

# Inherited Factor VII Deficiency in the Deerhound (Scottish Deerhound)

## Introduction

Blood clotting problems have long been known in both humans and animals. Many of those identified in dogs are well recognised as inherited problems. The best known is associated with von Willebrands Factor. In the past, diagnosis of these problems has relied on blood clotting tests to identify affected animals. Unaffected “carriers” could only be identified through the results of breeding. Sequencing of the canine genome and other recent advances in genetic testing are now allowing us to identify actual genetic defects in our dogs. This will in time give us the tools to control and eradicate many canine genetic diseases.

A clotting disorder, Factor VII Deficiency (FVIID) is well recognised in humans where about 1 in 500,000 people are affected. Most live quite normal lives. The condition has been known to exist in dogs since it was first identified in Beagles about 40 years ago. The recent investigation of a non-fatal, but very severe, bleeding episode after surgery in the USA, has led to the discovery of FVIID in the Deerhound. DNA testing revealed they can suffer the same genetic defect known to cause FVIID in the Beagle, Alaskan Malamute and probably therefore some other breeds. This article describes some of what is presently known of the condition and its genetic cause. It explores the problems and responsibilities that fall to Deerhound breeders as a result of the discovery.

## Blood Clotting and Factor VII

Blood clotting (“coagulation”) is the process that controls bleeding. It involves the production of a solid mass of cells and protein fibres (blood clot) from the normal cells and liquid constituents of circulating blood. It is essential to control the leakage of blood from wounds or within the body such as bruising and haematomas. As soon as a blood vessel wall is breached, contact between blood and tissue (or foreign substances) from which it is usually separated, sets off a complex chain reaction. The smallest of blood cells, platelets, clump together at the site and a number of blood proteins (clotting factors) react with tissue proteins (tissue factors) and calcium in the blood to create a web of protein fibres over the platelet plug to seal the leak. This clot organises and strengthens before it is removed as normal blood vessel tissue repairs the defect. Clotting is a complex process that can involve more than 20 different blood proteins called blood clotting factors. A deficiency or absence of one of these factors can prevent normal blood clotting.

Different factor deficiencies result in different patterns of bleeding disorder. FVIID is generally considered one of the less severe clotting problems, rarely resulting in fatality. FVIID affected dogs do not bleed to death from minor cuts or injuries but

have an increased bleeding tendency during surgery or after injury. They do not usually appear to develop spontaneous bleeding. Some affected dogs have required blood or plasma transfusions after severe bleeding. It appears that many FVIID dogs lead normal lives and their condition remains unrecognized throughout life. We already know that many Deerhounds in the UK carry the disorder. We do not have widespread reporting of resulting bleeding problems.

## **Inheritance of the Disorder**

FVIID is caused by a mutant gene. It does not reside on the sex chromosomes so its distribution occurs irrespective of the dog's sex. All Deerhounds inherit one copy of the gene from each of sire and dam. They are only affected if both copies are abnormal

Clear dogs have no copies of the mutant gene. They will not suffer the condition nor pass a mutant FVII gene to any offspring

Carrier dogs have one copy each of the normal and mutant genes. They do not suffer from the condition and do not have a bleeding disorder. They do pass a mutant copy of the gene to about half of their offspring. Their offspring may therefore be clear, affected or carriers. This will be determined by the gene inherited from the other parent.

Affected dogs have two copies of the mutant gene. They will have little or no factor VII in their circulation and will be affected by FVIID. They will pass a mutant copy of the gene to all their offspring that will all be either carriers or affected. Again, this will be determined by the gene inherited from the other parent.

With this pattern of inheritance the condition is said to be inherited as an Autosomal Recessive Disorder. The mutant gene can be passed down through generations not only by affected dogs but also by carriers who will appear and be normal. Combined with gene testing our knowledge of this mode of inheritance allows us, over time, to reduce or eliminate the condition in Deerhounds by taking note of this problem in our normal, careful selection of breeding stock.

## **Testing**

Until recently FVIID could only be diagnosed by measuring the level of Factor VII in the blood. Dogs could be screened for coagulation by assessing their blood clotting speed and characteristics but these are not reliable diagnostic tests for FVIID. No test could identify FVIID carriers, only affected dogs.

A team lead by Dr. Beth Callan at the Josephine Deubler Genetic Disease Testing Laboratory of the University of Pennsylvania School of Veterinary Medicine now have a DNA (gene) test that can identify the genetic status of clear ("normal"), carrier and affected dogs. Samples of blood or specially taken DNA mouth swabs are submitted to the laboratory in Pennsylvania. Results, received about three or four weeks later, classify the dog as either:

**NORMAL**

Homozygous (two copies) for normal gene. Will never develop or pass on FVIID

**CARRIER**

Heterozygous (one of each). Carries one mutant and one normal gene

**AFFECTED**

Homozygous (two copies) for FVIID mutant gene. Suffers the disease

This test is only available in the USA. Blood samples must be taken by a vet and can only be sent by special courier. Mouth swabs can however be more easily taken and submitted through the normal mail system. Testing costs \$75 per sample. We have found the service to be most professional and reliable.

## Can Factor VII Deficiency be treated?

Factor VII has a very fast turnover in the blood. In humans it has the shortest “half-life” (3-5 hours) of all the blood clotting factors. Whilst special human factor VII rich plasma is used by transfusion in some emergency situations this is not available for dogs. Plasma from a normal dog may help in an emergency, however frequent treatment is needed because the life span of factor VII is short. Furthermore avoiding the requirement will always be preferable. Knowing that a Deerhound has FVIID allows extra precautions to be taken during surgery and extra care after injury. Vitamin K is required for dogs to synthesize Factor VII. However FVIID affected dogs are not deficient due to lack of this vitamin so its use is unlikely to be of benefit.

It seems that affected dogs do not often present with a bleeding problem. The Deerhound that caused attention to focus on this issue did bleed severely after major abdominal surgery. There have been other reports of severe or fatal haemorrhage in the breed but so far not noticeably more frequently than other breeds of dog. The frequency with which the gene has so far been detected in British Deerhounds suggests that if FVIID often causes serious bleeding then many more reports of this should have been expected

## How widespread is the problem

At the time of writing around 50 UK bred Deerhounds have been genetically tested for FVIID. As they are very unevenly distributed across the breed they cannot be reliably considered a random representative sample of all UK Deerhounds. However, carriers have been detected broadly across those tested. Not all are in any way closely related. Testing here and in the USA suggests that the condition is widespread throughout the breed.

## What if my Deerhound is Affected?

Affected Deerhounds appear to almost always lead normal lives. As they could experience clotting problems, to reduce the risk of serious bleeding the following action may help:

- Make those treating the hound aware of the problem before surgery and when there is significant illness or injury.
- Be prepared to step in and help to stop bleeding in the case of significant injury or wounds
- Avoid where possible the administration of drugs that contribute to bleeding problems e.g. Aspirin, Trimethoprim/Sulphadiazine Antibiotics, Warfarin,

## **How could we eliminate the condition from the breed?**

We could immediately stop breeding from all affected and carrier dogs and bitches. This is impractical given the apparent widespread occurrence of the defective gene. It is also genetically dangerous as it reduces significantly and rapidly the diversity of our already relatively small gene pool. Additionally it places us in the trap of breeding for one characteristic above all others. This is always dangerous whether the characteristic is one of genetics, conformation or type. Heavy rapid selection for one characteristic alone carries the risk of inadvertent selection for other defective or undesirable characteristics, problems or diseases.

If we choose to act on this problem our first priority should be to avoid breeding affected dogs. This could be achieved by the following:

- Test all breeding stock before breeding unless they are known clear by virtue of their certain parentage.
- Avoid where possible breeding carriers and affected Deerhounds together.
- Where this advice is ignored, test all offspring and take responsibility for their health status.
- Ensure that purchasers of puppies are aware of the condition, their puppy's status and its implications.
- Remember we all have legal responsibilities and duty of care to those to whom we sell puppies.

However, as this condition appears to be rarely of clinical significance and carriers appear widespread, some may argue that limited, informed, breeding of carrier to carrier where there are other, good reasons for the breeding may help preserve the genetic diversity of the breed in the short term whilst the overall level of the condition is reduced. In time, such breedings should not be necessary and carriers need only be bred to clear mates as more are available. The eventual goal would be to only breed from clear animals allowing the condition will be eliminated from the breed.

## **Should I test my dog?**

Deerhounds never intended as breeding stock may benefit from testing to discover if they suffer from this bleeding problem. Knowing that a Deerhound is FVIID affected could be very important before or during any major elective or emergency surgery. Testing may therefore benefit any Deerhound of unknown status, however, if either their dam or sire was clear, they cannot be affected.

## **In Conclusion**

Over 600 inherited disorders have been recorded in dogs; over 6000 in humans. Deerhounds suffer fewer known genetic disorders than many other breeds. We can however expect more to be revealed over the next few years. Some will be for more serious conditions than this. We may eventually have tests for genes predisposing to bone cancer or dilated cardiomyopathy. In the great scheme of things FVIID is rarely serious but it can be fatal. It may, and on the present evidence is likely to, have been present in the breed for longer than any of us as breeders.

As breeders we have a responsibility to acknowledge its existence and to take whatever action we consider necessary. We must take note in this of our responsibility to the dogs we breed and the owners to whom we sell them. However we must never forget our other collective responsibility for the whole breed. . More serious genetic shocks are surely on the way. We can deal with them all, carefully, responsibly and without destroying the breed we all love. In the words of that most famous guide to the galaxy – DON'T PANIC

## **Genetic Testing Procedure**

For details of testing procedures visit the University of Pennsylvania School of Veterinary Medicine website at:-  
[http://w3.vet.upenn.edu/research/centers/penngen/forms/factorVIIdeficiency\\_ScottishDeerhounds.htm](http://w3.vet.upenn.edu/research/centers/penngen/forms/factorVIIdeficiency_ScottishDeerhounds.htm)

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