

The 2009 AKC-CHF National Parent Club Canine Health Conference

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While the conference this year was somewhat pared back, gone were the posters, and the numbers of attendees were reduced, although a number of veterinary students were invited, the contents of the full day and two half days of seminars and discussion sessions were as interesting and lively as ever.

On Friday afternoon we kicked off, after welcome speeches by CHF CEO Terry Warren and Steve Remspecher for sponsor Nestle Purina Pet Care, with Christine Haakenson, CHF Director's discussion of the CHF Grant process. I now am fluent in understanding the difference between OAK and ACORN grants. There is a maximum of 8% of donated money that can go to pay for overheads, which is good. It was noted that Purina donated \$6 million for research, rescue and health education programs from their program where folks send in weight circles from their animal feeds. Only 20% who sign up for this program actually send in their weight circles. Something to think about. The next presentation was by Margaret Poindexter, AKC's general counsel, who discussed the club's compliance operations, inspecting kennels, DNA and other measures taken to ensure the integrity of the registry. We then broke into groups for "round-table" discussions on various topics. This was a misnomer as we went to various areas in the two conference rooms, and were in a long line, often drowned out by noisier groups in the same room. Still there was a lot of interesting information in the group I attended "**Genetic Tests: How to Interpret Results and Incorporate Them Into Your Breeding Program.**" This discussion was led by Danika Bannasch DVM, PhD who as well as doing genetic research at UC Davis breeds and exhibits Nova Scotia Duck Tolling Retrievers. As a result they have or will have soon 10 genetic health tests for various diseases that afflict the relatively rare breed. Add to that the various phenotypical tests for hip dysplasia, eye disorders, thyroid etc, and it becomes a complex process of not only trying to avoid breeding two dogs carrying the same disease to each other, but weighing the relative effects of the diseases, how debilitating each one is, whether it has a late onset when non genetic diseases could be expected to also take their toll, degree of penetrance and accuracy of the test. Penetrance is something Danika is

working to establish in various diseases, and basically measures how many dogs with the genotype for a particular disease will actually get sick with that disease. If penetrance is low then risking breeding two affecteds with an autosomal recessive disease is a risk worth taking if their other good points are sufficiently outstanding. Not all genetic tests identify the actual gene responsible for the disease, they may be markers for a region of genetic material that is usually passed on with the actual gene. Markers are easier to identify, but somewhat less accurate than the actual gene. Again how accurate they are will differ from test to test. There was a lot to think about. Of course right now we have no genetic tests for Beardies. We hope that will change before much longer with a marker for Addison's at least. We were all jealous of the representative of the Pharaoh Hound Club as his breed appears to be free of genetic disease, and they only run OFA hips and CERF as most owners came from other breeds and they do so from habit. Danika encouraged us to support the CHIC DNA data bank, saying they process the DNA better than most research labs and it is available for all approved research.

Saturday we returned bright and early for the scientific presentations. These will gradually be released (some already have been) both on video and as audio podcasts. So I will just include the highlights here for the sake of brevity. Our Keynote speaker Mike Sampson spoke about the **One-Health/One-Medicine** initiative which attempts to strengthen the exchange of knowledge between human and veterinary medicine. More than 70% of human disease also occurs in animals. Of the Center for Disease Control (CDC's) category A (most serious diseases) 57% are zoonotic, and 100% of those in Category B (next most pressing) along with the majority of emerging diseases in category C. Dr. Sampson told us that due to H1N1 flu being misidentified as a swine flu (it's a human disease which other animals have caught from us) the cost to the pig industry was more than \$17 million a day. Loose lips sink more than ships.

Matthew Breen is always a popular speaker and he did not disappoint. His topic was **Canine Cancer & Comparative Genomics: New Technologies, New Opportunities**. As the genomes of more and more species are unravelled it is possible to identify regions shared between species and related to particular diseases. Making it easier to identify the particular genes not only relating to specific diseases, but the function of individual genes. Dogs and humans not only have very similar genetic make-up, they share a similar lifestyle and with shorter generation time are a good model

for human disease. This means there is more money for genetic research in dogs, and they as well as humans benefit from that research. By looking at tumorous tissue from more than 500 dogs not only are they beginning to be able to identify the genetic signature of the broad cancer types - lymphoma, hemangiosarcoma, soft tissue sarcomas, osteosarcomas and brain tumors - but to identify those patients who are good candidates for existing therapies and those who will die anyway within a few days or weeks. Owners knowing there is a good chance they will have more than 9 months with their companion are more likely to go ahead with expensive therapies. At present, for example, only 5% of the 100,000 to 2000,000 cases of canine lymphoma identified each year are treated and the \$3000 to 6000 price-tag is probably a good reason when there is no guarantee of success. For one therapy they have identified the 75% of dogs that will survive less than 9 more months with that therapy and the 25% who will live much longer. This will be applied to other treatments and other tumor types. Dr. Breen predicts in 10 years we and our animals may be having our genomes tested while we wait to see the doctor or vet, who will compare it to our last genome, note the changes and treat us accordingly.

David Vail talked about **Clinical Trials in Veterinary Oncology: Past, present and future**. New cancer drugs are only 6 to 8% effective, it is important to quickly identify the most promising of these and again dogs are a wonderful model for developing treatments for both species. Dr Vail discussed new delivery techniques - putting drugs in liposomes or bacteriophages to attach to new blood vessels - rapidly forming in tumors - or other more tumor specific sites so that only the tumors and other rapidly dividing cells will be affected and the rest of the body spared from the toxic effect of most of the drugs used to treat cancer. Similarly tomotherapy radiation combined with CT scans ensures only the tumor is radiated.

Ebenezer Satyaraj spoke on **Immunonutrition** - which looks at the detrimental effects of malnutrition, age (neonate or old age) and stress on the immune system. Antigen presentation is diminished and as a result individuals are more prone to succumbing to infectious disease, and more likely to develop autoimmune diseases or cancers. Neonates have only 50% of the immune capacity of healthy adults. The elderly have a reduced ability to make immune cells in bone marrow. Stress leads to a more rapid destruction of immune and other cells. In all groups vaccine response will also be diminished. Adequate and appropriately balanced amino acids,

vitamins and minerals are especially important for nourishing the immune system.

New Diagnostic and Therapeutic Investigations of Neurological Disease in Dogs was Simon Platt's topic. With any neurological disease immediate and accurate diagnosis is crucial for the best results. The use of MRI, including the 3T MRI he gets to use at the University of Georgia, is rapidly expanding our understanding of the cause and best treatment of these diseases. 50% of epilepsy though is still classified as idiopathic because the cause has not been determined. Intravenous valium remains the initial treatment of choice (the effect is far more rapid than rectal valium) but there are some promising new therapies. There is a new preparation of intranasal midazolam. It is introduced as a liquid but forms a gel in the nose which adheres to the mucosa and maximizes absorption. Maximal levels are reached within 3 minutes, longer than the average actual seizure, but in dogs who have repetitive seizure episodes this is really appreciated. Up to 20% of seizures don't respond to traditional seizure drugs like phenobarbital and the bromides. New drugs that show a lot of promise are gabapentin, zonisamide and levetiracetam. A new extended release formulation of the latter, Lacosamide, is particularly useful as the short half life and need for frequent dosing with many of these drugs in dogs limits their current use. Syringomyelia is a disease of Cavalier King Charles Spaniels (CKCS) and Brussels Griffons primarily in which the cerebrospinal fluid (CSF) is pushed out of the brain into the spinal cord with each heart beat. In the worst cases parts of the brain are also pushed out. It is inherited, although severity varies markedly. Surgery is of questionable benefit and there is no other treatment. Dogs get more brain tumors than humans but the types and classes are very similar. Outcome is influenced by age as well as neurological status. In humans MRI can predict outcome with 65-96% accuracy, and the degree of edema (fluid accumulation) correlates well with malignancy. MRI can be used for the same purpose in dogs although biopsy is needed for definitive identification. Speed of uptake of injected contrast material can help identify the tumor type, determine the best treatment and the prognosis. Examination of CSF is not helpful. Strokes present differently in dogs than in humans. Often the dog is blind on one side, and circles in one direction with difficulty in balancing. It can be hard to differentiate from old dog vestibular disease without an MRI, and is mostly seen in dogs over 7, especially greyhounds and spaniels. Most strokes in humans result from high blood pressure but this is rarely if ever the cause in dogs. Spinal strokes are common in large breeds and border collies and result from small pieces of disc material entering the spinal fluid. In the first 5 days after a cerebral stroke levels of the neurotransmitter

glutamate increase, it has been speculated that using glycine, which has opposite neurological effects, in early stroke might be helpful. Cytokines also increase in the first 5 days after a stroke, and anti-inflammatory drugs may be helpful. Most exciting is the use of stem cells derived from the patients own fat cells. These are very potent and very safe. Meningoencephalitis is most common in toy dogs and 80% of the inflammation seems to be immune mediated. Toys are also more susceptible to post vaccination meningitis.

Mark Oyama's presentation **Matters of the Heart: Advances in Canine Cancer Research** was equally packed with exciting new material, although fortunately Beardies are not at high risk of genetic heart disease (I have a lot more information on these that I will omit here). Mitral valve disease (MVD) results in more than 75% of all canine heart disease. In breeds in which it is inherited it may well manifest after the dog has been bred. Collagen is progressively lost from the valve and replaced by extracellular matrix so that it becomes thicker and weaker, blood flows back from the left ventricle into the atrium rather than out through the aorta to the rest of the body. Ultimately this causes congestive heart failure, heart enlargement and activates neurohormones. Certain drugs especially those that increase serotonin, ergot alkaloids (used for treating migraines) and dopamine agonists (used for human Parkinsons) as well as the banned fen-phen can all increase the risk of mitral valve disease. The mitral valve cells can make serotonin. Too much causes vasoconstriction. It can also damage the valves on the right hand side of the heart. A human drug that blocks serotonin shows promise for slowing the progression of MVD. Nutrition (amino acids) and environmental factors are also being explored for their effect on causing/preventing/slowing MVD. Small dogs, (especially CKCS) are more prone to MVD.

On Sunday morning, Danika Bannasch presented **Dalmatian Bladder Stones: not just a Dalmatian problem**. Dogs (and other mammals) excrete excess purine from their blood in their urine. This is usually excreted as allantoin, but Dalmatians as well as humans and great apes lack the enzyme to do so and excrete uric acid instead and this can lead to bladder stones. All Dalmatians are homozygous (have two copies) of the mutated gene causing this condition, and so do dogs of other breeds (Black Russian terriers and bulldogs most often) that form uric acid stones. The mutation seems to be old and shows up with variable frequency in other breeds (JRTs, GSDs, Weimeraners, Giant Schnauzers, American

Staffordshire terriers and Australian shepherds being among the more common). While all Dalmatians have the mutation, expression is variable - meaning not all will have a major problem with stones. Penetrance is also variable, so some dogs will have no problems despite being genetically predisposed to do so. Another effect epistasis may be at work. This is the result of a second gene masking the effect of the first. Not all genetic tests will apply to all breeds and have to be proven accurate in each breed before they can be offered to breeders. This has proven to be especially true in the case of progressive retinal atrophy where several different mutations have been found with similar disease manifestation but affecting different breeds. Other concepts Dr. Bannasch discussed included allele frequency - how common the mutation is within the breed, and very difficult to determine; and the relative risk of disease if a dog carries the allele which is usually 2 to 5% in complex diseases like autoimmune diseases. Questions breeders need to consider - but appreciate we still need answers to many of them - are: if a disease is in the breed; if it is treatable and if so how expensive or effective is treatment; how severe the disease is; the age of onset; is the mode of inheritance known; what is the penetrance; has it been proven that the mutation for an available test actually causes the disease - surprisingly this is often lacking.

Brian Zanghi spoke about **Nutrients to promote physical recovery in active dogs**. Giving dogs rapidly digestible carbohydrates immediately after vigorous exercise replenishes glycogen (the body's glucose store used for aerobic exercise) within 4 hours and completely restores it within 24 hours. Physical activity causes muscle fiber damage, soreness, inflammation and fatigue. Oxidative stress contributes to muscle cell damage, and reactive oxidative substances result from exercise. Antioxidants can reduce the damage, but some like Vitamins C and E can also increase the formation of reactive oxidants. Protein given post exercise probably acts to minimize damage by providing the amino acids needed for muscle cell recovery. Using carotenoids as antioxidants also helps maintain blood glucose levels and reduces markers associated with tissue damage.

Canine Herpesvirus-1: a new pathogenic role for an old virus was the subject of Eric Ledbetter's presentation. Most of us worry about canine herpesvirus-1 (CHV-1) as the cause of severe illness and mortality in fetal and neonatal puppies when the dam with no previous exposure contracts the disease. Dogs over 2 weeks of age usually show no signs of illness or those they do exhibit are very mild. It is probably the most common infectious

organism affecting dogs worldwide. Like the related human herpes viruses that cause chicken pox and shingles and those in other species once contracted the virus stays in the body for life and can be reactivated. Certain drugs (corticosteroids, cyclosporines, cyclophosphamide, epinephrine), surgery, trauma, stress, fever and ultraviolet light can all trigger recurrence. In other species herpes viruses have been the most common cause of blindness. Dr. Ledbetter's research has found that CHV-1 is the most common cause of viral conjunctivitis in dogs, and he has also linked initial and recurrent infection with outbreaks of ulcerative and nonulcerative keratitis (corneal infection). Outbreaks are most common in confined colonies of dogs. He has shown that infecting dogs with CHV-1 causes conjunctivitis and keratitis not just that affected dogs carry the virus. Immunosuppressed dogs are likely to revert to the neonatal disease form, and can go blind and may die. An antiviral drug to treat CHV-1 is awaiting testing. In the meantime he favors vaccination to prevent infection and remove the risk of lifelong recurrence of the active disease. However, currently the only vaccine is only available in Europe. Steroids should not be given to treat conjunctivitis (many of the ophthalmic ointments contain them) as if the cause is CHV-1 it could exacerbate the disease and result in corneal ulcers. Dr. Ledbetter also told us to expect more genetic tests for eye diseases especially those that cause blindness and/or pain and gene therapy to treat affected animals. He reported improved success in surgery to treat retinal tears and detachment; vastly improved ocular imaging; endoscopic cyclophotocoagulation via a tiny endoscope to treat glaucoma with reduced risk and increased efficacy - depending on the breed acute glaucoma must be treated within hours to 3 days to save sight.

The final presentation was Ziad Ramadan's on **Metabanomics: A tool for nutrition research**. Metabanomics measures all the products of metabolism in a single biological sample and correlates them to known physiological or pathological states. It does it using complex multivariate analysis -way over our heads! We can appreciate the hoped for result, biomarkers indicating changes in health and disease so that diet and other parameters can be manipulated to reduce the incidence of disease. Ultimately, diets can be truly tailored for every individual to maximize health and longevity. The field is only in its early stages, but like much of what we heard during the course of the weekend we have seen the future and it is fascinating. I'm already looking forward to the next conference in 2011.

