

NATIONAL IRISH WOLFHOUND ASSOCIATION

Irish Wolfhounds have been known to suffer from severe, unexplained internal bleeding in the days following routine, uneventful surgery that can very quickly result in death. The information in the following paper explains what is happening and what can be done to prevent it. The medication to prevent post-operative bleeding is available from several US veterinary supply pharmacies at a very reasonable cost.

Post-Operative Bleeding in Greyhounds, and What It Means for Deerhounds

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Every few months I hear of another Deerhound that has unexpected bleeding after surgery. The stories are much the same. Dogs typically emerge from surgery in good shape and go home with their owners, only to begin bleeding 24 to 36 hours later. The bleeding doesn't originate from a single blood vessel; instead, blood seems to seep from every vessel that was cut during surgery. Indeed, the only vessels that don't bleed are those that were specifically tied off or cauterized during surgery.

Some Deerhounds that have delayed post-operative bleeding survive, but only with heroic and expensive supportive care. Many don't. Some dogs are simply found dead the morning after surgery.

The recent discovery of an inherited Factor VII gene mutation in Deerhounds led some people to speculate that this might explain the delayed post-operative bleeding. (Factor VII is one of many proteins that help create a blood clot.) Unfortunately, the Factor VII mutation does not explain the problem in Deerhounds. Delayed post-operative bleeding has occurred in dogs with two normal Factor VII genes.

The biggest mystery surrounding delayed post-operative bleeding is also the biggest clue to what may be happening; specifically, the time when bleeding begins. It is as if the Deerhound forms normal blood clots after surgery, but those clots "come unglued" the next day. In other words, the problem is not in the dog's ability to form a blood clot, but instead in the dog's ability to maintain the blood clot for a normal length of time.

Another clue that points in the same direction is that some Deerhounds with delayed postoperative bleeding had pre-surgical workups that included tests to evaluate blood clotting function, and the test results were normal. This also suggests that the problem is not in the dog's ability to form a blood clot.

This mysterious, seemingly random, often fatal problem has led owners to be afraid every time their Deerhound undergoes surgery, or even to forgo elective surgery altogether. Now there is a ray of hope from an unexpected source: retired racing Greyhounds, or more specifically, a group of veterinary researchers at Ohio State University (OSU) who have dedicated themselves to studying that particular dog population.

A few weeks ago, I discovered a paper published in 2008 in the *Journal of Veterinary Internal Medicine* with the provocative title, "Postoperative Bleeding in Retired Racing Greyhounds." What particularly caught my attention was that the bleeding in Greyhounds occurred a day or two after surgery.

The lead author, Dr. Ana Lara-Garcia, was on the faculty at OSU when she wrote the paper, but has since moved to England to take a position at the Royal Veterinary College in North Mymms.

But the second author—Dr. Guillermo Couto—is still at OSU actively investigating the unique physiology of sighthounds, using racing Greyhounds in the USA and Galgos in Spain as his subjects.

I had a long conversation with Dr. Couto about post-operative bleeding in Greyhounds. Importantly, I learned that OSU had identified an effective drug that can treat the condition if it occurs and that even can be given after surgery to prevent delayed post-operative bleeding.

The Greyhound Story

The published paper describes the results of a study in 88 retired racing Greyhounds (36 males and 52 females) that underwent elective surgery to be neutered at OSU. The paper is so well organized and written that I will simply paraphrase it.

The authors first describe the lines of evidence that led them to study bleeding in Greyhounds:

- There were anecdotal references to excessive bleeding on some Greyhound websites or Greyhound health manuals.
- A web-based survey in 2006, which gathered information on disease prevalence and major causes of death in 747 retired racing Greyhounds, revealed that “bleeding disorders” were one of the four most common causes of death, accounting for 8% of all deaths. In addition, “hematologic diseases” were reported in 3.3% of the dogs, and “spontaneous and postoperative bleeding” accounted for about half of the hematologic disease.
- The authors had observed a tendency for Greyhounds to bleed excessively after minor injuries or simple surgical procedures like neutering or dewclaw removal. Because OSU is a major site for healthcare of retired racing Greyhounds, the authors were in a unique position to notice this tendency to bleed.
- Over a 3-year period at OSU, 10 of 38 Greyhounds that had a limb amputated because of osteosarcoma had severe delayed post-operative bleeding that required intensive care, including blood transfusions, and that resulted in long hospital stays and high medical bills.

From this evidence, the authors developed two theories about Greyhound “bleeders”—either they did not make normal blood clots, or the blood clots they did make were being dissolved too soon.

It may sound odd to you that dogs can dissolve blood clots as well as make them, but clot dissolution actually is an important normal process. The Greyhound story will make more sense if you understand more about how blood clots form and dissolve, so I’ll pause to briefly explain.

How Blood Clots Come and Go

You may not realize it, but blood is poised to clot at any moment. As soon as blood is exposed to damaged tissue or to the air, it starts to clot. This is vitally important to minimize blood loss from an injury. The process of clot formation is called coagulation. Coagulation involves the coordinated activity of circulating cell fragments called platelets, more than a dozen proteins in the blood called coagulation factors (such as Factor VII), and many other proteins that regulate the interactions of these components.

On the other hand, blood must stay in liquid form to circulate freely. If a clot forms in a blood vessel—even a small one—it may cut off the blood supply to a tissue, and the tissue will die within minutes. The result can be fatal, as in the case of a heart attack. That is why dogs (and we) also have a system to quickly dissolve blood clots by a process called fibrinolysis. Fibrinolysis involves the coordinated activity of several different proteins in the blood.

In a normal dog, coagulation and fibrinolysis exist side-by-side in an exquisitely delicate balance. The blood is simultaneously ready to form clots and dissolve clots at a moment’s notice.

The Rest of the Greyhound Story

The OSU researchers did a panel of blood tests before and after surgery to evaluate the coagulation and fibrinolysis systems. They also monitored Greyhounds for post-operative bleeding, scored on a scale of 0 (none) to 4 (severe). Then they compared the blood test results in bleeders and non-bleeders.

None of the 88 Greyhounds bled during surgery or shortly thereafter, but 26% (23 dogs) had delayed post-operative bleeding 36 to 48 hours after surgery! Bleeding was scored as grade 1 in two dogs, grade 2 in 14 dogs, grade 3 in five dogs, and grade 4 in two dogs. Bleeding was confined to the surgical site, never occurring in distant areas. Both findings—that bleeding was delayed and that it was not happening all over the body—suggested that the problem was with clot maintenance, not clot formation.

Coagulation test results were similar in bleeders and non-bleeders, but fibrinolysis test results differed. The fibrinolysis system was more active in bleeders than non-bleeders before surgery.

Taken together the study results suggest very strongly that Greyhound bleeders bled because their fibrinolysis system was turned up high before surgery, so that blood clots dissolved too quickly after surgery. To put it another way, Greyhound bleeders had shifted the balance between coagulation and fibrinolysis more toward fibrinolysis.

But Why?

Why would so many Greyhounds have a tendency for enhanced fibrinolysis, when this could lead to excessive blood loss after an accidental wound or routine surgery? The answer appears to be that humans unintentionally selected for this trait when they created this premier racing and hunting athlete.

Greyhounds differ from other breeds in ways besides the visible ones. Many of the differences are in the cardiovascular system—not just the heart and blood vessels, but also the blood itself.

Greyhound blood has more red blood cells per unit volume, which allows the blood to carry more oxygen but also makes the blood thicker than the blood of other breeds. Greyhounds have larger hearts and thicker arteries than other breeds—large enough not only to cope with thicker blood, but also to pump that blood faster and at higher pressure than in other breeds. All of this is necessary to send enough oxygen to a Greyhound's massive muscles to produce the explosive acceleration for which the breed was selected over thousands of years.

But there is a price to pay for this sort of high performance circulatory system: blood racing faster and at higher pressures through the vessels produces more damage to the vessel walls.

Blood vessels are lined by a thin layer of cells called endothelial cells. Like roof shingles in a high wind, these cells regularly shear off, exposing the tissue beneath. The exposed tissue triggers a tiny blood clot to form. This micro-clot covers the gap and gives the adjacent endothelial cells time to repair the damage, both by spreading themselves more thinly and by dividing to make new endothelial cells.

Each time a micro-clot forms, there is a risk that the blood clotting process will get out of control and make a clot so big that it blocks the blood vessel, or even trigger blood clots to form throughout the blood stream. That's where the fibrinolysis system comes into play, to make sure the micro-clot forms only where it's needed and that it stays intact only as long as necessary.

Because Greyhound blood is thicker and moving faster, Greyhounds experience more endothelial cell damage and form more micro-clots than other breeds. This, in turn, can put their fibrinolysis system into high gear. And this shifts the balance more toward clot dissolution than clot formation.

What This Means for Deerhounds

Honestly, I think that you could substitute the word Deerhound for Greyhound throughout this article. The delayed post-operative bleeding that has occurred in many Deerhounds seems identical in every respect to what is described in Greyhounds. And that actually makes a lot of sense.

The most important point in the Deerhound standard is that "a Deerhound should resemble a rough-coated Greyhound of larger size and bone." As it happens, Deerhounds do not just look like Greyhounds on the outside; they also work like Greyhounds on the inside.

Like Greyhounds, Deerhounds have thick blood moving at high speed and under high pressure, and consequently have more frequent blood vessel damage and micro-clot formation. As a consequence many Deerhounds almost certainly have fibrinolysis systems that are hyperactive, putting them at risk for delayed post-operative bleeding.

The OSU authors also speculated that the situation in Greyhounds probably existed in other sighthounds. They put it like this (with italics added by me):

"The [state of enhanced fibrinolysis] in retired racing Greyhounds could be an adaptational mechanism to racing or an evolutionary trait designed to prevent clotting of blood with high viscosity... that circulates through large muscle masses, as has been reported in human athletes... [and] in transgenic mice [with high viscosity blood]. ...*It is very tempting to think that a similar phenomenon may occur in [all] sight hounds and that they have evolved to be "hypocoagulable" in order to prevent intravascular thrombosis during strenuous exercise.*"

What Can You Do?

There are clinical situations in which enhanced fibrinolysis occurs in humans, leading to an increased risk of bleeding. In such situations, patients are treated with the drug aminocaproic acid (Amicar®), which inhibits fibrinolysis.

Researchers at OSU have just finished a clinical trial in 100 Greyhounds undergoing spay or neutering surgery, to see if aminocaproic acid would reduce or prevent delayed post-operative bleeding. The results are not yet published, so I cannot share them with you. But I can tell you that the results led OSU to change its standard surgical protocol so that every Greyhound is now given aminocaproic acid for 5 days after surgery. The aminocaproic acid dose for a 30-kg (66-lb) Greyhound is 500 mg every 8 hours, which is about 17 mg/kg (8 mg/lb).

I think we should adopt the same approach for Deerhounds that OSU has taken for Greyhounds. Every Deerhound that undergoes elective surgery should be given aminocaproic acid for the next 5 days to reduce the risk of delayed post-operative bleeding. Aminocaproic acid is available in 500-mg scored tablets. The dose should be as follows:

Aminocaproic Acid Dose for Deerhounds	
Dog weight	Dose every 8 hours
55 to 79 lbs	500 mg (1 tablet)
80 to 104 lbs	750 mg (1½ tablet)
≥105 lbs	1000 mg (2 tablets)

I do not make this recommendation lightly. Every drug carries the risk of side effects, and aminocaproic acid has not been studied in Deerhounds. However, aminocaproic acid has been studied in Greyhounds in a controlled clinical trial, which is more than can be said for many of the drugs we use routinely in Deerhounds. More importantly, the veterinary researchers at OSU

concluded that the benefits of aminocaproic acid in preventing life-threatening delayed postoperative bleeding far outweighed the risk of potential side effects.

Amicar® was approved for human use in 1964, at a time when relatively little animal testing was done with human drugs. It is available as an injectable liquid and as pills. The product label contains two references to potential side effects in dogs, but only when the drug is given intravenously:

- "Fatty degeneration of the myocardium has been reported in dogs given intravenous doses of aminocaproic acid at 0.8 to 3.3 times the maximum human therapeutic dose." The maximum human dose is about 32 mg/lb, so the dose range reported to cause fatty degeneration of the heart in dogs is about 26 to 107 mg/lb. This is approximately 3 to 13 times the dose recommended to prevent delayed post-operative bleeding (8 mg/lb).
- "An intravenous... dose of 2,300 mg/kg was lethal in the dog." This is about 1,045 mg/lb, or approximately 130 times the dose recommended to prevent delayed post-operative bleeding.

When the OSU clinical trial results are published, we will have a better idea of the incidence and nature of side effects in dogs given Amicar® by mouth. I will share this information as soon as it is available.

Thanks to studies in retired racing Greyhounds, I believe we finally have a likely explanation for the delayed post-operative bleeding that has occurred in many Deerhounds. Better yet, there is a readily available drug that offers the promise of preventing the condition and saving Deerhound lives. For my part, I will not put another of my Deerhounds through surgery without giving aminocaproic acid for 5 days afterwards to reduce the risk of delayed post-operative bleeding. I urge you to consider doing the same.

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