. However, if two of those mixed (short-hair/longhair) cats are mated together, the resulting offspring will be ¼ longhair i.e., having two longhair genes). By convention, the dominant allele of a gene is given an upper case letter, while the recessive allele is given a lower case letter. For the hair length gene, L is the shorthair allele and l is the longhair allele.

We can show this in a diagram called a Punnet Square:



If the shorthair cat carrying longhair is mated to another shorthair cat carrying longhair, the resulting offspring in a litter of 4 kittens will (on average) have one shorthair that does not carry longhair, two shorthairs carrying longhair and one longhair offspring. This is, of course, a very simple example. However, as you can see, genetic outcome can be predicted to some extent, although the ratios in a single litter may not reflect the “average”. If you plan a breeding program that maximizes the genes for which you are selecting, you will have this type of result. That does not take into account the role of the dice that gives you a litter of 5 shorthair cats! If you are trying to select for any particular trait, it is highly unlikely that you will get the desired result unless you start with a cat with that trait.

Sex Linkage

The X and Y chromosomes (X from the female and Y from the male) do not look alike. However, as a pair, they determine the sex of the offspring. These chromosomes are called sex chromosomes. The other chromosomes that carry other information are called **autosomes**.

Females have two X chromosomes and males one X and one Y. The male normally produces an equal number of sperm with either the X or the Y chromosome. As his mate will only be producing eggs with X chromosomes, an equal number of female (XX) and male (XY) offspring should be produced. The perfect ratio of 1:1 (male to female) is only realized over many litters, and breeders know that most of the time there are more males than females.

Determining the Mode of Inheritance

Suppose that you have a litter in which several of the kittens appear to be less robust than their littermates. Further,suppose that in the next few weeks these weaker kittens appear to be growing more slowly and appear less energetic. What do you do? Obviously, the first step is visit your vet for an examination.

As this is a hypothetical example without details, let us suppose that after appropriate tests, the vet concludes that these kittens have a hole in the septum between the two sides of the heart. This abnormality results in a mixing of oxygenated and deoxygenated blood. What caused the problem? Was it simply a developmental accident, an environmentally-induced condition, or is it genetic? This particular problem could arise from any of the three factors.

As a rule, if only a single kitten is affected, the problem has not turned up before in related litters, and the problem does not occur frequently in the breed, it is likely a developmental accident. Nevertheless, given the usual under-reporting of health problems, especially those that may be genetic, careful consideration should be given to repeating this particular mating again.

On the other hand, if all, or even the majority of the littermates were affected, one might be more inclined to look for something in the environment that could have disturbed the normal developmental process. Another serious consideration is the possibility that the parents carry a recessive gene(s) that caused this problem.

Dominant mutations have a significant impact on health, and will, in most cases, result in death before reproductive age is reached. There are exceptions, such as Huntington's Disease in humans or polycystic kidney disease (PKD) in several species, including cats. Any late-onset genetic disease, whether dominant or recessive, represents a potential problem. A dominant gene allows for a waiting game: one can wait for the progeny to reach an age where the problem would normally have developed, then breed unaffected animals with reasonable assurance that they are not undetected carriers.

Doing the necessary crosses to establish the mode of inheritance can be an expensive and time-consuming task, to which is added the thankless prospect of finding pet homes for kittens that are unsuitable for the breeding program. Consequently, test matings are seldom done on a scale sufficient to produce numbers that can be subjected to statistical analysis, except in a research laboratory. Since the feline genome map has been completed, it is now easier for some institutions to do these test matings to determine mode of inheritance. For breeders, neutering or spaying are viable options.

One alternative is retrospective analysis of pedigrees of affected animals. As one generally needs a number of related animals occurring over several generations, the problem will likely already have become fairly common before it is identified. The accuracy of such analyses is directly affected by the number of relatives for which data exists - a strong argument for the open exchange of information between owners, breeders, veterinarians and researchers. When looking at the “affected” pedigrees, it is important to know what happened to ALL of the offspring of each breeding reflected in the pedigree, not just the affected cat. This is extremely difficult since not everyone wants to share information. In some species, all offspring are tracked in a database, thus giving the prospective breeder a lot of information about the mating prior to actually producing offspring. This is not true in the cat world, although the writer would encourage this practice since it would help to minimize abnormalities in outcross breedings as well as line breedings.

Genetic Load

One of the biggest mistakes that breeders make is assuming that their animals are healthy and do not carry alleles for genetic diseases or abnormalities. This misconception leads many breeders to argue that it should be possible to breed animals with a desired conformation while avoiding undesirable traits. In a perfect world, this would be possible. Breeders do concede that some unfortunate individuals do carry recessive alleles for certain diseases, but believe that if they choose their breeding stock carefully, they can avoid these problems. And, if problems do occur, it is due to "bad luck", the lack of direct genetic tests for recessive alleles; because another breeder has been concealing something; or because it “came from that cat”.

The truth is that it is virtually impossible to avoid genetic disease. Geneticists believe that most species carry a "**genetic load**" of 3-5 recessive lethal genes. The difference between humans and cats is that humans have something in excess of 2500 identifiable genetic diseases which have been studied or whose causes are currently being uncovered by geneticists. Most of these diseases are extremely rare and thus seldom come from both parents to produce an affected child except by accident. This is because we as humans are “random-bred”. We are not bred to our sisters, cousins, fathers, or uncles, on a routine basis. For cat breeds, however, this is not the case. Cat breeds have a few common genetic diseases that may have come along with the development of the breed. It is the frequency of these problems, rather than the number of different ones, that is the true indicator of genetic health in a population.

We live in fortunate times. Geneticists have just recently completed the mapping of the feline genome, a daunting task made a little easier by the location of genes that are related to similar diseases in the human. Leslie Lyons, University of California (Davis) has written a chapter in the latest version of a book edited by Dr. John August which includes information about the feline genome project undertaken by several laboratories around the world. When a direct genetic test becomes generally available for a specific disease, the test will identify defective genes carried by individual cats. Take for example, polycystic kidney disease in cats. This disease is caused by a dominant gene. (The cat only needs to have one copy of the mutant allele to have the disease – two copies cause them to die during development in the womb or at birth). The test that was developed by the University of California at Davis along with researchers in Kansas State and Ohio State University allows breeders to test their cats at any age and their kittens at birth to look for the defective gene. Thus, a breeder can mate a known carrier of the defective gene to a non-carrier and select for breeding those offspring that do not have the defective gene. The other animals are spayed and neutered and placed in good homes with information on the disease for the new veterinarian and owner. In a couple of generations, the disease can be eliminated from that breeding program.

Some diseases are much more complicated. A discussion of specific abnormalities or diseases, "Heritable Diseases and Abnormalities in the Cat", can be found at http://catgenes.org/pdf/heritable-diseases.pdf. These diseases may have multiple genetic components, may be malfunctions of the immune system or combinations of both. For these issues, the geneticists are challenged to reach a new level of their craft. Breeders are forced to rely on their instincts and careful selection to keep their stock healthy until a definitive answer comes along.

Inbreeding and Line Breeding

Inbreeding and line breeding can be confusing words and the concepts are often confused as well.

Inbreeding is the practice of breeding two animals that are related (i.e. have one or more common ancestors). The degree of inbreeding may be assigned a value between 0 and 1, called the inbreeding coefficient, where 0 indicates that the animals have no common ancestors and 1 is a clone of the cat. Inbreeding produces animals that acquire the same allele from both parents as a result of their common ancestry. Thus, it increases number of genes that are homozygous. However, it does not discriminate between good alleles and bad, and therefore is just as likely to make genes homozygous for bad alleles as for good ones.

Inbreeding occurs in most pedigreed domestic animals as the result of several common practices:

Some breeders own a small number of animals and breed only within their own group.

Many breeders believe that outstanding animals can only be produced by inbreeding -- by doubling up on the good alleles while somehow avoiding the bad. This is sometimes called the "Winner" effect.

Some breeds are based on a small number of foundation animals and inclusion of new members into the breed is prohibited.

Line breeding is a form of inbreeding practiced by some breeders -- often by ones trying to maintain a recessive color -- where a son (or less commonly a daughter) is bred to a relative generally less closely related than a first cousin.

If we lived in a world where all the genes followed the simple rule that there may only be good alleles, which are dominant, and bad alleles, which are recessive, then inbreeding could be an effective tool for improving a breed providing the latter were rare.

Unfortunately, when inbreeding (and even line breeding) occurs, both "good" and "bad" alleles can be affected. If the mating enhances a bad trait, and this trait continues to be enhanced, eventually an individual or breeding line could be weakened due to the trait that has been enhanced. We often see this in breeding programs where lines are inbred or line bred until the resulting offspring become smaller and less healthy, more susceptible to disease, and often have a reduced lifespan.

The only animals that are routinely inbred to a high level are laboratory mice and rats. There, the breeders start breeding many lines simultaneously in the expectation that the majority will die out or will suffer significant **inbreeding depression**, which generally means that they are smaller, produce fewer offspring, are more susceptible to disease, and have a shorter average lifespan. However, the resulting animals may have specific traits that are desirable, such as mice with no hair (called nude mice) or mice with specific diseases to be studied as models for human disease. This also results in a line of mice that are genetically extremely similar and will respond to laboratory test conditions in the same way.

Geneticists have developed new tools during the past 20 years, including the ability to detect genetic material in blood samples down to the molecular level. In addition to seeing genetics of population (**population genetics**) such as what the colors of cats are on an island in the pacific, these geneticists can now measure the diversity in genotype (the genes that make up traits).

This discovery led to the theory of "neutral isoalleles" and the concept that heterozygosity (mixed genetic makeup) might actually be a good thing. (Breeders know this intuitively and periodically go to outside breeding programs for "outcrosses".) Although this concept is controversial for geneticists, anyone interested in protecting an endangered species is very concerned with maximizing genetic diversity. The Florida panther is an example. This animal is genetically homozygous for so many traits due to its environmental influences and lack of new genetic material. It has become susceptible to a variety of viruses including Feline Infectious Peritonitis and a variety of other immune disorders, since resistance to disease is dependent on heterozygosity in the genes responsible for the functioning of the immune system. Scientists have been and continue to work with this group of animals to introduce new genetic material into the gene pool to diversify the genes and make the animal healthier (for more information, see articles by Steve O'Brien at the National Cancer Institute).

The winner effect has been discussed, that is the over-use of a recognized male or female. Many breeders believe in the efficacy of this practice because they will be increasing the frequency of occurrence of the genes that made him/her a “winner.” What they may not realize is that they are increasing the frequency of all genes carried by this animal, whether they be good, bad or innocuous -- and that winning animals, like any other animal, carry a number of undesirable recessive alleles that are masked by wild-type alleles. Think about what happens when many breeders work with the same genetic material: all breed their females to one male, then all breed the offspring to another male, and then repeat the process with a third male. The result is that if there is an immune system weakening, a weak or defective hip joint, a defective sternum, crossed eyes, or some other undesirable trait, it is enhanced many fold through this type of selection.

Genetic Diseases and Abnormalities in Cats

Many breeders label any problem that appears to be inherited a "genetic disease". However, though there are legitimate genetic diseases, there are also a variety of problems that have an inherited component, but are of a fundamentally different nature. Dealing effectively with any genetic problem requires an understanding of the relationship between the genes (genotype) and the phenotype (the way the animal looks).

Inborn Errors in Metabolism

Inborn errors in metabolism are a group of abnormalities in genes that have been recognized for hundreds of years. They are the easiest to see because they require a direct intervention to prevent fetal or newborn death. Some can be managed by careful attention to diet; others cannot. A particularly nasty example is Tay-Sachs disease in humans, which involves an enzyme important in lipid metabolism. Individuals who have two alleles (homozygous) for a deficiency in this enzyme accumulate a compound called a ganglioside in the nervous system. They appear normal at birth but progressively lose motor functions and die around 3 years of age. There is no treatment.

Another inborn error is phenylketonuria in the human. The newborn with this metabolic disorder caused by an inability to process phenylalanine quickly causes brain damage. In the early 1960’s, a test was developed for every newborn and as the children with this abnormality were identified, special food was given to supplement the lack of metabolic ability in these affected cases. Using this food stopped the brain damage and allowed these individuals to live a full life. Most of these conditions involve mutations that lead to the production of a nonfunctional enzyme, or one that is totally absent. In heterozygotes, the single good copy of the gene is generally able to produce sufficient enzyme to handle the normal workload. However, in a few cases, carriers as well as affected individuals have to be careful about their diet, or may exhibit less severe phenotypic effects.

We have several of these inborn errors in cats. Glycogen storage diseases, lysosomal storage diseases, and others have been identified. Fortunately, most of these errors result in kittens that are short-lived or born dead, thus limiting the errors to the specific individuals who were mated. However, there are some lines of cats (in several breeds) that have exhibited such issues. Again, these breeders acted correctly in finding a researcher veterinarian who could help them to identify the problem and work with the affected animals. For a more detailed discussion of specific inborn errors, see "Heritable Diseases and Abnormalities in the Cat" at http://catgenes.org/pdf/heritable-diseases.pdf.

Structural Abnormalities

There are many structural abnormalities in the cat. From patella luxation and hip dysplasia to xyphoid cartilage abnormalities, structural defects occur at random in cats. As we selectively breed pedigreed cats, we enhance the opportunity to see these abnormalities occur. A discussion of the most common and well-known structural abnormalities can be found in the article on "Feline Structure" at http://www.cfa.org/articles/structure.html and "Heritable Diseases and Abnormalities in the Cat" at http://catgenes.org/pdf/heritable-diseases.pdf.

Other Abnormalities

Such issues as blood type incompatibility in cats have been around a long time. They have recently been studied in depth and articles have been written to describe the problem. A discussion of the most common and well-known issues can be found in the article on "Heritable Diseases and Abnormalities in the Cat" at http://catgenes.org/pdf/heritable-diseases.pdf.

What Can Breeders Do?

As a breeder, you are a practicing geneticist. To breed effectively you need to know something about genetic principles that have been discussed in the early part of this article. To enhance the possibility of good breeding, you need to know something about how to select breeding stock and what to do when issues arise. To care for the resulting offspring, you need to know how to care for groups of animals – whether they are herds of cattle or a cattery of felines.

The genetics we have talked about so far is sometimes called "Mendelian genetics" after the Monk who grew peas in his garden. There is also a science called "Population genetics" which deals with the distribution of genetic traits (alleles) in a population and the effects of mutation, selection, inbreeding, etc. on this distribution. A basic knowledge of both is critical not only to your own success, but also to the survival of the breed with which you work. Genetics at the level of DNA is called "molecular genetics".

A long time ago, geneticists believed that there were only two alternatives for a gene - "good" alleles that functioned normally and "bad" alleles that didn't. If things were this simple, then the task of the geneticist-breeder would be simplified to one of identifying the bad alleles and trying to eliminate them from the population. Such a simplistic model could be modified to allow for different "good" alleles, but it should not matter whether you have one or another. These early geneticists expected to find little genetic variability in a population. The majority of individuals were expected to be homozygous for the good allele for most genes.

With the recent introduction of modern biochemical and molecular studies, geneticists studying populations found far more variability (diversity) than they had expected. There are a number of possible reasons for this, and even the experts are not in total agreement on the most likely reason(s). However, geneticists have also discovered that populations lacking genetic diversity often

have significant problems and are at greater risk from disease and other changes in their environ ment. The conclusion is that genetic diversity is desirable for the health and long-term survival of a population.

Is there much diversity in cat breeds? Cats do not come in varying sizes to the degree that dogs, horses, or many other animals do. Their size differences may be from 5 pounds to about 30 pounds. However the genetic makeup that shows us the distinctive things about breeds, such as

their coat textures, patterns, colors, whether or not they have a tail, or folded ears or no hair at all makes them diverse. Also, the places they come from may have influenced their gene pool.

Once we could only see the phenotype of cats. Now thanks to the technology that lets scientists see into the very genetic makeup of each animal or breed, we can begin to see the diversity of the gene pool, or lack thereof. The challenge for breeders is to restrict the variability of the genes that make the breed distinctive without sacrificing the variability/diversity that is necessary for good health and long-term survival of the breed. In some cases, this has not been achieved, and we are now paying the price in terms of high incidence of specific genetic diseases and increased susceptibility to other diseases, reduced litter sizes, reduced lifespan, inability to conceive naturally, etc. This is not solely the responsibility of cat breeders. This same issue affects breeding populations of all types worldwide.

Why has this happened – and do we have to accept it as an inevitable consequence of creating a pool of cats we call a breed? I do not think we need to accept this.

The principal reasons for limited genetic diversity are:

1. Many breeds have been established with too few founders or cats that are already too closely related.
2. Many registries are closed for almost all breeds. Therefore you cannot introduce diversity from outside the existing population easily.
3. Most selective breeding practices have the effect of reducing the diversity further. In addition, selection is often being made for the wrong things
4. Even if the founders were sufficiently diverse genetically, almost no one knows how their genetic contributions are distributed among the present day population. Consequently, breeding is done without regard to conserving those contributions that may be of value to the general health and survival of the breed.

If a database of genetic makeup for all cat breeds were designed without regard to the showing, or desirability of "winners," such a database would enable breeders to identify which individuals are most likely to carry the genes that defined the breed. Genes that defined health or structural issues within a breed, such as crossed eyes, or poor hip sockets could be found as well. Measures might then be considered by breed groups as a whole to rebalance the breed in order to ensure that the remaining diversity is more evenly distributed and that therefore is less at risk of loss.

The Havana Brown breed is a good example. Breeders of Havana Browns in the US decided that an outcross for this breed was necessary to increase the vigor of the breed, reduce its susceptibility to infection, and increase its size a little. A suitable outcross program was approved by the breeders, in conjunction with geneticists, and outcrosses were done. The results were healthier animals, with greater size and the same (single) color for which the breed was named.

At the level of the individual breeder, understanding the issues within their particular breed and observing for possible signs of inbreeding depression will enable that breeder to make intelligent,

informed choices when selecting mates. This understanding will also allow breed groups to discuss what to do in general when the health and vitality of their breed is beginning to decline.

Registries for pedigreed cats worldwide are facing the same issues that have been described here. Some registries in Europe have elected to not register cats with mutations such as tailessness, white cats (who may carry the gene for deafness), folded ears, etc. Other registries have elected to register and continue to work with these cats. Still other registries require screening for certain heritable diseases before the cat can be included in that breed's official study book. None of these registries are wrong in what they have decided.

Selecting Good Breeding Stock (from an article by Susan Little, DVM)

Before selecting stock it is important to consider the number of animals in the cattery, their overall health, their interactions with one another, and the things we have reviewed earlier in this article. The challenge is not to add animals without a reason, and not to overpopulate the cattery with animals that do not advance your breeding program. The reminder I have used is to decide how many animals make a good breeding program for the cattery and post that number on the refrigerator where you can look at it daily. If the number is exceeded, then one of the current animals will need to be spayed or neutered and placed in a good home.

Whether you are selecting foundation cats for a new cattery or contemplating adding breeding stock to an established cattery, it is important to understand how to select breeding stock. Breeders can start by identifying their specific goals clearly when considering the addition of new breeding stock. Important skills for the breeder to acquire include a good understanding of the breed standard, the ability to recognize excellent examples of the breed, and the ability to judge one's own cats impartially to recognize strengths and weaknesses. It is also important to keep accurate breeding and health records so that information will be available for selection criteria.

Catteries may require new breeding stock for several reasons:

1. To improve the overall look of the cats as compared to the breed standard
2. To improve reproductive performance of the cattery
3. To improve the overall health of cats produced

There are a number of ways in which breeders can add new breeding stock to a cattery:

1. Selecting a kitten produced within the cattery
2. Purchasing a new kitten from another cattery
3. Purchasing a mature cat from another cattery
4. Using outside stud service for the cattery's females with the intention of keeping kittens for breeding
5. Leasing a mature cat from another cattery for a specified period of time

Selection implies choosing cats for breeding on the basis of individual merit or on the basis of family performance and characteristics. In general, selection causes a small decline in heterozygosity, perpetuation of certain genes, and increasing similarity. Mature cats may be selected primarily on individual merit, whereas kittens may be selected primarily on the basis of family performance. Selection criteria should include health, reproductive performance and phenotype. In general, successful breeders select toward a breed standard based on good temperament and sound conformation and select away from breed-related health issues and other detrimental factors (poor temperament, poor reproductive performance, etc.).

The first goal of the successful breeder is selection for good health and temperament. Good breeding stock is healthy and as free of inherited defects as possible. Select against breeding stock with:

1. Poor overall health, susceptibility to infectious diseases
2. Any inherited defects (including cryptorchidism)
3. Poor temperament with other cats or with people
4. Conformational faults or anomalies

Physically view as many siblings or relatives as possible in order to have a good understanding of the phenotype of the lines you are contemplating. In the case of young kittens, it will not always be possible to evaluate these factors fully until the kitten is mature. Therefore, you can evaluate these factors in the kitten's closest relatives, especially parents and full siblings. Check on the health of the litter to see that they have all grown normally and have been free of disease from birth. Kittens with eye disorders or poor health are not good candidates for breeding programs.

A cat being considered for potential new breeding stock should be:

1. Free from signs of illness (such as upper respiratory infections, diarrhea, ringworm, etc.)
2. Tested negative for feline leukemia virus and feline immunodeficiency virus
3. Tested negative for intestinal parasites
4. In good body condition

5. Screened free from breed-associated genetic diseases, such as polycystic kidney disease, hip dysplasia, hypertrophic cardiomyopathy, etc.
6. Blood typed, if the breed has a significant amount of blood type B cats

Reproductive performance is often overlooked when new breeding stock is selected. If care is not taken, poor reproductive performance can be propagated into future generations. It has been suggested that reproductive performance cannot be evaluated fully until a cat has produced at least 3 litters. Queens that have a poor reproductive performance record by the third litter are unlikely to improve. Young kittens should be evaluated by the reproductive performance of close relatives. Evaluate young males by the performance of the father and full brothers. Evaluate young females by the performance of the mother and full sisters. Select mature male and female cats that have good libido, good breeding behavior, and good fertility (average or above average for the cattery or the breed).

The stud male is the most important cat in the cattery due to simple statistics. The stud male can sire many more offspring in a lifetime than can any queen. In general, breeders need to apply higher standards for health, reproductive performance and phenotype when selecting a stud male, and if he is not up to par, be prepared to neuter him in favor of an offspring or another addition to the cattery. Also, be aware that the show cat, the most perfect specimen, may not be the best breeding stock. His brother or another sibling could be a better breeding candidate than the show cat himself. A secret to keeping good breeding stock available in these uncertain times is to keep a littermate (male or female) when you are showing another cat heavily so that the breeding stock is available to the cattery if something happens to the show cat. This can be accomplished as well by a group of catteries working together.

Mature queens being considered as new breeding stock have:

1. Normal estrous cycles
2. Normal parturition: no history of complications with labor and delivery
3. Good mothering skills: no history of cannibalism or abandonment
4. Normal milk production
5. Normal kitten birth weights, low neonatal mortality rates

Prepotency is the term used to describe a male or female cat that possesses the ability to produce offspring bearing a strong resemblance to that parent. The term is more often applied to males because it is easier to recognize this trait in them due to the larger number of offspring they produce. Prepotency may occur as an individual becomes more homozygous for both dominant and recessive traits. Prepotency can be a valuable asset in a breeding cat, but remember that both good and bad features are reproduced in the offspring. Using a prepotent male of superior phenotype can enhance the appearance of kittens produced by a cattery, and using a male known to produce healthy kittens can benefit the long-term health of a cattery and a breed.

The popular sire (or "winner") effect occurs when a given stud cat is overused in the breeding population. Sires may become popular because they are a top winning cat or have sired many winners or because they are known to be free of certain genetic diseases. Recognition programs such as the Distinguished Merit program of the Cat Fanciers' Association (CFA) can actually encourage breeders to flock to certain cats because of their proven track record. However, these programs recognize only the ability to produce show winners, not the overall health of the cat, or its reproductive performance, so caution should be used.

In less populous breeds the effect of overuse of certain cats can be extensive. When one cat's genes are widely propagated, any unknown detrimental recessives the male carries will also be propagated, perhaps to be uncovered in future generations. This can be the mechanism behind the foundation of a new genetic defect. Popular sires also block the contributions of other stud cats and an artificial population bottleneck can occur.

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