

# Canine Leukocyte Adhesion Deficiency: the Irish Setter Mystery Disease

by Mary M. Woodsen

Canine Leukocyte Adhesion Deficiency (CLAD for short)– a rare and deadly disease found only in Irish Setters–is the ultimate mystery disease. No one knows how long it's been around, or even the true extent of the damage it causes. And in the country where it was first named - the United States - who has even heard of it? Practically no one.

What is CLAD? This autosomal recessive disease, closely related to LAD (Leukocyte Adhesion Deficiency) in humans and BLAD (Bovine Leukocyte Adhesion Deficiency) in cattle, renders white blood cells – the immune system's infection busters – unable to “stick to,” then destroy, invading bacteria and yeast cells. Many affected pups get navel infections soon after birth. Others fall prey to repeated severe infections: gum disease, bone infections, diarrhea, tonsillitis, dermatitis, pneumonia; you name it. Many become feverish. Death is often sudden – and sudden or not, it's inevitable.

Here's the scenario: a young puppy gets an infection, and the vet gives it antibiotics. The infection gets worse-or a second one kicks in. The vet switches antibiotics. Still no recovery. The vet does cultures and increases the antibiotics but the pup dies, and the vet says, 'Boy, that was a very bad case.' But of what?

Maybe CLAD.

Several factors may have kept this killer from being recognized in the United States. First off, it's rare.

Affecteds never breed, which keeps down the incidence of disease. And we're not attuned to it. When we see a pup with dissimilar symptoms–navel infections *and* gum disease *and* tonsillitis *and* pneumonia—we think, poor thing, all at once; what a streak of rotten luck! Or the pup shows only one of those symptoms so we think that's what the problem was. Then the pup dies before we've gotten to the root of it. And again, the age of onset itself is a factor. We anticipate that the very young (symptoms generally show up by eight weeks of age) are more prone to succumb to disease. And when two or three pups in a litter succumb, as is often the case, we figure an infectious agent—such as staph or strep—was the primary cause. After all, infectious diseases are a major cause of mortality in newborn pups.

So if CLAD isn't even recognized in the United States, where do we know it from? Scientists in Sweden and Great Britain have done the bulk of the research on CLAD because it is a recognized problem in those countries.

And now researchers led by Dr. Leif Andersson at the Swedish University of Agricultural Science in Uppsala have released a mutation-based DNA test that absolutely and unequivocally identifies normal dogs as well as carriers of CLAD. (Affecteds die before they could ever be tested.) They've tested over 200 Irish Setters from Europe and they have found that 10% are carriers.

It does seem odd that a disease like this should continue to go unrecognized in the U.S. Indeed, it is possible that we simply don't have the problem here; end of discussion. But two factors weigh against this conclusion. Most obvious – it was first clinically described here. Dr. Harland W. Renshaw's careful research at the Department of Veterinary Microbiology and Parasitology at Texas A & M University's College of Veterinary Medicine – way back in the mid-'70s – conclusively proved the genetic basis of the disease. (Back then, he called it “Canine Granulocythopathy Syndrome.”) The other factor? Irish Setters are popular dogs. Breeding stock flows across national boundaries.

Concerned about this mystery disease? Dr. Gunilla Trowald-Wigh at the Swedish University of Agricultural Science has cared for every single pup with CLAD in the project leading up to the test. She tells us what to look for:

Several very sick puppies in the same litter are indicative of an inherited immunodeficiency in the Irish setter, CLAD. Repeated infections of any sort, particularly when coupled with gingivitis (gum disease) omphalophlebitis (navel infections) and osteomyelitis (bone infections) should always ring an alarm. In fact, sometimes the first symptom is only lack of appetite and fever—but it's always followed by something else: by one or more of the trio mentioned above; and/or by tonsillitis, pneumonia, diarrhea, or dermatitis. And white cell counts in blood samples are sky-high—it's the body's attempt to make up for their collective inability to destroy the invading micro-life. The one constant with CLAD seems to be gum disease. Every CLAD pup Trowald-Wigh has examined has had the red, swollen gums, excessive salivation, and halitosis (bad breath) that signal gingivitis.

Puppies with omphalophlebitis are swollen and warm at the navel, and often run a fever. These pups cannot

## CLAD, CONTINUED...

form ordinary pus; instead, lesions are weepy with a reddish, serumlike discharge. Sometimes the pups manage with antibiotics for a few weeks – then get new infections (tonsillitis, for example) at other sites.

Bone infections often show up in the jaws (mandible) and/or knees (carpal joint). These joints become swollen and thick. It hurts the pups to open their mouths, and some of them are unable to stand or walk.

Trowald-Wigh notes that diagnoses of craniomandibular osteopathy and methaphyseal osteopathy sometimes mimic CLAD. Dogs with these conditions have pain in their jaws and/or in the methaphyseal regions of their legs. Sometimes they, too, are feverish. But these pups never get gingivitis and aren't prone to infection.

"I guess that a lot of breeders and almost all owners in a country not having recognized the disease are unaware of the disease; also many veterinarians," Trowald-Wigh says. "In Sweden most breeders and most veterinarians know about CLAD after 10 years of information. I have no opinion of the incidence of CLAD in United States but I would be surprised if you did not have the disease.

Veterinarians and breeders must be informed."

Concerned owners can use the new genetic CLAD test to be sure that this devastating disease doesn't crop up in their kennel as they breed for all those other desirable traits. If you have had pups that died of chronic or recurring infections, it would be wise to test the dam, the sire, and any littermates that you plan to use for breeding.

Dogs that are carriers must be bred only to dogs that test as genetic normals, or "clears." They should never be mated with untested dogs. Clears, on the other hand, may be bred to any dog – but if the other dog is untested, all pups from the litter that are used for breeding should be tested.

How can you get this test done? Write to OptiGen for detailed instructions at 33 Thornwood Drive, Suite 102, Ithaca, NY 14850, or download the instructions from the OptiGen website at [www.optigen.com](http://www.optigen.com). Then make an appointment with your veterinarian. Your veterinarian will have the necessary supplies to collect the blood. These instructions will tell your veterinarian what sizes and types of syringes and containers to use, and will give you all sorts of important information on storing and shipping the sample, including international and

warm weather shipping instructions. (Be sure your appointment is for early in the week to avoid shipping the sample over the weekend.)

Running this test takes a considerable amount of time. Depending on the number of samples in hand, the time to finish your test will vary. Turnaround time is generally two to three weeks. Tests are run on a "first come-first served" basis. Results are reported only to the owner and (by policy of the ISCA) to the DNA registry of CERF.

It makes the most sense to test dogs that are good breeding prospects. Even very young pups can be tested for CLAD. All test results are certain and can be determined from birth. And these results are exactly accurate. This means that test results will never change with age and will be the same whenever it is repeated.

Optigen performs this patented test by exclusive license in North America from the Swedish group, and is the only laboratory in the United States that has blood samples from dogs known to be either affected or carrier with which to verify the results. The price is reduced if both the CLAD test and a test for Progressive Retinal Atrophy (PRA) are done at the same time. ♣