Report on the 2015 AKC Canine Health Foundation National Parent Club Canine Health Conference

- Dr. Nancy Kelso, Chairman, Collie Health Foundation Grants Committee

A repeated message repeated throughout the conference was of one health: what we discover in veterinary medicine can often directly relate to human medicine.

1. Stem Cell (SC) Therapy for Supraspinatous Tendonopathy
Jennifer Barrett, DVM PhD

Regenerative Medicine currently include:
1. Stem cells (SC)-
Embryonic are the ultimate stem cell as they are pluripotent since they can be directed into producing any cell in the body, which is compared to adult stem cells are multipotent. (can form many but not all cell types). Current research is focused on adult stem cells. Adult stem cells are easier to acquire, are more controllable and less likely to allow cancer to thrive. From adult stem cells, proginator cells are derived. They are stem cells, which are oligopotent, or unipotent, meaning they have more limited ability on what cells they can create,

Adult stem cells have a trophic function. They can:
Generative new tissue
Supply growth factor
Chemotactic progeninator cells
Supply an extracellular matrix
Angiogensis (grows blood vesses)
Anti-apoptosis (fat deposition)
Immunomodulator
Antifibrotic (antiscar)

In veterinary medicine there are hundreds of ways to make but most commonly they are derived from bone marrow or mesenchymal cells (adipose or fat is most commonly used).

Comparing Adipose stem cell (ASC) to Bone marrow stem cell (BSC):
ASC: grow faster (take 29 hrs to double), are more concentrated, currently are primarily used for anti-inflammatory. Commonly used today with in house kits (they are using the FDA approved human Ingeneron) and Vet Stem or other commercial labs.
BMSC: take 46 hours to double, currently appear better for cartilage or bone

2. Platelet Rich Plasma (PRP)- typically derived from the patient's own serum or plasma. Produce Growth Factor (GF), which mixed with SC, is very beneficial. The GF protein is critical for cell division and makes a matrix that the SC thrive and grow on.

The goal of regenerative medicine is to cure an injury, not repair since repair or musculoskeletal conditions lead to scar generation, which is never as good. The current study take Supraspinatous tendonopathy diagnosed by ultrasound and treat with PLP and SC. For dogs to be entered in the study they can only have one shoulder affected. Later trials will involve dogs with elbow disease. The process involves collecting fat from the patient sending it to Vet Stem Lab then the product once returned is injected by ultrasound guidance into the supraspinatous tendon, followed by rehab. Thus far there have been favorable responses (12 weeks) in the pilot study. The current study is randomized, controlled and blinded: some patients receive plain plasma as the control, Adipose sc with PRP and PRP alone. It's a short tiral where all are rescued at the end and given the benefit of regenerative medicine. The results are promising, although more eligible participants are needed. Contact Drs. Canapps's office, VOSM (Veterinary Orthopedic and Sports Medicine) in Annapolis Junction, MD.

2. Regenerative Medicine Techniques to Treat Cartilage Disorders
Brian Saunders DVM PhD DACVS

This session covered his research and advancement in canine regenerate medicine application to dogs with osteochondrosis and other common joint ailments such as osteoarthritis. Osteochondrosis is any defect in cartilage with a variety of causes. There is heritable OC caused by the development of a thick cartilage flap if growing dogs, which dislodges and causes pain. The pain is analogous to having a pebble in your shoe. Other causes of OC are trauma, fracture, sepsis, hip and elbow dysplasia. Treatment of OC is surgical debridement; however, articular (hyaline) cartilage is very poor at regenerating and replaces with the less adequate fibrocartilage (never as good as hyaline). Traditional regenerative medicine supplied anti-inflammatory properties but did not resurface the hyaline cartilage. Other treatments being looked at:

1. OATS (Osteochondral Transplant) takes healthy tissue from the patient's non-weight bearing surface of the knee and transplanting it into the defect (autograph) has been used in humans, horses and dogs.

2. Regenerate osteochontral plugs, using regenerative medicine, taking the patient's stem cells and add a scaffold so that they can be engineered to look like normal cartilage that can be placed in a joint, and unlike OATS do not require a donor site. The chondrogenic plugs currently being made from stem cells derived from synovium, bone marrow and implanting into rodents thus far. This research is still in process and is unpublished but looking very promising.

At this time canine stem cells hold much promise in orthopedic disease and tissue engineering. Extensive characterization of SC to serve as foundation for tissue entineers and SIPS/Salt hydrogels look very promising in vitro and are biocompatible in vivo.

3. Bright Mind Plaform
Yuanlong Pan, BVM, PhD
Nestle Research Center

Senior dogs often show problems with cognitive function such as:
Inability to perform normal navigation, loss of recognition of people or dogs, loss of knowledge, slower to get up, loss of muscle mass, decrease attention to surroundings, and intermittent, unexplained anxiety At about 7 years of age the glucose metabolism in the brain changes. With 25% of the body's glucose normally used by the brain, especially the frontal cortex and hippocampus, decreasing glucose metabolism correlates with decreasing brain size with age. Medium Chain Triglycerides (MCT)(coconut oil is a primary source) can be used as an energy source for the brain by producing ketones; therefore, compensate for the brain's decreased ability to produce it's own glucose. Especially useful if fed with a low carbohydrate food, which forces the body to use fats for energy. Ketones are a normal end product of fatty acid metabolism and are not the same as ketoacidosis. Simply stated, the gut absorbs MCT's. they are transformed by the liver into ketones, and serve as an alternative energy source during a low carbohydrate diet. In addition, ketones do no require insulin for metabolism.

A study in 2010 British Journal of Nutrition confirmed that MCT's did convert to ketones (with a low carbohydrate/protein diet), and fed long term (months to years)(20 grams of MCT/day) improved function in humans with Alzheimer disease. In the dog study, dogs fed MCT's made 50% fewer mistakes on cognitive function tests fed a diet of 5.5% MCT.

4. Senior Cognition and Brain Aging
Gary Landsberg, BS DVM DACVB DECAWBM

Cognitive Dysfunction Syndrome (CDS) in dogs is a neurodegenerative disorder of senior dogs (seen as young as 6 years old), characterized by a gradual cognitive decline and increasing brain pathology, after other medical conditions are ruled out. The diagnosis is normally made based on clinical signs described the acronym DISHA: Disorientation, altered social interactions, altered sleep wake cycle, house soiling, altered activity level. In addition and increase in fear, anxiety and irritability, and learning deficits are associated with cognitive dysfunction.

Brain changes associated with CDS include a decrease in frontal lobe volume, reduction in neurons, an increase in toxic free radicals, and the accumulation of beta-amyloid plaques with similar sequence, distribution, and biochemistry as in human Alzheimer patients. Early detection allows for early intervention and slowing of the disease.

Treatment:
1. Environmental enrichment (play, exercise, train)
2. Selegiline (L-deprenyl)- labeled in US

3. Nicergoline
4. Propentogylline (increase blood flow, used in Austrilia)
5. Natural therapeutics:
-Hill's b/d diet (uses anti-oxidants, fatty acids, and mitochondrial co-factors), which was demonstrated to be effective.
-Purina Bright Minds diet- uses ketones for an alternative energy for the brain
-Senilife/Activait: phosphatidylserine, antioxident
-SAMe (S-adenosylmethionine- methyl donor
-Apoaequorin (Neutricks)- calcium buffer
-DHA fatty acids

5. Osteosarcoma
Bruce Smith VMD, PhD

Osteosarcoma is a common and devastating bone caner. At the time of amputation, dog's chest radiographs are clear of metastasis, but it is long believed that microscopic metastasis is present, and therefore the rapid reoccurrence. Oncolytic Viral Treatment is the new treatment using engineered adenovirus (the common CAV2 and CAV1). These vaccines are tumor or cancer specific. This means in normal cells it stops, but in cancer, the virus reproduces. The reproduction causes the body to react and spread virus, which in turn causes to body to react and kill tumor cells. This process has been found to last about a week.

In his first study, dogs with no radiographic evidence of osteosarcoma metastasis had the affected limb amputated. Forty-eight hours post-op they received the virus. The dogs went home and received the standard osteosarcoma carboplatin chemotherapy. In this trial with amputation but without treatment, the dogs lived an average of 6 months. The four dogs with amputation, standard chemotherapy and O-CAVE1 lived 4 months, 6 months, 8 months, but one greyhound lived 26 months. The second study involving more patients just ended this summer where 20% of the dogs had long-term survival also had long-term titers. The next research necessary is to figure out why some individuals respond, as well as additional research on the vaccines and immunology.

6. DNA Methylation in Canine Lymphoma
Jeffrey Bryan DVM MS PhD DACVIM

Epigenetics: how our experiences (chemicals, stress, diet, exercise) affect our DNA) as well as our past relatives. For example, Jewish relatives of holocaust survivors' genes are affected today. Another example is women who smoke leave damaged genetics not only to themselves, but to their children and their children's children….

DNA methylation occurs primarily in mammalian cells. After DNA replicates, methylation is added. The methylation tells which DNA should replicate, and which should not. If methylation occurs this tells the cell NOT to replicate this DNA. There is a methylation breakdown in cancer. Then the wrong DNA replicates and t cells no

longer control he rate of replication. Very little is known about methylation except in canine lymphoma there is a loss of methylation. It is also known that MDR1 is not modulated by methylation.

The future use of this study is that drugs that demethylate and work in humans may also assist dogs. Current research is being done, especially in Golden Retrievers Colorado is studying a particularly aggressive B cells in Golden's (B cell lymphoma is typically "better" then T "terrible" cell lymphoma in most dogs) and have found two genes (myc+ and bcl2+) associated with this particularly aggressive B cell lymphoma. DNA methylation has been confirmed. Missouri is currently defining the methylation of these genes. The final step is to ID and characterize these genes in subpopulations w/in Goldens with B cell lymphoma. This potentially would benefit humans and pets, to catch those at high risk before they have cancer, and define which patient will respond to chemotherapy.

7. Precision Medicine in Oncology
Doug Thamm VMD DACVIM

This form of therapy has gained popularity in human trials, designed to match targeted therapeutic, based not on tumor type or site of origin, but on the presence or absence of DNA mutations or activated cell signaling pathways that are predicted to confer sensitivity to specific drugs. This approach has gained popularity after the studying that the average FDA approved drug only helps ¼ to 1/20 of those taking it.

An important application of precision medicine is in dogs with the mdr1 mutation. For example, in a cancer that normally responds to doxorubicin, the 1/3 dose that would be tolerated in a homozygous mdr1 mutant dog is not sufficient to affect the cancer; however, the 2/3 dose that heterozygote mdr1 mutant dog, may be beneficial.
Another example is Mast Cell tumor in dogs, which is very common and previous staging, has proven less then adequate. A current study took c-kit sequencing and KIT IHC on any stage or grade of MCT. Specific genetic mutations were found to have a worse prognosis. Having a predictor of the cancer can help clarify what treatment is best suited. This process has also been used in familial osteosarcoma. This research is in its infancy.

8.. Quality of Life in Senior and End of Life Years
Alice Villalbobos DVM FNAP

Dr Villalobos proposes that we look at End of Life as being a specific and separate stage of life, no always associated with old age because it may occur at any age. End of Life has 3 stages: the well stage, the decline stage, and the trajectory towards death stage. We can do many good things for senior and geriatric dogs to keep them in the well stage with excellent quality of life (QOL) for as long as possible. Using the HHHHHMM QOL scale. Keeping our pets alive help to extend the quality and length

of life human's life. For example: People who own a pet generally live 3 years longer, and humans that suffer a heart attack are 4x more likely to survive if they have a pet and have a shorter hospital stay.

QOL Scale:
Hurt
Hunger
Hydration
Hygiene
Happiness
Mobility
More good days then bad

Use this QOL scale to improve and extend life
"What would our grief be if we had twice as much time?"

QOL Death: 2 steps
1. Sedation prior to an IV catheter or euthanasia
2. Euthanasia (don't take them to "the back")

Email her for a booklet @ veterinarians taking better care of themselves due to the repeated stress of owners and their pets. Veterinarians have topped the list of suicides.

9. Fungal Microbiome of Healthy and Allergic Skin
Jan Suchodolski, DVM PhD

Microbiome should replace the word microflora. Microbiota is a collection of microorganism in an ecosystem. For example there are 100 trillion bacteria in the gut, 90% of the cells in our body are bacteria, our body has 100x the number of genes in the bacteria in our body then in our genome. We are in the infancy of fully understanding the body's microbiome.

Gut bacteria a beneficial to fully develop a functional GI, immune development, provides nutrients, and protects us from pathogens. The intestinal microbiota is generally stable over time, influenced by genetics and environment, and generally resistant to change. Humans have 95% of our DNA in common with each other yet our bacteria are 90% different from one and other. In disease states the microbiome changes (Inflammatory Bowel disease, metabolic syndrome, asthma, diabetes, obesity, stress and anxiety.). Our current cultures of GI bacteria will only show 1% of the bacteria in the gut (the aerobic ones). Many are anaerobic or undiscovered; however, with current PCR genetic sequencing (which looks at the DNA of each microbe) many more have been discovered. Most of the bacteria in the GI tract are anaerobic (vs the well known E coli which only accounts for 1%) and fungal organisms. Growing fungal organism and anaerobes is difficult but PCR

techniques have helped to find and define both bacteria and fungal organism. To date 40 different fungal organisms have been recognized in the gut.

Dysbiosis occurs when the whole microme is off, and that's not just overgrowth. There is a paradyne shift, which causes a loss of the protective and beneficial function of the GI microme.

Dysbiosis causes:
1. reabsorption of deconjugated bile acids, leading to malabsorption
2. bacteria produced fatty acids that inhibit fluid absorption
3. distruction of bush boder enzymes
4. decreased absorption of monosaccharides, amino acids, and fatty acids
5. Lack of protective factors of the normal microbiota

Dysbiosis occurs in many diseases and in IBD. IBD is mulitfactorial, caused by genetics, GI microbes, immune system and environment/food. Studies have shown in IBD of both dogs and humans there is a shift in the microme: less bacterial diversity, decreased Firmicutes fungi, and increased Proteobacteria. Another example of dyspbiosis is the western diet typically high in protein, fat and carbohydrates, which decreases gut diversity and exacerbates inflammation. Antibiotics mimic dysbiosis where sometimes the gut never fully returns. A study done by Ilseung in 2012 fed young mice subtheraputic levels of antibiotics for 7 weeks and found these mice had significantly more body fat and insulin resistance compared to the controls.

The skin is it's own complicated microbiome and ecosystem, even more diverse then the gut. The canine skin microbiome :

1.characterized by a diverse microbiome:
2. marked individual variability and among the different skin sites on the body
3 . haired skin is more diverse then mucocutaneous junctions
4. allergic dogs have a less diverse microbiome
5. mite sensitized atopic dermitis dogs have dysbiosis of the microbiome (abundant Actinobacteria and firmicutes)
6. healthy pet dogs are colonized with more abundances of gammaproteobacteria

His AKC CHF study was to describe the canine skin's fungal microbiome in dogs with healthy skin and dogs with allergic skin disease. He found 80 mold genera induce hypersensitivity in allergic individuals. Dogs with a history of allergic skin disease exposed to malassezia induced gene expression resembling diseased skin and Malassezia correlated with disease severity in dogs with allergic dermatitis

He found over 120 fungal organisms by using pcr, which did very by the location of the body. Dogs with allergic skin disease had more and different fungi then dogs with healthy skin, except in the ear. Perhaps in the future this will lead to us applying topical medications with healthy bacteria to the skin and other therapies.

10. The Cutaneous Microbiome and Resistome of Health and Atopic dogs
Charles Bradley VMD, DACVP

Canine atopic dermatitis (allergic skin disease) is a common condition, affecting approximately 10% of the canine population, and affected dogs often develop recurrent bacterial skin infections. As in human medicine, antimicrobial resistance is increasing, and presents a major challenge to successful treatment of these conditions. Atopic dermatitis is a type I sensitivity reaction by IgE, where pruritus (itching) occurs. There appears to be a genetic predisposition, and it is a diagnosis of exclusion. No single test will diagnose.

Starts with late onset type 1 hypersensitivity>causes inflammation>causes itching> then skin barrier changes occur> which leads to a change in the microbiome. There are two camps of thought on the genetics. Clearly there are breed predispositions, as well as regional.

1. High IgE production (a mutation has been found in Westies; however it's not always associated with disease).

2. Epidermal barrier defect: in humans filaggrin is a hot topic. Filaggrin is the glue that holds the epithelial cells together. Two genetic mutations have been found in humans.

In his study he did pcr and cultures to determine what aerobic bacteria was found: orally, axillary, inguinal and pinna (ear). The most common bacteria on human skin is staph aureas, but in dogs different Staph are present (pseudintermedius and schleiferi. The skin microbiome changed during atopic flares. Anitibiotic resistance was found commonly in both normal dogs (1.5-3% methicillin or multidrug resistance found) and atopic dogs, although there was a higher degree antimicrobial resistance following antibiotic administration. In fact, there was a horizontal spread of methicillin resistance (from one pet in the house to another). The current study is looking if methicillin resistance was already there and it grew after antibiotic usage.

Current therapy is designed to manage atopic disease. Unfortunately it is not cured. Treatment involves:

1. Controlling pruritus (itch): corticosteroids, cyclosporins, oclacitinib, and antihistamines
2. Supporting skin: fatty acids, phytosphingosine, topical therapy
3. hyposensitization (sq and sublingual)
4. Ask are antimicrobials really needed? Topicals are often more effective. If antibiotics are used dispense at least 3 weeks at a time and rechecking skin cytology at your veterinary is extremely important! First empiric choices: clindamyin, smz/tmp, first generation cephlasporins, lincomycin, . Second tier: 2nd and 3rd generation cephlasporin, doxycycline, chloramphenicol, aminoglycocides,, and Third

tier only used after culture that this is the only choice: fluoroquinolones due to the rapid progression of resistance including horizontal spread.

Veterinary Consensus statement on when to culture:

1. cocci present >6 weeks after treatment
2. intracellular rods present
3. less then 50% reduction of lesions after appropriate therapy
4. emergence of new infection after 2 weeks of treatment
5. multidrug resistance present in any individual of household

The bottom line: Culture, Use topical and are antibiotics really needed?

11. Gastric Dilatation-Volvulus: Big Problem for Big Dogs
Laura Nelson, DVM, MS, DACVS

Surveys by Pipan (2012) and Glickman (2000 CHF was part of this study) try to define risk factors. These studies trying to find risk factors but are confusing as they historically list some association but not causation.

Mortality ranges from 10-43%, but most progressive emergency services are 10% overall and 6% post op. Increased mortality if: depressed on arrival (increase 3x), comatose (36x), greater then 5 hours signs (15x), perioperative or post operative arrythmias, splenectomy (32% mortality) or partial gastric resection (35% mortality).

Plasma Lactate is an area receiving a lot of attention. Initial studies showed a single lactate if <6% had 99% survival and > 6% 58% survival. Another study showed 90% survival if lactate <9% and 54% survival if lactate >9%. Lactate is released when circulation is reduced, to internal organs, result of cell death. More importantly the prognosis has been better determined by following lactate. Levels that improve have been associated with a better prognosis and clarify which patents need the most aggressive treatment. At this time it is not recommended to decide treat based on lactate alone.

Mainstay of treatment is shock treatment and surgical repositioning with gastropexy. A study of prophylactic gastropexy showed 11% future gastric dilatation compared to emergency gastropexy with 9% reoccurrence rate. These dogs had dilatation, not torsion.

Current research is looking at etiology (cause) and looking into gastric motility (nerve studies), intestinal motility, genetics, microbiome and the gas. Where does the air come from? Sample have shown a high CO2 and H2 compared to room air, concluding that bacterial fermentation is likely. The low gastric pH should limit bacteria but a higher pH (>4) is found in some breeds. Do bloat prone dogs have more gas-formers?

Studies on motility are currently looking into 3 hormones important for digestion: Motilin (increases in positive feedback loop with 5-HT and level peak with phase 3 contractions), 5_HT (Increases with phase 2 pressure in duodenum, and stimulates motilin), and Ghrelin (a growth hormone related protein that peaks during phase 1 contractions and inhitibs motilin to stop phase 3). Currently we know that phase 3 motility is decreased in dogs after naturally occurring GDV. More motility studies are being done looking at radioscintigrapy, tracer studies, measuring electrical resistance, and the smart pill (measures pH, temperature, pressure and time). Michigan State College of Veterinary Medicine is currently looking into how inherited gastric dyshythmia predisposes large-breed dogs to GDV, and the effect of prophylactic incisional gastropexy on markers of gastric motility in dogs, using a novel wireless device. Genome analysis is looking for canidate gene analysis with a special interest in motilin and ghrelin.

12. Bloat: What is New in 2015?
Elizabeth Rozanski, DVM DACVIM, DACVECC

Most do well post op but why don't' all?

1. Gastric Necrosis and rupture
2. Multiple Organ Dysfunction Syndrome (MODS)
3. Euthanasia due to the cost of care and co-morbidity

MODS: Failure of one organ system may be tolerated but as more fail, mortality increases. Systems commonly involved are cardiac, pulmonary, coagulation, liver, GI and renal. These can be caused by infection, vascular compromise by blood clots, and reperfusion injury (low oxygen to cells when circulation is lost, followed by return of circulation and oxygen, then the release of free radicals).

Most common causes of mortality are aspiration pneumonia, coagulopathy (treat with plama & if PT/aPTT normal consider anticoagulant therapy for microthrombosis), arrythmias (treat with lidocaine and sotalol). Some research is showing that lidocaine may be good to prevent reperfusion injury.

Prevention: educate new dogs owner so the signs are recognized early, consider pet insurance for the catastrophic problems (GDV cost $2000-8000), and prophylactic gastropexy?

New research is looking into the cardiac dysfunction since it associated with a poorer outcome and is poorly understood (Troponin/ NTPro BNP markers, ECG, and echo). Other research is looking into intragastric pressure measurements, gastro-hepatic ligament length, microbiome (of feces, stomach and blood) and the genome.

Other interesting topics in her research:

1. Shih tzu has a high rate of pulmonary hypertension
2. Female dogs in diestrus (2 months after heat) are hypercoagulable and clotters, which includes bitches with pyometria
3. Golden and husky (northern breed) predisposed to spontaneous pneumothorax.
4. 10-40% of dog in ICU have no protective titer to distemper and parvo. Significance unknown.

Veterinarians should review VetCOT for education and collaboration on emergency medicine.

13. Inflammatory Bowel Disease and Chronic Intestinal Inflammation
Kenneth Simpson BVM&S, PhD

Etiology (cause):
1. Luminal Antigens: diet (allergies or intolerance) and microbiome
2. Host genetic defects
3. Mucosal barrier defects
4. Defective Immunoregulation (some adaptive and some innate)

IBD is defined by the location and type of inflammation present:
Examples of IBD:
1. Boxer with granulomatous colitis (also in other breeds such as French bulldog). Currently blood is needed on affected dogs for research since the same GWAST analysis is looking at the same candidate region in boxers, frenchy, and humans. This is the CD48/SlamF1 genes which have been associated with killing E. Coli genes. Invasive E Coli has been confirmed in affected dogs. This explains the fact that this disease in antibiotic responsive (enrofloxin, amoxicillin and metronidazole for 6 weeks although improvement is seen in 2 weeks, in addition some immunotherapy).

2. German Shepherd IBD typically responds to tylan or oxytetracycline. The TLR5 gene has been affected causing over reaction against flagellettes in the GI tract. It is believed that having the susceptible gene along with environment and bacteria together contribute to IBD.

3. Wheaten Terrier with lympho-plasmocytic enteritis responds to hypoallergic diet. Univ of PA is working on looking at Wheaten's with protein loosing nephropathy and enteopathy.

4. Irish Setter with gluten sensitive enteropathy (autosomal recessive associated with TLR5 SNPG22A) believed to be an IgA deficienct is also antibiotic responsive
5. Sharpei have inherited Cobolamine Deficiency (chromosome 13 4SNPs)

6. Protein Loosing Enteropathy/ Lymphangiectasia primarily seen in Yorkie. Causes low blood protein to the point of ascites (fluid build up in the abdomen). Diagnosis is based on classic ultrasound appearance (ascites with hyperechoic speckles and linear striations in SI) and endoscopical biopsy (dialated lymphatics). The prognosis is poor since only 50% respond (low fat/high protein diet, MCT (1-2ml/kg/day), try cyclosporine +/- pred, diruetics, low dose aspirin, tylan). Current study at kw55@cornell.edu

7. Hemorrhagic Gastro-Enteritis (HE) is a clinical syndrome affecting many breeds, and is believed to be a clostridium toxin or paracute dysbiosis. HE can be life threatening and requiring IV fluids, antibiotic (bacteria translocate), and GI protectorants.

These studies once again show the importance of one medicine and how our canine research and human research support each other.

14. Advances in Canine Cardiac Genetics
Josh Stern DVM PhD DACVIM

There are currently >1600 known inherited disease in dogs (>200 cats) with over 100 genetic tests available, yet today there are only 4 mutations and genetic test available for canine cardiac disease.

Inherited Cardiac Disease include congenital: subaortic stenosis (SAS), Patent ductus arteriosus, pulmonic stenosis, tricuspid valve dysplasia and acquired: Mitral valve degeneration, dilated cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy

SAS is the #2 congenital heart defect in canine, most commonly affecting large breeds and signs range from none to severe life threatening and life expectancy of 19 months). Auscultation is not good enough in breeds at risk. Many dogs develop a murmur when exited (50% of Goldens and 80% of boxers). All dogs need a doppler echocardiograph to diagnose. In goldens check aortic velocity at the subcostal site: Equivocal 2-2.5 m/sec 2, mild 2.5-3.5, moderate 3.5-4.5, and severe > 4.5, as well as seeing turbulent flow (as apposed to laminar flow common in excited dogs). These numbers are easy to underestimate but hard to over estimate so take a high number seriously. The signs are syncope (fainting), sudden death or heart failure. Research is being done on a new stretching devise, which in the short term alleviates signs.

Current genetic understanding is an autosomal dominant with variable penetrance. The current SAS research in goldens and Rottweilers (chromosome identified but WGS needed), and additional mapping is needed in Dogue de Bordeaux, bull mastiff, Bouvier and Bull terrier.

In Inheritied acquired heart disease Myxomaous Mitral Valve Degeneration (also called mitral valve endocardiosis and mitral valve diseae) is the #1 heart disease

seen. This is similar to mitral valve prolapse in people. It is commonly seen in all breeds, but especially smaller breeds of dogs. The Cavalier King Charles Spaniel is highly over represented. In fact current genetic studies want sample from those CKCS over ten years old without a murmur. To date there have only been 3 normal in 100's of CKCS, considering that this is possibly a fixed trait. More funding and continued research is necessary to move this project forward. In addition Whippet is overrepresented too and there is currently and AKC CHF genetic WGS study underway.

15. Evidence-Based Recommendation for Reduction of Infectious Disease in Canine Group Settings
Jason Stull, VMD MPVM PhD DACVMP

It only takes one individual to cause a disease outbreak. He researched 43 canine pathogens (12 viruses), bacteria (14), parasitic (13), mycotic (1), and emerging (3 which includes flu. Cornell is currently doing flu work on current outbreaks)

The key concepts in these preliminary drat recommendations are presented here.

Topics that must be taken into consideration:

1. Risk is not uniform for an individual dog or event
2. Pathogens vary (route, spread, severity, environmental stability)
3. Practices and policies can limit introduction and spread

Ten Recommendation Areas and he expect to be published in the next couple months:

1. General: having a vet involved, enforcing and informing that only well dogs are invited
2. Vaccinations (see AAHA core and non-core), verify that vaccines were given at least 1-2 weeks prior)
3. Pest and Wildlife control (remove their feces, remove garbage and organic debris)
4. Vector and vector-borne disease (see CAPC) integrated pest management (monitor individuals and groups, as well as control the environment)
5. Gastro-intestinal disease (pick up stools, raw diet pathogens)
6. Environmental disinfection/hygiene (use cleanable material, hand hygiene, bathe)
7. Decrease dog-to-dog contact (examples at doggie day care have small, permanent groups)
8. Facility design and traffic control (isolation has no traffic)
9. Exclusion (two week isolation period)
10. Recognizing and controlling outbreaks (surveillance programs, record keeping, monitoring, and outbreak management)

See: http://go.osu.edu/prevent_K9_disease

16. Be Very, Very Quiet..I'm Hunting Brucellosis
Matthew Krecic DVM MS MBA DACVIM

Brucella in dogs, is most commonly B. canis although dogs are also subseptible to B. aborus (bovine) and B. suis (porcine). Brucella is intracellular making it impossible to cure. It is zoonotic (humans can be infected) and reportable to some states. The signs vary from none to reproductive failures or back pain. Unfortunately it lives through frozen semen.

Brucella is a worldwide disease, and common in the US. A survey in southern US found 8% of strays were seropositive for brucella and it is likely highly under reported. There is no prevention or cure. Purdue University is developing a Center for Animal Welfare Science to research and give guidelines to commercial breeders. Ohio passed a Commercial Dog breeding act in 2012 defining high volume breeders (>9 litters/year or >60 puppies/year) and requiring them to test all breeding dogs, and that they test negative to B. canis.

Brucellosis testing is currently recommended by AKC and Society of theriogenology (see the SFT position statement: http://sft.site-ym.com/?page=PositionStatement). It is recommended to test breeding males and females every 6 months, or prior to every breeding. When bringing in new breeding animals to a kennel, test prior, keep isolated for one month and retest to assure still negative before co-mingling,

No test is 100%, and current tests include:
1. Rapid Slide Agglutination (zoetis makes an inhouse kit)
2. IFA- looks for antibodies (most common commercial lab screening test)
3. PCR looks for any DNA of the brucella
4. Tube agglutination looks for antibodies
5. AGID only currently done at Cornell and looks for antibodies. Do this test if screening test is positive (although check with your state veterinarian if reportable).
6. Blood or tissue culture is the gold standard but is difficult to culture and is infectious to humans.

17. Can We Predict Cranial Cruciate Ligament Disease (CCLD) in Dogs?
Dominique Griffon DMV MS PhD DECVS DACVS

A large-scale multi-centric study has just been completed to validate the ability of this equation to predict the status of Labrador Retrievers with or without CCLD. A study out of Illinois estimated that 6% of labs will be affected. In addition, 40% of all dogs that are affected in one leg will also become affected in the other. In her study non-invasive measurements were made on normal and affected dogs using exams, radiographs, and CT. Three muscles were measured, bone angles measured (tibial plateau angle and femoral anteversion angle) as well as fat to muscle ratio calculated. Fat content had a high predictor value but unfortunately is not useful in a clinical setting.

It's long been known that women athletes are predisposed to ACL injury due to an imbalance of hamstring muscle to extensors, and that neuromuscular training can decrease the risk by 80%. This study found that risk of CCLD increased with: Increased gastrocnemius (calf) muscle>Increased standing hock angle> increased the energy on the hock and stifle>increased the extensor muscle on the hock. An equation was created and validated. This formula provided good specificity (92%) to predict if the other leg would be affected but needed to improve sensitivity (73%). That is it labeled some dogs at risk that shouldn't be.

18. Canine Degenerative Myelopathy (DM)
Joan Coates DVM MS DACVIM

This session covered canine degenerative myelopathy as a disease model for translation of therapeutic strategies to amyotrophic lateral sclerosis (Lou Gehrig's Disease). DM is caused by a gene mutation SOD1 (which is a common enzyme in the central nervous system to remove free radicals). The gene is autosomal recessive with age related incomplete penetrance, and it is suspected to have modifying genes. There has been a second gene found in Burmese Mountain Dogs. This causes a degeneration of the spinal cord with distinct histopathology. It generally affects older dogs and within one year they are non-ambulatory. It is a diagnosis of exclusion (normal MRI, normal spinal fluid analysis, and electromyography is normal early in the disease). There is some look at pNFH protein in the spinal fluid as a marker of nerve degeneration. The current test for SOD1 done at her lab indicates susceptibility or at risk. Homozygous dogs are at risk but this does not mean that they will all become affected. Dogs that are heterozygous are carriers and less likely to develop signs, and normal are unlikely to develop signs and will pass on a normal protective allele to their offspring.

Stages:

1. Early in the disease there is upper motor neuron (UMN) ataxia (spastic) of the pelvic limb, decreased propioception and sensory, yet no pain. Signs initially are often asymmetric. A neurologic exam will localize it to T-L location at this stage.

2. Non-ambulatory pelvis

3. Forelegs affected and urine/fecal incontinence. It's at this time it goes from an UMN disease to lower motor neuron disease (LMN) with flaccid and severe muscle atrophy

4. Loss of breathing, swollen legs and flaccid tetraparesis. Natural death is from loss of respiratory ability.

The prognosis is poor and treatment has consisted of physical therapy and a cart. Novel treatment strategies are being looked at. Dr Miller at Washington is looking at knocking down the proteins produced by SOD1 (RNA repression), which at this time

given SQ in rodents has slowed the progression. There is currently a NIH grant evaluating safety, and an AKC CHF small clinical trial (12 dogs double blinded).

19. Update on the Latest Canine Epilepsy Research Developments: Genetics, Drugs and EEG's
Ned Patterson DMV PhD

Treatment:

1. Drug: although 20-30% are refractory in canine and humans
phenobarbitol (20-30% serious liver issues, pu/pd (drink and urinate excessively), increase appetite and weight gain)
KBr (potassium bromide) also pu/pd, increase appetite and sedation
Zonisamide (zonegran)
Levetiracetam(Keppra)
Others: Felbamate
Topiramate- another AKC CHF grant found this drug to be safe, well tolerated and effective in status epileptiicus. Although more studies need to be done it looks promising, including a potential for IM use. It is not currently available in the US.
Gabapentin
Fosphenytoid used in humans but short acting (half-life of 3hrs) in dogs. Is being studied with an NIH grant.

Status Epilepticus is a state where seizures continue one after another and has 30-40% mortality. Dogs need immediate veterinary care. They are first give diazepam IV if not better, then phenobarbitol or levetiracetam IV (20mg/kg IV), and finally if not better, general anesthesia. Although no study has been done to determine the best action after diazepam.

2. Surgically remove the seizure focus

3. Vegal nerve stimulators (NC State 50% improved when used on dogs already on two or more medications) and medial bionics are looking at an EEG to alert you when a seizure will happen.

4. ketogenic diets and specific fatty acids (next lecture)

His current AKC CHF grant was to identify genetic variants associated with epilepsy in Aussies and Vizslas and begin initial development of a genetic screening test, and to identify genetic variants associated with drug-resistant epilepsy in Aussies and Vizslas. No genes have been identified, and like hip dysplasia is likely polygenetic. So they have also been looking at microRNA (affects gene regulation by binding to RNA and preventing production of it's protein) and microRNA may serve as a useful biomarker. More studies need to be done.

20. Nutritional Management of Canine Epilepsy
Holger Volk DVM PhD DipECVN MRCVS FHEA

Epilepsy is not one disease but has many factors (genetic, environment) and possible etiologies. Everybody has a seizure threshold in which a seizure is triggered. By modifying the environment there is the potential to improve seizure control. Diets have been looked into.

1. Hypoallergic diet

2. Omega 3 Fatty Acids have been studied in humans with conflicting results

3. Ketogenic diets: high fat and low protein and carbohydrates (3:1) has good efficacy in humans. Neurons function on ketones, but glial cells that trigger seizures use glucose. Dr Patterson's study showed no benefit in dogs.

4. Medium Chain Triglycerides (MCT) like in cognitive dysfunction. A London study looked into a ketogenic diet with MCT in a randomized, crossover trial of poorly controlled seizure dogs while continuing their medication. The results are still being analyzed but results subjectively are looking good. In addition the MCT's work quickly with 3/21 seizure free, 7/21 > 50% seizure reduction, 5/21 reduction and 6/21 no response. Therapeutic blood levels (of whatever the patient was one) were monitored before and after the diet and showed no change.

5. Canapanoids are starting to be studied, some benefit seen with THC but not great

A great smart phone App is the Pet Epilepsy Tracker by the Royal Veterinary College: for more information www.rvcpetepilepsytracker.co.uk

21. Cancer Research- how you can help: see www.modianolab.org/studyinfo/Breen_LabStudies.shtml has links to these three researchers

Dr. Kersin Lindblad-Toh (The Broad Inst) is banking cancer and DNA. They are currently studing osteosarcoma mutations (greyhound, Rotts and Irish setters), Lymphoma and hemagiosarcoma in goldens and hemangiosarcoma in other breeds. They want to develop a Canine Cancer Genome Atlas to mimic the same that is being attempted in humans. This is a huge task.

Dr Breen at NC state (breenlab.org) is currently accepting sample and doing a lot of genetic research. Most submissions of samples require submission in their special medium, although they are developing a test to work on formalin samples.

Tests soon to be released:
1. cytogenetic test on free catch urine that has >99% sensitivity to detect bladder cancer, three months prior to signs. It appears to be working in humans too, and can

detect 85% of all bladder cancers. These cancers contain the genetic material it is detecting from the most common type of bladder cancer.

2. A cytogenetic test to predict with >90% accuracy how lymphoma will respond to standard CHOP or doxyrubacin therapy,. The test is also working in humans.

3. A cytogenetic assay to identify>96% of histiocytic neoplasia from other round cell cancers. Histopathology often misdiagnoseds as lymphoma. The dog test is due out in 2015, and the human version is being tested
.
4. Genetic assay to identify risks in Goldens of lymphoma or hemangiosarcoma (has been published in PLOS genetics). This test is not designed cause an over reaction by breeders and pull all these dogs from the breeding population, but to make educated breeding decisions.

Dr Jaime Modinao (Minnesota): www.modianolab.org
Studying a variety of cancers with Breen lab and accepting samples, see website
Also studying hemagniosarcoma and circulating tumor cells and treatment
Another study has bioengineered a drug with 2 tumor targeting elements linked to a lethal bacterial toxin so that they attack the tumor micoenvironment and cancer with no effects elsewhere in the body.

There genetic research in cancer is exploding and I applaud anyone who can look above the pain of their loss of a pet to submit samples to these researchers.