THE 2021 AKC CANINE HEALTH FOUNDATION **NATIONAL PARENT CLUB HEALTH CONFERENCE**

BY CAROLINE COILE

The 2021 AKC Canine Health Foundation National Parent Club Health Conference was a virtual event this year. I confess it was nice to attend at home in my shorts, but the experience drove home the value of networking with researchers as well as with parent club health representatives. Plus, there was no good food. Nonetheless, there was still plenty of good information, divided into topics of dermatology, cancer, neurology, and cardiology. There's never space to cover every presentation, but here are the highlights of the cancer and neurology sessions. I'll cover the dermatology and cardiac session next month.

ENVIRONMENT AND CANCER

In her talk "Environmental Cancer Risk in Dogs and People," Lauren Trepanier, DVM, PhD, DACVIM, DACVCP, of the University of Wisconsin-Madison, reported on her research examining the role of household and neighborhood influences on lymphoma and bladder cancer. First, they compared the environments of 56 Boxers with lymphoma to 84 Boxers, 10 years and older without lymphoma. They did this by questionnaire to the owners, by using Google maps to find neighboring sources of pollution such as crops, golf courses or power plants, water utility data, EPA pollution data by county, and NATA pollution data. They found that Boxers with lymphoma were more likely to live within 2 miles of an active crematorium (odds ration of 2.2), within 2 miles of a chemical supplier (odds 2.3) and within 10 miles of a nuclear power plant (odds 5.8). Risks also included formaldehyde (found in off-gasses from paints, paneling and medium-density fiberboard); 1.3-butadiene (found in car exhaust and industrial air pollution); and ozone (which does not itself cause cancer but is a marker of pollution with volatile organic compounds). How can dog owners avoid these risks? Aside from moving, we can choose low-VOC paints, paneling and wood products; avoid idling our cars, and of course, advocate for stronger air pollution controls for us and our dogs.

In a second study Trepanier looked at factors that might influence bladder cancer in dogs. In some humans and dogs, bladder cancer is known to have environmental causes. Half of all cases in people are linked to smoking, and 20% to industrial jobs or herbicide applicators. The risk is higher in industrial areas, but the responsible chemicals are unknown. Dog bladder cancer may in fact be a good model for human bladder cancer, as dogs and humans share environments, and the disease is naturally occurring. Canine bladder cancer resembles the more invasive form of human bladder cancer that is difficult to treat effectively. In dogs, bladder cancer is more common in Scottish Terriers, Westies, Beagles, and Shelties; in obese dogs and females; and in areas with herbicide use. Using the same types of data as in the Boxer lymphoma study, the researchers compared 66 dogs with bladder cancer to 70 unaffected dogs, 11 years or older. They found that dogs with bladder cancer were from households that used more insecticides (odds ration of 4.3); were more likely to live in a county with high ozone levels (odds ratio 4.6); and lived in counties with 3-fold higher levels of total trihalomethanes in tap water

(P<0.0001). The latter is a very significantly high finding. Trihalomethanes are by-products of disinfection in tap water. Note that they can be removed by some water filtration units, so it may be worth finding the levels in your county and, if needed, investing in a unit to remove it.

The researchers went further and compared possible bladder-cancer causing chemicals in the urine of dogs and people in the same household. The most interesting finding was that these chemicals, which included metabolites of arsenic, 2,4-D weed killer and acroleins (found in cooking fumes) were present in dog urine at much higher levels than in human urine.

In the question and answer period, the question was raised about long-lasting flea and tick medications. Trepanier replied that the older organophosphate dips and sprays were in fact associated with bladder cancer but that newer spot-on treatments are not. Another question asked about chlorine in pools. This was not included in the present surveys but may be in future ones. She pointed out that there is lots of potential information, including the availability of frozen urine samples, from the ongoing Golden Retriever lifetime study. Trepanier plans to conduct further studies looking at gliomas and nasal carcinomas and is recruiting affected dogs for these studies. If you would like to participate, contact her at lauren.trepanier@wisc.edu.

THE LIFE AND TIMES OF THE HERO DOGS OF 9/11

Continuing the thread of environment and cancer (and other diseases), Cynthia M. Otto, DVM, PhD, DACVECC, DACVSMR gave the keynote talk, a final report of the health of the 9/11 search and rescue dogs. These dogs were exposed to high levels of hazardous materials including asbestos, metals, dioxin-like matter, polychlorinated biphenyls, volatile organic compounds, and smoke and dust, and they did so without wearing masks, respirators, or boots. While human responders reported a barrage of illnesses even while wearing protective gear, what about the dogs who were actively sniffing and traversing not only the buildings, but the Freshkills landfill where debris was taken, and doing so for weeks and even months?

Otto and team followed these dogs, which consisted of 31 German Shepherds, 28 Labs, and 12 Goldens with a mean age of 5 years. Surprisingly, even at the time most dogs remained relatively healthy, with cuts (at 9 events per 1000 search hours) and weight loss the main complaints. A toxicology screen showed no evidence of lead, mercury, PCBs, or other organic compounds. Deployed dogs had slight pulmonary changes and cardiac changes compared to control dogs, as well as some higher liver values, but the latter resolved within the year. By year 5 post 9/11, deployed dogs had some different blood values, such as higher alkaline phosphate, glucose, and cholesterol. As for cancer? There was no difference between deployed dogs and control dogs.

MORE CANCER

Two other talks revolved around prognostic markers in canine breast cancer and targeted therapies in lymphoma. Susan Volk, VMD, PhD, DACVS, of the University of Pennsylvania, states that about 50% of canine mammary tumors are malignant, but it's hard to know which ones will spread out of control. In breast cancer the underlying collagen matrix may be tumor-permissive or tumor-resistant, depending on the size, density, and organization of the collagen fibers. Tumor permissive matrixes allow cancer cells to divide and migrate more easily. Identifying the underlying collagen matrix could allow veterinarians to make more informed decisions about treatment options.

Also, from the University of Pennsylvania, Nicola Mason, BVetMed PhD, spoke about precision medicine in canine lymphoma. Precision medicine, which is tailoring treatment to molecular subtypes of cancer, is becoming the norm in human cancer therapy. This could also greatly improve canine therapy and outcomes as we know what to look for. At least 10 different subtypes of canine lymphoma have been identified. The challenge is balancing how many genes to look at versus expense and practicality. The best balance is probably with targeted gene sequencing, which looks at about 300 genes. Their gene panel is still in its validation phase, and still too early to know if it will pan out. Other panels are available elsewhere but Mason cautions that such veterinary-aimed panels and tests don't require the stringent FDA analysis that analogous human tests would and may not be what they purport to be. She adds that tests that supposedly detect cancer in the blood are subject to the same criticism.

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CBD AND EPILEPSY

Owners of epileptic dogs know the challenge of balancing anti-seizure medication with quality of life. Stephanie McGrath, DVM, MS, DACVIM, of Colorado State University, is continuing her research of CBD and epilepsy in dogs. In a pilot study McGrath's lab had found that 89% of dogs treated with CBD showed some reduction in number and severity of seizures. That study is now being expanded to include 60 dogs; results are expected this year. Interestingly, preliminary data suggests that dogs treated at a dose of 2.5 mg/kg had a better response than those treated at the higher dose of 4.5 mg/kg. Not all dogs responded, but those that did had a greater than 50% reduction in seizures. Future studies will focus on the lowest effective dose to control seizures, as well as safety and CBD, and other conditions such as mobility and anxiety.

MUO AND THE MICROBIOME

Nicholas Jeffrey, BVSc, PhD, MS, DECVS, DECVN, DSAS, FRCV spoke about meningoencephalomyelitis of unknown origin

(MUO) in dogs. MUO is an autoimmune condition striking mostly small dogs suddenly, causing brain and spinal cord inflammation and affecting coordination, balance and mobility—-and its incidence is increasing. It has been called canine multiple sclerosis. Its cause is unknown, but there appears to be a link with changes in the gut microbiome. Jeffrey has found that dogs with MUO have different levels of *Prevotella* microbes compared to controls. Unfortunately, it's not practical to give dogs *Prevotella*, but in his new study he is giving it through pills containing fecal matter from dogs with high levels of *Prevotella*. It's too soon for results, but if positive, it may open the door for treating MUO.

DEGENERATIVE MYELOPATHY

Degenerative myelopathy (DM) has a late onset (9-14 years) characterized by progressive hind limb weakness that progresses forward to the point the dog can't walk within a year; eventually the dog is completely paralyzed and loses the ability to swallow or breathe. There is no treatment.

Since the SOD1 mutation and resultant DNA test for DM was discovered over a decade ago, there's been increasing interest—and misunderstanding—regarding testing. In a recent survey of 152 genetic disease variants looking at more than 100,000 dogs, the DM (SOD1) mutation was ranked #1 in disease allele frequency in both mixed breeds (8%) and purebreds (5%). Dogs homozygous for the SOD1 mutation are AT RISK for DM. Not all will develop it, and the risk varies depending on breed, with some breeds having a high risk and others a very low to almost non-existent risk. This leads to speculation about other genes that might also need to be present, or even environmental factors. To further complicate matters, carriers in some breeds (Ridgebacks, Chessies, Bernese Mountain Dogs, German Shepherds, Australian Shepherds, Alaskan Huskies, and some mixed breeds) sometimes also develop signs of DM, though they tend to do so at a later age. (Note that a different mutation is responsible for DM in Bernese Mountain Dogs).

In the current study, Joan Coates, DVM, MS, DACVIM, at the University of Missouri, sought to determine how the SOD1 genotype affects the risk of developing DM in different breeds. They found no difference in probability or age on onset attributable to sex. Of the more than 2000 dogs they compared, they only had sufficient numbers (more than 100) of Ridgebacks, Boxers, Bernese Mountain Dogs, German Shepherds, Chessies and Pembroke Welsh Corgis. (Borzoi, Poodles and Cardigans had more than 50 dogs, followed by Bloodhounds, Canaan Dogs, Kerry Blues, NSDTRs (all more than 30), Shiloh Shepherds and Puli (15 or more)). Of the six major breeds, Ridgebacks developed DM at the earliest age. Overall, by 12 years of age, over 50% of homozygous at-risk dogs developed a DM-like disease and over 60% developed signs when older. Heterozygotes had an increased risk of developing DM before 12 years of age, but even so fewer than 5% developed signs by 14 years of age.

As canine DM represents the best naturally occurring model of human ALS (Lou Gehrig's disease), a major goal to help both dogs and people is to use dogs as models to develop therapies. Since DM dog spinal cords contain a type of SOD1 that correlates with disease severity, Coates hypothesized that perhaps using selective messenger RNA targeting could slow or stop SOD1 production. Introducing MRNA to the part of the nervous system presents difficulties, but they tried several techniques on dogs. Seven affected dogs completed the clinical trial, which lasted one year during which the dogs received the treatment monthly while under anesthesia. Their gaits were evaluated on a standardized rating scale by researchers blinded as to their treatment group. All dogs continued to worsen, but the median time it took them to reach non-ambulatory stage was longer in treated dogs compared to historical controls. However, the difference was not statistically significant.

Courtesy of the Canine Chronicle