The Genetic Basis of Disease in Dogs

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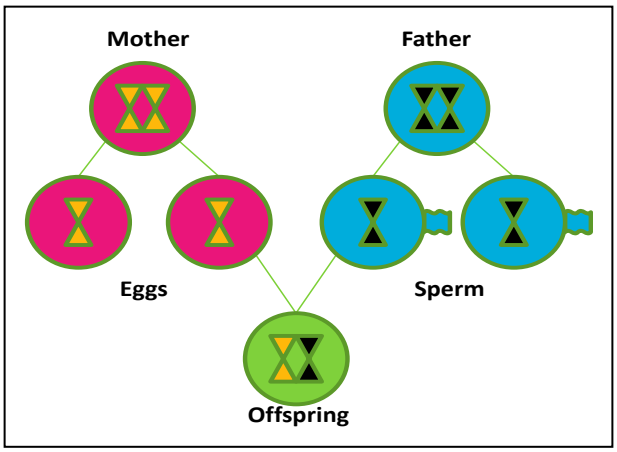
The dog population has a different genetic structure to many other species, such as humans, due to selective breeding that resulted in the development of specific dog breeds. Dogs suffer from a wide variety of diseases, often similar to those suffered by people, and in many cases these diseases are more prevalent in certain dog breeds, suggesting a genetic component to disease. It is of the utmost importance, when trying to reduce the incidence of a disease in a dog population, that the basic genetics underlying the inheritance of disease are understood. Today we will discuss the unique genetic structure of the dog, and we will look briefly at the different components of the genome – the chromosomes, genes and DNA. We will also discuss the various modes of inheritance by which a disease (or any other trait) can be inherited.

The basic structure of genes

Genetic information in all complex organisms in the world is encoded in deoxyribonucleic acid (DNA). This is specific code of just 4 different nucleotides. The order of the nucleotides is the code which determines the production of proteins in every cell of the body.

There is so much DNA in each cell that it is tightly packed and stored in chromosomes. There are 78 chromosomes in each cell in the dog, and they are arranged in pairs (38 pairs of autosomal chromosomes, 1 pair of sex chromosomes). A region of DNA that codes for a particular protein is called a gene. There are many hundreds of genes in each chromosome. As each chromosome is paired, there are, in most cases, two copies of each gene in a cell (the exception being in male animals, which have an X and a Y chromosome, instead of two X chromosomes).

Most cells in the body have the full complement of chromosomes. Only the reproductive cells (the eggs and sperm) have exactly half the number of chromosomes. This means that when the egg and sperm fuse, there is the correct number of chromosomes. This also means that each animal gets half of its genetic information from its mother, and half from its father.



Mutations in genes

In many cases, diseases occur because of mutations in genes, resulting in abnormal proteins being produced by the cells of the body, or the complete absence of a protein necessary for certain functions in the cell. Mutations can occur for many different reasons, and in many different ways. For example, radioactive material can damage DNA and result in mutations. Sometimes, the complex process of copying DNA goes wrong, a mistake is made which is not corrected, and a gene becomes faulty. Mutations that are not corrected are nevertheless copied every time a cell divides, and the mutation can be passed down, through the reproductive cells, to future generations.

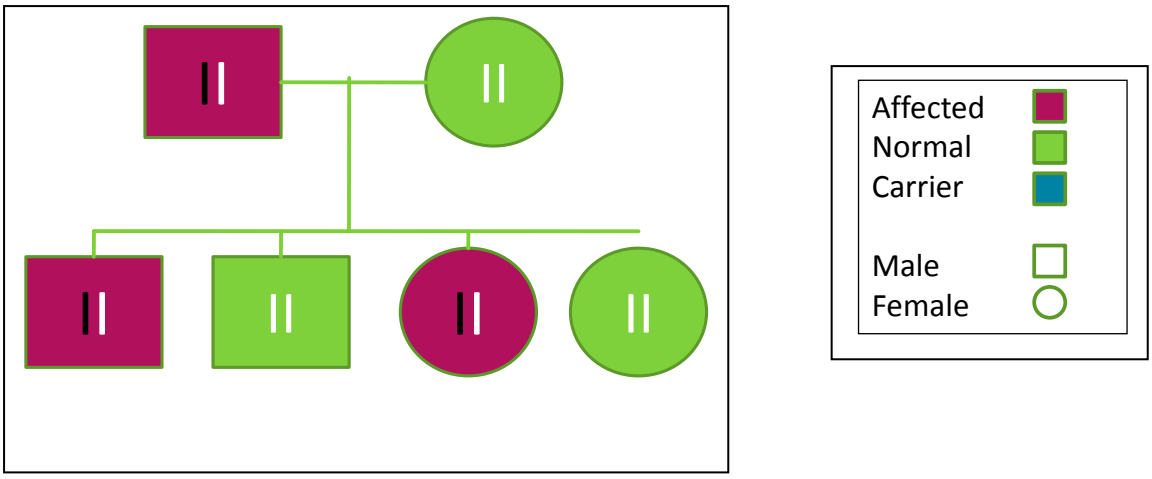
Inheritance of genetic traits and disease

Each cell in an animal has two copies of a gene, one from the mother and one from the father of that animal. The inheritance pattern of a disease or trait gene will vary depending on the number of abnormal copies of the gene and the interaction of normal and abnormal genes. Depending on how the gene is inherited, different numbers of offspring are likely to be affected, the disease may appear to skip generations, and different numbers of male and female offspring may be affected.

Clearly the knowledge of how a disease is inherited is therefore extremely important when making decisions about breeding animals with disease. Although many diseases follow basic inheritance patterns, it must be remembered that in reality genetics is much more complex, and environmental influences, further mutations and other factors may influence whether or not a disease gene is expressed in the body, even if it is inherited. This latter phenomenon is known as incomplete penetrance (i.e. a gene is inherited as expected but for some reason some individuals that have the disease gene will not develop disease).

Autosomal dominant inheritance

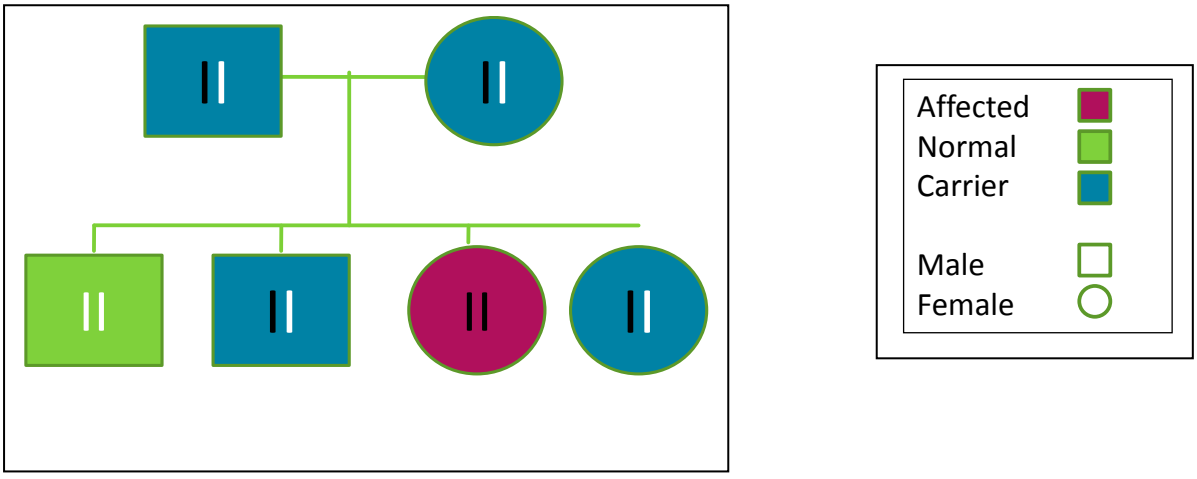
In this pattern of inheritance, the gene is inherited on one of the autosomal chromosomes (i.e. not the sex chromosomes, X and Y). The diseased gene is also dominant, which means that the animal only needs to have ONE copy of a gene in order to develop the disease. In autosomal dominant inheritance, the disease is likely to occur in every generation, and males and females are equally affected. It is important to recognise this pattern of inheritance, as animals that carry the disease gene will always have affected offspring, even if they are mated with a normal animal. Offspring of affected animals have at least a 50/50 chance of developing the disease



Autosomal recessive inheritance

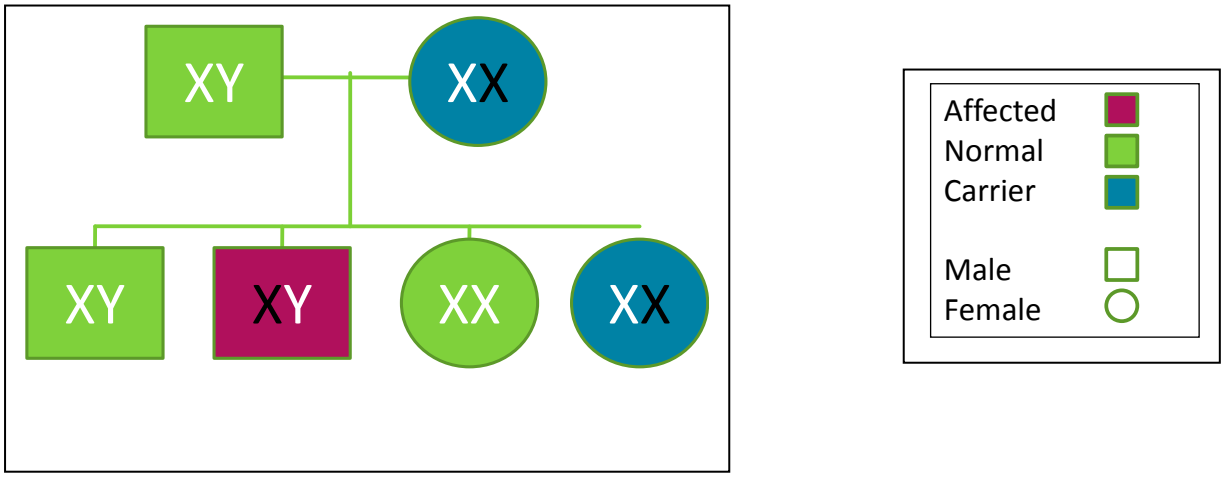
In autosomal recessive inheritance, the disease gene is again carried in one of the autosomal chromosomes. This means that there is no difference in the number of males and females affected by the disease. In recessive inheritance, however, TWO copies of a gene are required in order for disease to develop. This means that the animal must inherit one gene from its father and one from its mother. Both the mother and the father may only have one copy of the disease gene, may therefore never develop the disease, but they will have affected offspring. In carrier animals (i.e. those with just one copy of the disease gene), the 'normal' gene that is paired with the disease gene prevents the disease gene from being expressed.

This mode of inheritance is important to recognise as dogs that have the disease gene but are outwardly normal (carrier animals) may have offspring that develop the disease. The disease may appear to skip generations. The numbers of affected offspring in a litter from carrier parents is approximately one in four.



X-linked recessive

In X-linked inheritance, the disease gene is found on the X chromosome. As the disease is recessive, two copies of the gene are required for disease to occur. Male animals, however, have only ONE X chromosome. Therefore, if they inherit the disease gene on their X chromosome, they do not have a matching gene to suppress the effect of the recessive gene, and therefore they will develop disease, even if they only have one abnormal copy of the gene. Males are therefore much more likely to develop the disease. Female animals are more likely to have one disease gene and one normal gene on their other X chromosome, and therefore they are most likely to be carriers of the disease. The disease cannot be transmitted from father to son. Females only develop the disease if they have an affected father (and a carrier or affected mother). If a female animal has the disease, all of her male offspring will also develop the disease, and all of her female offspring will be carriers.



Other forms of inheritance:

- X-linked dominant
- Mitochondrial inheritance
- Complex

Why is this important?

As you can see from the differences detailed above, the mode of inheritance of a disease can have a great influence on the number of animals that may be affected by that disease, and therefore will have an effect on how animals should be bred. For example, in autosomal dominant inheritance, an affected dog will always have affected puppies, even when bred with a completely normal dog. In contrast, if the disease is autosomal recessive, then breeding an affected dog with a normal dog should result in only carrier puppies, and a much reduced incidence of disease.

As briefly mentioned above, in reality, genetics is complicated by other factors, such as environmental influences (e.g. the effect of exercise or nutrition on the development of hip dysplasia) or incomplete penetrance of the disease. There is a great deal that we are yet to learn about genetics, and in many cases we simply do not understand the reasons why some dogs develop disease and others do not.

Breeding of dogs should take in to account knowledge of the diseases that are common in that population of dogs, but selective breeding against a disease should be undertaken cautiously. Eliminating all dogs affected by one disease may dramatically reduce the gene pool, and thereby increase the risk of development of other diseases. Breeding to reduce the incidence of a disease in a population involves careful planning, knowledge of the mode of inheritance of the disease, and input from geneticists, breeders and vets.