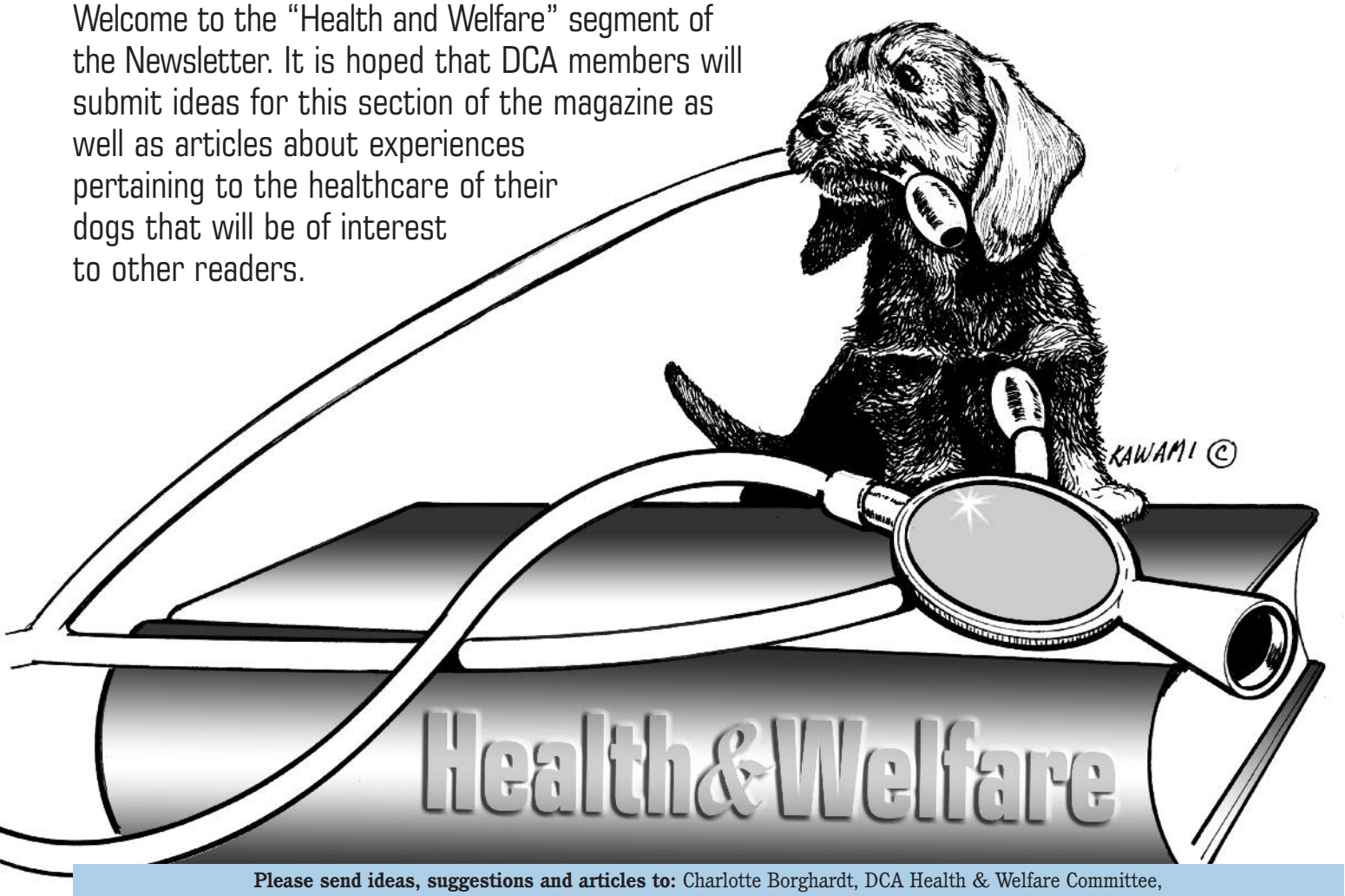
Welcome to the "Health and Welfare" segment of the Newsletter. It is hoped that DCA members will submit ideas for this section of the magazine as well as articles about experiences pertaining to the healthcare of their dogs that will be of interest to other readers.



Please send ideas, suggestions and articles to: Charlotte Borghardt, DCA Health & Welfare Committee, P.O. Box 1126, Sierra Vista, AZ 85636-1126, teckelhofaz@yahoo.com

"Brittle Bone" Gene in Dachshunds Discovered

New Genetic Test Can Help Breeding

submitted by Carrie Hamilton

An international research team headed by Prof. Dr. Cord Drögemüller and Prof. Dr. Tosso Leeb from the Institute for Genetics at the University of Bern has discovered a gene mutation that causes Brittle Bone Disease (Osteogenesis imperfecta, or OI) in Dachshunds. This serious hereditary disease also occurs in other species and shows similar clinical symptoms in Dachshunds and humans. It expresses itself as soon as birth in newborns with extremely brittle bones and teeth. In dogs, the affected animals must be euthanized if they do not die shortly after birth. In humans as well as in dogs it is caused by hereditary changes in the genome (gene mutations), which are responsible for the production and development of collagen.

Collagens are the most common proteins in human and animal bodies and give the bones their elasticity. Recently a new mutation in an additional gene which is needed for the correct formation of collagen was found in Dachshunds with Brittle Bone Disease (OI). A search for abnormalities in the genes of five affected Dachshunds with severe Brittle Bone Disease showed that all had a mutation on the same gene – resulting in the incomplete development of a specific helper protein for collagen. This hereditary defect of the so-called SERPINH1 gene leads to Brittle Bone Disease in dogs. Brittle Bone Disease or OI in Dachshunds is a genetically caused disease. As the mode of inheritance is recessive, the mutation must therefore be present in both parental copies (alleles) of the gene. Only then is the Dachshund affected and therefore both parents of affected dogs must be carriers. Hence it is prudent to test breeding animals to determine they are free of the OI predisposition. Brittle Bone Disease or OI is not gender specific and can therefore affect male and female puppies. The recessive mode of inheritance means that only homozygous animals actually are affected. Heterozygous animals are therefore healthy. All parents of affected puppies, which outwardly cannot be distinguished from unaffected Dachshunds, are heterozygous carriers of the mutation. As so-called carriers they can pass the mutation on to their offspring. As long as no genetic test was available, such carriers could only be identified after the occurrence of puppies with Brittle Bone Disease.

It is not currently known how wide this hereditary fault is spread in the Dachshund breed. Therefore the frequency of the OI mutation in the actual breeding population is unknown. Recently, in two independent litters of Dachshunds suspected of Brittle Bone Disease, which were also falsely identified as so-called 'swimmer puppies', the parents of the affected puppies were identified as carries of the OI mutation (OIC) via the new genetic test. Thus, one may certainly conclude a distribution of the OI mutation in Dachshunds.

With the newly developed genetic test, a suitable tool is available for breeders for the consistent fight against Brittle Bone Disease in Dachshunds. The new genetic test detects the OI mutation itself. This way it can be determined early in the life of an animal if it carries the undesired mutation OI, which is called OIC. Tested dogs, which do not carry this mutation and are therefore clear, meaning OI free, are called OIF. The genetic test can be administered for any breeding animal of any age via a blood test. The genetic test offers a simple and reliable opportunity for the selection of

genetically healthy Dachshunds. Thus, in the future, the occurrence of additional puppies with Brittle Bone Disease can simply be avoided.

The table depicts how the inheritance of Brittle Bone Disease actually happens. For example, from the mating of one genetically clear animal (OIF) with a carrier (OIC), half of the offspring may be carriers of the genetic defect. They are able to subsequently pass on the undesired mutation. If both parents are carriers one can actually expect sick offspring. The goal of breeding can only be the mating of two genetically clear parent animals, resulting in homozygous clear offspring.

If now, for example, an OIC tested sire is used that passes on the mutation to an average of half of his offspring, it depends on the dam whether she is genetically clear or a carrier. In the first case approximately 50% of the puppies are potential carriers, in the second case the percentage of carriers is even higher and every fourth puppy can succumb to Brittle Bone Disease.

The primary goal should be to breed carriers only to non-carriers. This guarantees that no further puppy falls ill with OI. Animal welfare must be the priority!

For the health of the breed, however, it is advisable in the near term to preferably use only OIF tested, meaning homozygous healthy parent animals, in order to eliminate the occurrence of sick puppies. Additionally, the test would no longer be necessary for the resulting puppies.

	Sire	X	Dam	=	Puppies
1.	Clear OIF	X X	Clear OIF	=	Puppies with sound bones All are OIF (clear)
2.	Clear OIF	X X	Carrier OIC	=	Puppies with sound bones 50% are OIF (clear) 50% are OIC (carrier)
3.	Carrier OIC	X	Clear OIF	=	Puppies with sound bones 50% are OIF (clear) 50% are OIC (carrier)
4.	Carrier OIC	X	Carrier OIC	=	25% puppies with brittle bone disease 75% puppies with sound bones Of that 33% are OIF (clear) Of that 67% are OIC (carrier)

Genetic Test

The test can be performed at the Tierärztlichen Institut der Georg-August-Universität Göttingen for the price of approximately $75. http://www.tieraerztliches-institut.uni-goettingen.de/moldiag.html

For the case that the OI mutation is present in the American Dachshund population as well, it might be realistic to ask a US veterinary genetic service lab (e.g. OptiGene) to offer this test as well. Please don't hesitate to contact Prof. Drögemüller directly to arrange a convenient solution.

Source:
Cord Drögemüller, Doreen Becker, Adrian Brunner, Bianca Haase, Patrick Kircher, Frank Seeliger, Michael Fehr, Ulrich Baumann, Kerstin Lindblad-Toh, Tosso Leeb: A missense mutation in the SERPINH1 gene in Dachshunds with osteogenesis imperfecta, 24. Juli 2009, PLoS Genet 5(7): e1000579.

Contact:
Prof. Dr. Cord Drögemüller
Institut für Genetik, Universität Bern
Bremgartenstr. 109a, 3001 Bern, Schweiz
Telefon 0041 (0)31 631 25 29
Telefax 0041 (0)31 631 26 40
E-Mail: cord.droegemueller@itz.unibe.ch

Vaccines and Vaccination Protocols

The advent of canine vaccines has vastly changed veterinary medicine in the last 50 years. There has been a significant decrease in the number of dogs with infectious disease; before the vaccine was developed for distemper, it was the number one cause of death among dogs.

Now, where the distemper vaccine is used, cancer is the leading cause of disease-related death. The importance of vaccinations to our dogs' well being cannot be overstated. However, what are the guidelines? What are the "rules" to follow? How do we know how much is "too much?"

The purpose of a vaccine is to mimic an infection so that the immune system is introduced to the pathogens that will cause protective immunity without causing clinical disease. It is meant to ensure a faster, stronger response to the pathogen upon re-exposure. The purpose of re-vaccination is to maintain the immune system's "memory" of that pathogen so that the vaccinated dog continues to mount an attack with every exposure so that the infectious agent does not result in a disease state.

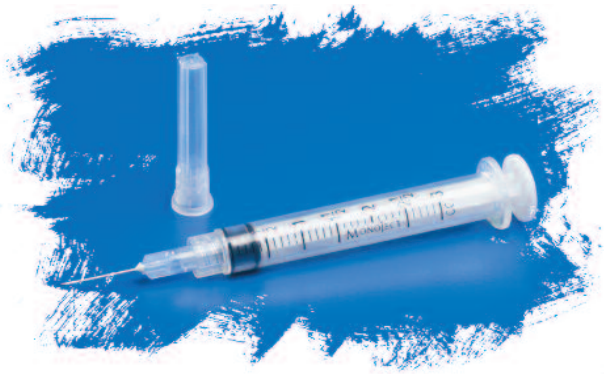
Types of Vaccines

There are several types of vaccines. They include conventional vaccines (modified live and killed), recombinant vaccines (genetically engineered and proteins/ peptides) and DNA vaccines.

Modified live vaccines mimic natural infection. They are based on attenuation (reduction of virulence) of the original virus such that they are limited in their ability to cause illness. The vaccine virus follows the exact same path as the wildtype (original) virus does; replicating and getting distributed throughout the body, exposing all parts of the immune system to the pathogen against which you are vaccinating. This type of vaccine is useful because it generally provides a long-lasting immunity; though it can also inadvertently cause disease if the vaccine is inadequately attenuated.

A killed vaccine is made of a virus or a strain related to the virus that has been treated to make it non-viable (incapable of replicating and causing disease).

The advantage is that the immune system is presented with all of the viral components, especially with those that are conserved between the different subtypes. However, revaccination is necessary because of the shorter duration of immunity.



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Genetically engineered vaccines are among the most advanced vaccines

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Vaccines

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used in human and veterinary medicine. In veterinary medicine, recombinant vaccines involve inoculation with only selected genetic sequences derived from the disease producing virus or bacteria. The vaccine does not expose the individual dog to the whole organism. In dogs, recombinant vaccines have been found to be very safe, highly effective, and produce a long duration of immunity.

Vaccines that use proteins or peptides from the pathogenic virus create vaccines that are highly specific—these vaccines are very pure and adverse reactions are rare. The fact that they are highly specific is also their downfall; they are not ideal for protection from organisms that tend to mutate.

DNA vaccines entail injecting highly specific DNA sequences into muscle in a manner that leads to the production (expression) of specific proteins. These vaccines are effective because they elicit both the humoral (pertaining to antibodies) and cell-mediated immunity. The only DNA vaccine licensed for use in the dog is approved as an aid in the treatment (not prevention) of oral melanoma.

Depending on the vaccine type, different routes of administration are used: injection (parenteral), which can be subcutaneous or intramuscular, topical (intranasal) or transdermal (air pressure, through the skin).

Intranasal vaccines are typically modified live viruses and bacteria, and must never be injected. Because they mimic infection best, they provide best immune response. Side effects include mild to moderate clinical signs of disease.

Parenteral vaccines can be either modified live viruses/bacteria (MLV) or killed viruses/bacteria. With MLV vaccines, there is a faster immune response, but there can be side effects, and they should not be used in pregnant bitches. With killed vaccines, there is no risk of shedding, but boosters are necessary and the adjuvant (substance that carries the virus) has been attributed to causing cancer (fibrosarcoma) in cats.

Core Vaccines

Core Vaccines are those that are recommended for all dogs, barring special circumstances. These core vaccines include: distemper, parvovirus, canine adenovirus I/II, and rabies. While parainfluenza is no longer considered a core vaccine, it is generally included in the combo core vaccines and will therefore be discussed here. The following descriptions are taken from the University of Tennessee Breeders' Symposium abstract by Dr. Margret Casal of the University of Pennsylvania.

Canine Distemper Vaccine:

Currently, distemper vaccines are modified-live vaccines, which are very effective. It was previously thought that combining distemper and Parvo in the same vaccine would lead to a decrease or a delay in seroconversion to the distemper component. However, (Dr. Casal's) studies and those from Cornell have been unable to substantiate such claims. If a patient is immune deficient or pregnant, MLV vaccines should not be used, because they may cause disease in the patient or the fetuses, respectively. There is a recombinant Distemper vaccine currently available that could be used for those dogs in which MLV vaccines are not an option.

Canine Parvovirus (CPV) Vaccine:

Modified live vaccines are available for dogs. Killed vaccines are no longer available because of poor efficacy. Today's MLV Parvovirus vaccines are less attenuated (new-generation, high- titer, low-passage) than previous ones and are claimed to be able to "break through" maternally derived immunity earlier than the previous generation of MLV parvovirus vaccines. In a recent study 60 mixed-breed pups were vaccinated with these newer versions of the CPV vaccines at 6, 9, and 12 weeks. The results showed that all pups had seroconverted by 15 weeks of age, suggesting a faster response and higher serum neutralization titers. Alternatively, if there are immune deficient animals present, they may contract the disease from the vaccine virus. There are myths about the MLV Parvovirus vaccine suppressing the immune system. However, all of the scientific studies done to date have not been able to substantiate such claims. Another myth is that it is more difficult to immunize Rottweilers and Dobermans against CPV infections. While these dog breeds may develop more serious disease after natural infection, they mount immune responses to an efficacious vaccine just like any other dog. Lastly, Parvovirus outbreaks are not prevented with more frequent vaccination. The only way to prevent outbreaks is with proper hygiene, even if this means foot baths and limited contact. CPV is spread by contact with contaminated shoes, clothes, soil, toys and other dogs, while CDV is passed on almost entirely by direct contact with infected dogs.

Canine Adenovirus Vaccine:

Canine Adenovirus (CAV) type 1 causes infectious canine hepatitis and CAV-2 is part of the kennel cough complex. Because of previously reported side effects (Blue Eye) when using CAV-1 vaccines, all vaccine manufacturers now offer attenuated CAV-2 in their vaccines as it provides cross-protection against infections with CAV-1. Parenteral and intranasal MLV vaccines are available. Minor side effects are possible with the intranasal vaccine such as nasal and ocular discharge, and allergic reactions to the parenteral vaccine have been reported.

Canine Parainfluenza Vaccine:

This old tried and true vaccine comes in a parenteral and intranasal MLV form. It is an effective vaccine in the prevention of this component of the kennel cough complex. Side effects include those seen with intranasal CAV-2 vaccines.

Non-Core (Optional) Vaccines

These vaccines are recommended based on the lifestyle and location of the animal in question and include: leptospirosis, Bordetella bronchiseptica, Lyme disease, and parainfluenza virus. Again, the descriptions below are courtesy of Dr. Casal:

Leptospira Vaccines: Because all Leptospira vaccines are bacterins, their use may result in allergic reactions. The later the vaccine is administered during the puppy series, the less likely the allergic reaction.

Current AAHA (American Animal Hospital Association) guidelines recommend delaying this vaccine, especially in small breeds, until the CORE vaccines are completed. Most current Leptospira vaccines contain four different serovars: grippotyphosa, canicola, icterohemor-rhagica, and pomona. The vaccine is now purified, which may reduce allergic reactions and although titers drop significantly after 6 months, challenge with pathogenic forms of L. icterohemorrhagica and canicola one year after vaccination did not cause disease. Generally, this vaccine is recommended to be given in spring time, especially for dogs that come in contact with wildlife or city rodents.

Lyme Disease (Borreliosis) Vaccines: Lyme Disease in dogs can be prevented by the use of tick prevention and vaccines. The Lyme vaccines

have been criticized by some veterinarians as being ineffective. While it is true that some vaccinated dogs do contract the disease, it appears that vaccinated animals are less likely to contract the disease than unvaccinated animals. Vaccination is generally limited to dogs traveling to or living in high prevalence areas.

Bordetella bronchiseptica Vaccine: This is probably not a very effective vaccine, and there are not enough studies to document either short- or long-term efficacy. However, there are some kennels that require Bordetella vaccinations before the dog can be boarded. The intranasal vaccine seems to provide marginally better protection than the injectable form. The dog should receive a booster 2-4 weeks after the initial vaccination, if given the killed injectable vaccine. A single dose of the intranasal vaccine is likely to be sufficient in a puppy older than 14 weeks of age, when the maternal antibodies have dropped to undetectable levels.

Canine Influenza Virus (CIV) Vaccine:

In May, 2009, the USDA granted a conditional license for the first vaccine against Canine Flu. This vaccine is expected to reduce incidence, severity and duration of the disease but does not necessarily prevent infection altogether. (Conditional license means it has been proven safe with good signs of efficacy, but additional studies are needed to gather more information. The Canine Health Foundation has funded Grant 1105: Understanding the Dynamics of Canine Influenza Virus Transmission in Dog Populations and Intervention Strategies for Reducing Transmission, a study which will model the transmission of canine flu in a population with and without vaccination and will be a major component in determining the recommended use of this new canine flu vaccine.)

So how do you decide which vaccines to give your dog? You should work closely with your veterinarian to determine the risks involved with each animal and treat the individual patient based on their specific needs. Differences in risk of exposure to infectious diseases, age and health of the patient, and potential side effects of certain vaccines, make it next to impossible to recommend one single vaccination protocol for all dogs. Therefore, for optimal protection, each dog should be examined on a yearly basis even if vaccines are not to be given in that particular year. Health and life style changes can be assessed and the dog's vaccination protocol can be adjusted as needed. Dr. Richard Ford of North Carolina State University has assembled a website, www.dvmvac. com that carries the American Animal Hospital Association's guidelines for vaccinations, various definitions and a forum for questions and answers for both dogs and cats.

The Canine Health Foundation has funded research by Dr. George Moore at Purdue University on adverse reactions of vaccines (Grant 779). Visit our website, www. CanineHealthFoundation.org for more information about this study.

Special thanks to Drs. Margret Casal, Richard Ford and George Moore for their comments and suggestions for this article.

Canine Research & Education for the Canine Health Foundation, eaw@CanineHealthFoundation.org

STEWART

by Patrick Eddings