



**2006 Canine Health Foundation  
National Parent Club Canine Health  
Conference**

*Proceedings and Summary*



## The Story So Far

### **The Canine Health Foundation**

- Founded in 1995
- \$15 million in research grants
- Sixth biennial Parent Club Conference
- Research network from Netherlands to California
- Mission: *To develop significant resources for basic and applied health programs with emphasis on canine genetics to improve the quality of life for dogs and their owners.*



•Thank you very much for the opportunity to join you today. I'm here with some important news from the American Kennel Club Canine Health Foundation, based largely on research results presented at the Sixth Biennial Parent Club Conference in St. Louis late last year (October 21-23, 2005).

•As you see on this slide, CHF was founded in 1995, and has established itself as "the largest non-profit funder of exclusively canine health research in the world."

•The Foundation has established a research network that stretches from The Netherlands to California, and has distributed more than \$15 million in research grants.

•***As you'll see, that success depends on the commitment of club members like you. And there is still a great deal more to be done.***



## The Story So Far

### **Alliances Make It Possible**

- American Kennel Club
- Nestlé Purina PetCare Company
- Canine Health Information Center (CHIC)
- Orthopedic Foundation for Animals



\* Before I get to the details, we know that nothing happens these days without strong, productive alliances. And we know the progress we've made in canine health research would not have been possible without the enthusiastic support of the American Kennel Club, the Canine Health Information Center, the Orthopedic Foundation for Animals, and Nestlé Purina PetCare Company.



## The Story So Far

# The 2005 Parent Club Conference

- Sequencing of the canine genome
  - A huge opportunity to move forward
  - They said it couldn't be done...
  - Complete sequence released in December 2005
- Donations have never mattered more
- Other ways for clubs, individuals to help
  - Send samples (*but check first!*)
  - Conduct health surveys
  - Raise awareness



- The big news in St. Louis was that researchers have finished the job of sequencing the canine genome.
- The complete sequence was published in *Nature* magazine late last year. Concurrent with that publication, Cold Spring Harbor Laboratory Press released a book entitled *The Dog and Its Genome*.
- This was an incredibly ambitious project. And when CHF researchers first took it on, there was a fair bit of skepticism about whether it would succeed.
- But the work is complete, and the 2005 Parent Club Conference heard some wonderful examples of genetic research that is helping our dogs live longer, happier, healthier lives.
- And it may surprise you that canine genetics is delivering important benefits for human health research, as well.
- It all adds up to an increasingly important role for breed clubs as the organizations that collect blood and tissue samples, conduct health surveys, and raise awareness among breeders and owners.
- And, of course, your generous donations have never mattered more.



## The Story So Far

### **AKC CHF Research Grants**

- Biennial survey identifies five top health concerns
  - Last survey: Cancer, eye disease, epilepsy, hip dysplasia, thyroid disease
- RFP to 2,500 researchers world-wide
- Peer review
- Funding so far: More than 50 institutions in eight countries
- ACORN grants: up to one year, \$12,000



- The results reported in St. Louis were the end result of a steady stream of CHF-funded research grants.
- The Foundation conducts a biennial survey to identify the five top health concerns across all breeds.
  - Results of the last survey: Cancer, eye disease, epilepsy, hip dysplasia, thyroid disease
- Each year, a request for pre-proposal is sent to more than 2,500 qualified researchers around the world
  - Their responses are sent to a review committee that consists of veterinarians, medical doctors, and CHF staff
  - Full applications are sent to four subject specialists for peer review.
  - To date, the CHF has distributed funding to more than 50 research institutions in eight countries.
- CHF also offers small grants that we call ACORNs. They provide up to \$12,000 for researchers who want to test an idea, generate preliminary data, or complete a small project that runs no more than a year.
  - Projects can include clinical or laboratory studies.
  - The Foundation does try to balance the ACORN grants it approves for testing versus treatment.



## 'The Next Big Thing' Is Now

# Sequencing the Canine Genome

- Human health benefits from canine research
  - Parallels between canine, human diseases
  - Closer match to humans than traditional research species
  - Detailed pedigrees lead to quicker results
- Dogs benefit from human health funding



## 'The Next Big Thing' Is Now

- Again and again, conference attendees heard about important parallels between diseases in dogs and in humans.
- The canine genome project showed that the canine and human genetic maps are about 90% similar.
- That means dogs are a closer match for human health research than some of the traditional research species like mice and rats.
- Because breed clubs keep such detailed, meticulous records, we often have the pedigrees that researchers need to trace genetic differences and abnormalities back three generations or more.
- And it turns out that research with client-owned dogs is more effective than studies involving lab animals, since the dogs are less stressed and the cost of care is much lower.
- The end result: Human health agencies are turning to our dogs as a great source of information for their research.
  - Which means an important new source of funding for research on canine disease.



**'The Next Big Thing' Is Now**

## **Sequencing the Canine Genome**

*“The idea is to approach breeds that have dogs that are of interest, and to use free living dogs” for the research. This avoids ethical concerns and costs less than working with laboratory mice.*

*-- Karl Lark, PhD*



Dr. Karl Lark is a soybean geneticist who became interested in canine health research following the death of his Portuguese Water Dog, Georgie, in 1996. He told the conference...

“...One of the points we wanted to prove was that in fact it can be done. The idea is to approach genetic isolates, breeds that have dogs that are of interest, and to use free living dogs” for the research. That means working with dogs who are very much alive, and living with their owners. The approach avoids the ethical, humane, and cost considerations surrounding captive dogs, and turns out to be less expensive than working with mouse colonies in laboratories.



## 'The Next Big Thing' Is Now

# Case Study

## *The Portuguese Water Dog*

- The ideal research subject
  - Small population
  - Excellent pedigree records
  - 30 founders
  - 10 responsible for 90% of the gene pool
- Closer attention from corporate sponsors, NIH
- **Everybody wins**



•Dr. Lark didn't realize it until Georgie died, but the Portuguese Water Dog is an ideal subject for genetic research.

- The breed is small, with a total population of 9,000 to 10,000.

- Breeders have kept excellent pedigree records.

- The breed began with about 30 dogs, and 10 of those accounted for 90% of the present-day gene pool.

•So far, the Georgie Project has enrolled more than 1,100 dogs, and holds 900 DNA samples and 550 x-rays.

- Owners who supply blood samples now will also be asked to agree to autopsies when their dogs die.

- The database is being used to study two hereditary diseases that are relatively simple genetically: progressive retinal atrophy, and cardiomyopathy.

- With the sequencing of the canine genome, researchers have identified the genes that control the water dog's size and shape, and there is interest in studying more complex diseases that depend on multiple genes...like cancer, osteoarthritis, and the kind of autoimmune disease that took Georgie's life.

•With corporate sponsors and the National Institutes of Health paying closer attention to dogs, we're looking at a situation where everyone wins:

- Human health researchers and the patients they're trying to help

- Canine health researchers

- Owners who want their dogs to live longer, healthier lives

- ...and of course, the dogs themselves.

•And here's why... [next slide]



'The Next Big Thing' Is Now

## Sequencing the Canine Genome

*"The dog has a much closer genome to the human. More than 300 human genetic diseases are found in dogs. The different breeds are genetic isolates, so they're very important and very hard to find in humans."*

*-- Karl Lark, PhD*



•We've already identified more than 300 hereditary diseases that affect humans and dogs. When we say that different breeds are "genetic isolates," it means we know how to differentiate one breed from another at the level of genes and chromosomes – and those differences are making it possible to identify the genes that make a dog or a person more susceptible to a particular kind of disease.



'The Next Big Thing' Is Now

## Sequencing the Canine Genome

*"People are mutts," and flagging heritable risk factors is less straightforward in human research "because of the genetic background of cross-breeding that we have."*

*-- Dr. Jaime Modiano*



Dr. Jaime Modiano of the University of Colorado Health Sciences Center explained it a different way. But the message was the same: It makes sense to rely on purebred dogs with well-known pedigrees to track the genetic basis of disease.



'The Next Big Thing' Is Now

## Sequencing the Canine Genome

*“The real bottleneck now is getting samples, and samples that are accurately characterized. The rest is easier than it used to be.”*

*-- Kerstin Lindblad-Toh, PhD*



•So now that we've established the link between canine and human genetics, the main challenge is logistics. We'll hear more later about the process of gathering and submitting samples. But now that the basic science is well established, Dr. Kerstin Lindblad-Toh of the Broad Institute at Massachusetts Institute of Technology and Harvard University said it's all about the practicalities.



## Major Findings

### ***Results on the Horizon***

- Canine cancer
- Neuronal ceroid lipofuscinosis (NCL) and Batten's disease
- Stem cells: Mending heart failure
- Epilepsy and canine neurologic disease



## Major Findings

- Medical conferences are all about presenting the latest scientific findings, and the 2005 Parent Club Conference was no exception. For a full weekend in October, participants from across the country heard back-to-back presentations on the most important diseases affecting our canine friends...and on research results that will help them live longer, healthier lives.
- Some of the most exciting results had to do with:
  - Canine cancer
  - The genetic link between neuronal ceroid lipofuscinosis (which is why we will now refer to it as "NCL") in dogs and Batten's disease in children
  - The possibility of using stem cells to literally mend a broken heart, and
  - Epilepsy and other neurological diseases of dogs.

## Major Findings

# Canine Cancer

- Most serious canine disease
- Primary tumors often metastasize before they are diagnosed
- Human genome: 27,000 cancer-related aberrations
- Canine genome: Chromosomes harder to identify, but five linked to non-Hodgkins lymphoma



- Canine cancer research is relatively new. Dr. Jaime Modiano reported that most of the major advances in canine cancer over the past three or four decades have come from human research, but the information flow has reversed in the last two or three years: now we're studying disease in dogs first, for their own benefit and for the lessons we can learn for humans.
- One of the wonderful aspects of canine cancer research is that it often benefits children who are diagnosed with cancer at a very early age.
- But cancer is known to be a genetic disease, and it's also the most serious canine disease. It's that much more so because it's so insidious: too often, the cancer has spread by the time a primary tumor is diagnosed, and at that point it's often too late to save the dog's life.
- Dr. Matthew Breen of North Carolina State University explained the genetic basis for cancer.
  - He described chromosomes as a "biological filing cabinet" into which DNA is organized.
  - If you think of your own filing cabinet...or your email in box...it won't surprise you that genes sometimes get misfiled. And over the past 25 years, human health researchers have identified about 27,000 of these aberrations that can lead to cancer.
  - The aberrations matter because our genes have evolved in a way that enables them to exist and function normally if they're located in the right place on the right chromosome. When they relocate, they may end up interacting with other genes in a way that causes the uncontrolled cell growth that we know as cancer.
- That's what we know from human research. Canine cancer has been harder to study, for a couple of reasons.
  - Dogs have 78 chromosomes, compared to 46 in humans.
  - And the chromosomes are smaller, which makes them harder to work with when they're normal, harder still when we're trying to track aberrations.
- But researchers have identified five specific chromosomes in dogs that are linked to non-Hodgkins lymphoma, one of the top three canine cancers.

## Major Findings

# Canine Cancer

## *Non-Hodgkins Lymphoma*

- Lifetime risk of 1:10 to 1:20 in dogs, 1:50 in humans
- One-year canine survival rate: 55%
- Breeds at highest risk
  - Boxers, Goldens, Labradors, Scottish Terriers, Basset Hounds, Saint Bernards, Dobermans
  - All middle-aged dogs
- Specific genes: A work in progress



•Dr. Modiano has been doing specific research on non-Hodgkins lymphoma. As you can see on the slide, dogs carry a higher lifetime risk of this disease than humans, and just over half of them survive a year after diagnosis.

•There are two types of non-Hodgkins lymphoma – B-cell and T-cell. For many years, cancer practitioners believed there was no such thing as a good lymphoma – if B was bad, T was terrible.

•But Dr. Breen talked about one dog that had been diagnosed with T-cell lymphoma in 2001 and survived four years after conventional chemotherapy. Cancer specialists used to think that was impossible.

•Dr. Modiano said 60% of dogs with cancer have B-cell lymphoma, 35% have T-cell, and the rest are unidentified. T-cell cancers are more common in younger dogs and older breeds; B-cell tumors seem to show up more often in older dogs and more recent European breeds.

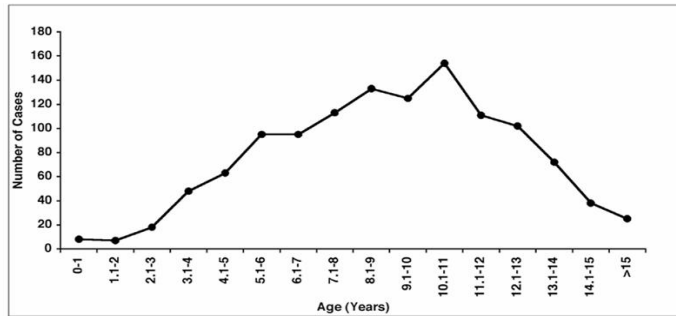
•There are differences in humans, as well – for example, Caucasians have more T-cell cancers than Asians.

•Researchers are still working to identify the specific genes involved, but Dr. Breen's research team has found a specific genetic aberration that may be linked to B-cell tumors in Golden Retrievers...and they think they may have identified the parallel gene in humans.

Major Findings

## Canine Cancer

### *Lymphoproliferative Disease and Age*



Here's another look at the age distribution of *lymphoproliferative disease*, a broad category that includes Hodgkin's and non-Hodgkin's lymphoma. This graph is courtesy of Dr. Modiano. It shows that the number of cases begins to spike around the age of three, reaches a maximum around age 10, then begins to decline.

## Major Findings

# Canine Cancer

## *Prevention and Treatment*

- Dogs and humans: Similar incidence, age of onset, location, progression, outcome
- Shared environment, shared susceptibility
- Canine cancer on the rise
  - Environmental factors?
  - Longer lifespans?
- *'Life is the single highest risk factor...'*



- Although cancer treatment is a top priority in human health research, there is also a great deal of interest in cancer prevention. The same applies to dogs.
- You've already heard that dogs and people have similar types of cancer. Dr. Modiano said there are also comparable histories of incidence, age of onset, location, progression, and outcome.
- And because pet dogs share our environment, it's possible that we're exposed to the same cancer risk factors.
- Some people believe the increase in canine cancer is linked to environmental pollutants or commercial products. It may also be that dogs are simply living longer, now that parvovirus and other preventable diseases are under control. For dogs or humans, Dr. Modiano commented that "life is the single highest risk factor for cancer."



## Major Findings

# Working with Cancer Researchers

Elaine Ostrander, PhD  
NHGRI/NIH  
Building 50  
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Bethesda MD 20892  
Eostrander@mail.nih.gov

Sample Coordinator:  
Dana Mosher  
301-451-9390  
Mosherd@mail.nih.gov  
*(DNA samples only)*

Kerstin Lindblad-Toh, PhD  
Broad Institute of Harvard and MIT  
320 Charles Street  
Cambridge, MA 02141  
Kersli@broad.mit.edu

Sample Coordinator:  
Joanne Lai  
Dog-info@broad.mit.edu  
www.broad.mit.edu/mammals/dog/  
*(DNA samples only)*



•One of the recurring questions at the conference was how best to send blood and tissue samples to the researchers who need them for canine health research. Here is the contact information for Dr. Elaine Ostrander, Dr. Kerstin Lindblad-Toh, Dr. Jaime Modiano, and Dr. Matthew Breen.

•<next slide>



## Major Findings

# Working with Cancer Researchers

Jaime Modiano, VMD, PhD  
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Health Sciences Center  
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Denver, CO 80214  
Jaime.Modiano@UCHSC.edu

Samples to:  
Cristan Jubala  
303-239-3327  
Info@modiolab.org

***(blood or tissue samples; please  
contact before sending!)***

Matthew Breen PhD  
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North Carolina State University  
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Rm. 348 CVM Research Building)  
Raleigh, NC 27606  
Cvm\_K9genomics@ncsu.edu

***(blood or tissue samples; please  
contact before sending)***



## Major Findings

# Canine Cancer

## ***Proper procedures matter!***

- *Work with sample coordinators*
- Match available sample to current need
- Send samples *quickly*
- Send reference samples from older, unaffected dogs
- Pay attention to waiver provisions
- *Fill out consent forms in full*



•I told you earlier that I would have more to say about the proper procedures for sending samples to researchers.

•You don't want to waste the time, effort, and money that you put in to send a blood or tissue sample. So it is *very important that you keep in touch with the sample coordinators* for the four labs. Different research groups can use different types of samples at different times, depending on the studies in which they're involved. You should talk to the coordinators before you collect a sample.

•Right now, the Ostrander and Lindblad-Toh labs are accepting blood samples only. The Modiano and Breen labs are interested in both blood and tissue.

•We'll circulate the two previous slides at the end of this talk.

•It's important to send samples very quickly, by courier, to make sure they're fresh when they reach the lab.

•The researchers need samples from sick dogs, but they're also interested in reference samples from older, healthy dogs.

•Please, please remember that the paperwork is important. Each lab has a slightly different waiver form, so you have to read each one carefully, make sure you agree with its provisions, and follow the instructions. Consent forms have to be filled out in full.



## Major Findings

# **Canine Cancer**

## ***Mark your calendar!***

AKC CHF Canine Cancer Conference  
Chicago, IL  
September 15-17, 2006

*More information: [www.akcCHF.org](http://www.akcCHF.org)*



- And mark your calendar for September 2006. That's when the Canine Health Foundation will be hosting a canine cancer conference in Chicago. You'll find details on the Foundation website in the next couple of months.

## Major Findings

# Neuronal Ceroid Lipofuscinosis (NCL)

- Multiple breeds
- Linked to Batten's disease in humans
- Major symptoms: Mobility problems, dementia, blindness
- Benefits of canine research: 30 generations of DNA, shorter breeding cycle
- Tests show fluorescent yellow material in cerebellum, retina



•Beyond cancer, the next genetic disease that received a lot of attention at the Parent Club Conference was neuronal ceroid lipofuscinosis. For your sake and mine, I'm going to refer to it as NCL.

•NCL is not hugely prevalent, but we can learn a lot from the way research on this disease has been carried out, and from the way dog and human research interests came together.

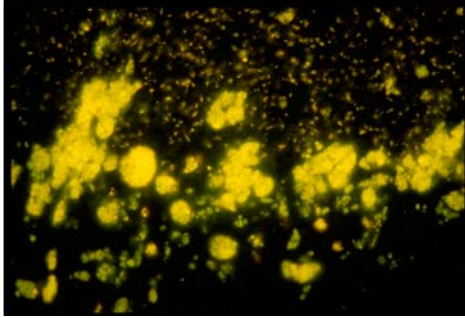
•NCL is a disease of particular interest to the Tibetan Terrier Club of America, but it appears in a number of different breeds.

- A terminal disease of the nervous system.
- Appears late in life.
- Characterized by mobility problems, dementia, and blindness.
- Genetically linked to Batten's disease in humans, a tragic and incurable disease that strikes children, takes away their abilities, and eventually takes their lives.

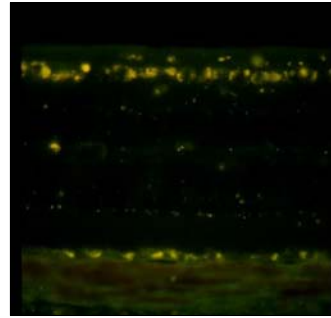
•It's characterized by an accumulation of cells that show up fluorescent yellow under ultraviolet light...<next slide>

Major Findings

## Neuronal Ceroid Lipofuscinosis (NCL)



Cerebellum



Retina



...and block the normal functioning of the cerebellum and the retina. This is actually a very disturbing picture for anyone who knows the science of NCL.

- NCL was initially confused with progressive retinal atrophy.
  - But when the Tibetan Terrier Club held its world congress a couple of years ago, the audience included parents of children with Batten's.
  - The two groups began comparing notes, and now they're working together to find a genetic marker for the two diseases.
  - So far, researchers have identified nine candidate genes in dogs, and six in humans.
  - They haven't found a match yet, but they aren't giving up.

## Major Findings

# Stem Cells

## *Mending heart disease*

- *'The body's innate repair tool'*
- Two key characteristics
  - Self-renewing
  - Able to differentiate
- Clinical treatments 10 to 15 years away
- Human health results apply to dogs, too



- Stem cell research is one of the hottest areas of medical science.
  - You might have heard the recent reports of fraudulent research at a stem cell lab in Korea, but it seems unlikely that one setback will be enough to derail an extremely important field of study.
- At the conference, Dr. Doris Taylor of the University of Minnesota described stem cells as “the body’s innate repair tool.”
  - She said aging essentially amounts to a failure of stem cells...
  - ...and that the use of stem cells for cardiac and vascular repair in dogs and humans is no longer a matter of “if”. The only question is “when”.
  - Clinical treatments are likely 10 to 15 years away.
- The two most important characteristics of stem cells is that they can renew themselves, and they can match the characteristics of the different cells with which they come into contact.
  - A stem cell injected into a vein will help rebuild the vein.
  - Injected into a heart, it will help build heart tissue.
- And here, again, this is an area where human health research can benefit dogs, and vice versa.

## Major Findings

# Stem Cells

## *Mending heart disease*

- Progression of heart disease
  - Inflammatory response may be a first sign
  - Scarring of the heart
  - Heart can't compensate; cells fail
- Cell therapy for damaged hearts
  - Dosage rates matter
  - A measure of success: Ability to pump blood



- Our organs and tissues are constantly repairing themselves, and stem cells make that possible.
  - For heart disease or any other condition, Dr. Taylor said an inflammatory response may be the first sign that stem cells are needed.
  - In heart disease, the muscle becomes scarred, and if the scarring becomes bad enough, the cells begin to fail.
- Cell and gene therapies are already available.
- In future, clinicians will try to prevent heart disease by growing new blood vessels, and eventually by growing new heart cells.
- Dr. Taylor's lab has been transplanting cells into damaged hearts since 1989. They aren't transplanting stem cells, but using immature muscle cells called myoblasts.
  - Research began with rabbits.
  - By 1998, the team had shown that it could thicken the myocardial wall and improve heart function.
  - Higher doses of 100 million cells produced the best results.
  - Human clinical trials opened in 2000.
- The success of cardiac therapy can be measured by the heart's ability to pump blood.
  - A normal heart pumps out 50-65% of ventricular blood with each beat.
  - Patients with heart failure may be in the range of 24%.
  - Rate improves to 32% following cell therapy.

## Major Findings

### **Canine Neurologic Diseases**

- *'Striking at the essence of the animal'*
- Help is on the way for...
  - Movement disorders
  - Epilepsy/storage diseases
  - Degenerative myelopathy



•Dr. Dennis O'Brien of the University of Missouri commented that epilepsy and canine neurologic disease “strike at the essence of the animal: their mobility, personality, and ability to learn, remember, and interact with their family, and may take away life itself.”

•He said the canine genome project and other advances in molecular genetics will help researchers address some of the key neurologic diseases in dogs, including movement disorders, epilepsy and other storage diseases, and degenerative myelopathy.

## Major Findings

# Canine Neurologic Diseases

## *Movement disorders*

- Cerebellar ataxia
  - DNA marker found in English Pointers
  - Staffordshire Bull Terrier research may help Old English Sheepdogs
- Progressive Neuronal Abiotrophy
  - Common in Kerry Blues, in Chinese Crested
  - Possible similarity to Parkinson's in humans



•The first of the movement disorders is cerebellar ataxia. Research so far has generated mixed results.

•In the early 1990s, Dr. O'Brien's lab found a DNA marker for English Pointers within a year.

•Subsequent research with Old English Sheepdogs was unsuccessful.

•The team is now conducting DNA studies with Staffordshire Bull Terriers, and is hoping the results will help Old English Sheepdogs, as well.

•Progressive neuronal abiotrophy is similar to cerebellar ataxia.

•Also known as Multiple System Degeneration (MSD).

•Common in Kerry Blue Terriers, Chinese Crested Dogs.

•Appears at three to four months of age.

•Characterized by exaggerated movements, immobility and falls at eight to 10 months of age, death within two years.

•May be genetically similar to Parkinson's disease in humans.

## Major Findings

# Canine Neurologic Diseases

## *Epilepsy/storage disorders*

- Cases in miniature wirehaired Dachshunds linked to a form of human epilepsy
- Storage disorder symptoms linked to abnormal accumulation in brain: Seizures, generalized weakness, blindness
- Neonatal encephalopathy in Standard Poodle
- “Chinook seizure”
- Link to NCL in sheep and mice



•Turning to epilepsy and storage disorders: Research has also found a genetic link between epilepsy in miniature wirehaired Dachshunds and Lafora’s disease, a form of human epilepsy.

•Both are storage diseases in which an accumulation of abnormal material in brain cells leads to seizures, generalized weakness, and blindness.

•Researchers are well on the way to isolating the gene for a form of neonatal encephalopathy that may kill up to 25% of the puppies in a litter of standard poodles.

•DNA research is under way to address a form of “Chinook seizure” in which dogs are aware of their surroundings, but experience tremors, rhythmic leg movements, and immobility.

•We talked earlier about neuronal ceroid lipofuscinosis (and I remember promising to refer to it as NCL).

•Researchers have also been looking at a storage disease that causes weakness and loss of coordination in American Bulldogs.

•Linked to the gene that causes NCL in sheep and mice.

## Major Findings

# Canine Neurologic Diseases

## *Degenerative myelopathy*

- Begins at age eight or nine
- Poor coordination leads to paralysis, spinal degeneration
- Current and pending studies involve German Shepherds, Corgis
- Existence and characterization of disease is controversial; causes are under study
- *Solid evidence is needed*



- Dr. O'Brien also talked about degenerative myelopathy.
  - An example of a disease where research is still at a very basic level, since not all neurologists agree that it even exists; neither has the disease been well characterized enough to be accurately diagnosed.
  - Age of onset: Eight or nine
  - Begins with poor coordination, leading to paralysis and spinal degeneration
  - Researchers are studying the disease in German Shepherds and Corgis.
- To prove the existence of degenerative myelopathy, it will be necessary to gather spinal cords post-mortem, so that pathologists can document the changes that have occurred.
  - This raises an issue that came up repeatedly during the conference: Heartbreaking as it is to give up a beloved companion for autopsy, it's important that owners take that step in the interest of furthering medical research and helping future generations of dogs live longer, happier, healthier lives.

## Major Findings

### ***Better Knowledge of Chronic Conditions***

- Diabetes
- Hypothyroidism
- Centronuclear myopathy
- Pancreatic acinar atrophy
- Dermatomyositis



•Beyond the most common acute diseases, the Parent Club Conference heard about new treatments for a variety of chronic conditions...including diabetes, hypothyroidism, centronuclear myopathy, pancreatic acinar atrophy, and dermatomyositis. <next slide>

## Major Findings

### ***Better Knowledge of Chronic Conditions***

- Nutrition and metabolism
  - Osteoarthritis
  - Protein metabolism
- Assisted reproduction
- Behavior and temperament
- Canine vaccination



•There were also presentations on dog nutrition and metabolism, assisted reproduction, behavior and temperament, and canine vaccination.

## Major Findings

# Diabetes

- High prevalence in dogs and humans
- Incidence has more than tripled since 1970
  - 50,000 amputations, 50,000 cases of blindness projected for 2005
- Many cases may go undiagnosed
- Susceptibility varies widely among breeds



- Dr. Thomas Graves of the University of Illinois talked about two disorders of the endocrine system, diabetes and hypothyroidism.
- As many of you know, diabetes is reaching epidemic proportions in dogs and humans.
  - The number of canine cases has tripled since 1970.
  - Veterinarians were projecting that diabetes would lead to 50,000 amputations and 50,000 cases of blindness in American dogs in 2005.
  - Symptoms of insulin-dependent diabetes include increased thirst, urination and appetite, weight loss, and cataracts.
  - As many as one-third of cases may go unreported.
- Any dog can get diabetes, but different breeds are more or less susceptible.
  - At one end of the spectrum, the odds ratio for Australian Terriers is more than 32:1.
  - For Boxers, it's only 0.07:1.

## Major Findings

# Hypothyroidism

- Commonly diagnosed...and misdiagnosed?
- Susceptible breeds: Golden Retrievers, Dobermans, Irish Setters, Miniature Schnauzers, Cocker Spaniels, Airedales
- Diagnosis more difficult in dogs than in humans
- Treatment without clear diagnosis may suppress pituitary, damage heart
- No value in routine or pro-active screening



•Hypothyroidism is the other major endocrine disorder in dogs, and here the situation may be a bit more complicated.

•A number of breeds are considered susceptible. But one of the key messages from Dr. Graves was that hypothyroid is often misdiagnosed.

•Clinical signs of hypothyroidism include lethargy, weight gain, dry hair or shedding, hair loss, anestrus, hyperpigmentation, cold intolerance, and low heart rates.

•But Dr. Graves said those signs are often misinterpreted in the absence of sound scientific proof.

•Part of the problem is that the standard tests for this disease are more difficult to interpret in dogs than in humans.

•Dr. Graves warned against treating hypothyroidism just because we think that *might* be the problem.

•The endocrine system is very complicated, with a lot of interactions among different hormones.

•So there are two problems with prescribing the wrong treatment:

•The right treatment for the wrong condition could suppress the normal functioning of the pituitary gland and damage the heart.

•The other risk is that a vet might stop diagnosing, so that a less obvious condition goes untreated and gets worse.

•Dr. Graves recommended against routine screening for hypothyroidism, since a positive test result might actually be a sign of some other disease.

## Major Findings

### **Centronuclear Myopathy**

- Previously known as muscular myopathy
- Prevalent in Labradors
- Clinical signs begin at one month of age
- Dogs can live 8.5 years and reproduce, but never regain mobility
- Carriers have included national winners
- Breeder awareness is crucial
- 'White list' identifies dogs with no predisposition



•Dr. Marilyn Fender of the University of Wisconsin talked about a new genetic test for muscular myopathy, or as it's now known, centronuclear myopathy. We'll just call it 'CNM'.

•The test is now being introduced internationally, and a major effort is under way to raise awareness among Labrador owners and breeders as well as their veterinarians.

•When CNM appears at one month of age, its symptoms include weight loss and an absence of tendon reflex.

•The disabling version appears at two to five months, and its signs include muscle weakness and reduced tolerance for exercise.

•The dogs can live 8½ years and pass on their genes, but they never regain mobility.

•Labrador CNM has become a major issue, in part, because a number of national winners have been carriers. This is one reason that Dr. Fender is putting so much emphasis on breed awareness, and on the development of a "white list" of dogs with no known predisposition to CNM.

## Major Findings

### **Pancreatic Acinar Atrophy**

- Degenerative disease of the pancreas
- Curtails enzymes required to digest food
- Prevalent in German Shepherds, Rough Collies
- Diagnostic test is 100% accurate
- Treatment is expensive, but 95% effective
- Late onset makes it impossible to identify carriers before they breed
- Researchers are seeking a molecular signpost



•Here's another disease that we're going to pronounce as an acronym. PAA is a disease that damages pancreatic cells and stops them from producing the enzymes that dogs need to digest their food.

•It is most prevalent in German Shepherds and Rough Collies.

•Its symptoms include weight loss, poor coat quality, and high fat content in fecal matter.

•Dr. Keith Murphy of Texas A&M University reported that the diagnostic test for PAA is 100% accurate, and 95% of dogs with PAA can be treated, though the treatments are expensive.

•A number of the German Shepherds in Dr. Murphy's studies came from the Department of Defense. One challenge is to keep up their enzyme treatments when they're in the field in places like Iraq and Afghanistan.

•PAA is caused by a recessive gene and begins fairly late in life, so carriers can't be identified before they breed. But Dr. Murphy and his team are closing in on a molecular signpost that will make it easier to track the problem earlier.

## Major Findings

### **Dermatomyositis**

- Degenerative skin and muscle disease
- Prevalent in Collies, less so in Shetland Sheepdogs
- Some similarity to muscular dystrophy
- Abnormal chromosome may be linked to merle coloring



- Dr. Murphy is also studying dermatomyositis, a degenerative skin and muscle disease that affects Collies, and to a lesser extent, Shetland Sheepdogs.
- The disease begins with crusting on the face and extremities.
- It's aggravated by stress, so the symptoms may tend to rise and fall.
- When it affects muscle function, it makes it difficult for the dog to eat, drink, and walk.
  - Muscle lesions can be serious enough that the dogs must be euthanized.
  - This occurs more frequently in Collies than in Shelties.
- It's similar enough to muscular dystrophy that the Muscular Dystrophy Association is taking an interest in Dr. Murphy's research.
- There is some possibility that dermatomyositis is linked to the genetic abnormality that causes merle coloring.
  - So this may be another case where a disease can be eliminated, but only at the expense of a truly lovely breed characteristic.

Major Findings

**Dermatomyositis**



Here are some photos of dermatomyositis, courtesy of Dr. Murphy...

## Major Findings

# Nutrition and Metabolism

## *Osteoarthritis*

- Most common joint disease in dogs and humans
- 20% prevalence, 70% in older dogs
- Nutritional approaches can manage obesity, reduce inflammation
- *'Humans are good research models for dogs'*



•Dr. Steven Hannah of Nestlé Purina PetCare talked about an approach to canine research that starts out with the whole dog, moves down to the clinical level of organs, tissues, and nutrients, then continues to the molecular level, before translating the results back up to the dog and the owner.

•He applied that approach to managing osteoarthritis, a joint disease that affects 20% of all dogs and 70% of older dogs.

- At the level of the whole dog, obesity is often a risk factor for osteoarthritis.

- At the level of organs and tissues, it occurs when the body loses its normal ability to repair and maintain cartilage.

- At the molecular level, an initial inflammation produces enzymes that break down the cartilage.

- Molecular nutrition can have an impact on the process.

•With that in mind, there are two main objectives for nutritional interventions:

- Reduce inflammation;

- Manage obesity.

•One participant asked whether there are correlations between humans and dogs in nutritional research, and you're going to love Dr. Hannah's answer. He commented that "humans are real good models for dogs, and I hope they do more human work."

## Major Findings

# Nutrition and Metabolism

## *Protein metabolism*

- Dogs need 20 different amino acids, 10 from diet
- Inadequate protein impairs growth
- Research supports low energy, moderate protein diet for large breed puppies
- High protein for older dogs supports lean muscle mass
- Severe calorie restriction reduces lean muscle



- Dr. Jill Cline from Nestlé Purina PetCare Research described the role of protein in dogs' daily diet.
- She warned that inadequate protein will impair a dog's proper growth.
  - There's an urban myth that low-protein diets will help prevent future skeletal problems in large breed puppies, but Dr. Cline said there's no truth to the rumor.
    - The latest research shows that large breed puppies should receive at least 25% of their calories from protein.
  - For older dogs, a high-protein diet will support lean muscle mass, while severe calorie restrictions will reduce lean muscle.

## Major Findings

### **Assisted Reproduction**

- Poor timing is still the biggest issue
- Two drug groups can manipulate the reproductive cycle
  - Drugs have pros and cons
  - Costs are high
- Embryo transfer: Careful synchronization, or larger breeding colonies
- Canine cloning: One clone required three years, 123 embryo transfers



- Dr. Frances Smith, President of the Orthopedic Foundation for Animals, talked about the different treatments available to assist canine reproduction. But she said the best strategy is still to get your timing right.
- Part of the difficulty is a uniquely long reproductive cycle in bitches. Reproductive science has made its greatest advances with species that cycle more frequently, like humans and cattle.
- There are two new classes of reproductive drugs, dopamine agonists and gonadatropin-releasing hormones.
  - Both can be used to manipulate the reproductive cycle, to schedule litters around national specialty events or hold off estrus for a long period of time.
  - But none of the drugs is approved for use in dogs.
  - The only one that is commercially available carries a warning that it may not be effective or safe.
  - And treatment costs range from \$130 to \$770 for a 70-pound dog, not including shipping and vet fees.
- Canine embryo transfer is another assisted reproduction option. But once again, success depends on careful timing, unless you've got a larger breeding colony with many bitches at different stages in the cycle.
- Canine cloning is on the horizon, but one successful clone in South Korea required three years, 123 attempts, and a great deal of money.

## Major Findings

### **Behavior and Temperament**

- Major cause of euthanasia
- Temperament eliminates 30-50% of service dogs
- C-BARQ Assessment questionnaire: Seeking a reliable measurement standard
  - 152 questions
  - >3,000 owners and breed club members
- 11 traits were common to most dogs
- Study identified differences among breeds



- We all know that canine behavior and temperament matter as much as any other disease or disorder.
  - It affects our enjoyment of our dogs and their enjoyment of their lives.
  - Behavior problems are a major cause of euthanasia.
- The starting point for work by Dr. James Serpell at the University of Pennsylvania was the lack of a single standard for measuring behavior and temperament. To this point, there have been three measurement methods, but they all have drawbacks:
  - Long-term observation in the dogs' usual environment may miss a behavior that is serious but infrequent, and may confuse a dog's actual temperament with the way it interacts with its owner.
  - Temperament tests are time-consuming, and they may not be accurate. And they're stressful, especially for puppies.
  - Owner and handler questionnaires are quick and affordable, but they may not be reliable.
- Dr. Serpell's Canine Behavioral Assessment and Research Questionnaire, or C-BARQ, poses 152 questions to dog owners and handlers, on the assumption that they're the ones who know their animals best. It was sent to more than 3,000 owners and breed club members.
- The survey identified 11 traits that are common to most dogs, regardless of breed, age, sex, or neuter status:
  - stranger-directed aggression
  - owner-directed aggression
  - stranger-directed fear
  - nonsocial fear
  - dog-directed fear/aggression
  - separation-related behavior
  - attachment and attention-seeking
  - Trainability
  - Chasing
  - Excitability
  - touch sensitivity
- The study did identify consistent differences among breeds
  - For example, Dachshunds and Rottweilers scored highest on stranger-directed aggression, Siberian Huskies lowest.
- Next steps:
  - Survey additional breeds;
  - Determine whether C-BARQ can be used to screen and select service dogs

## Major Findings

### Canine Vaccination

- More vaccines available, but adverse events may be understated
- Research requires large population, long study period
  - 3.5 million doses to 1.2 million dogs led to 4,678 events
  - Highest prevalence in Dachshunds, Pugs, Boston Terriers, Miniature Pinschers, Chihuahuas
  - Adverse events increased 25% for each additional vaccine on the same occasion



- Dr. George Moore of Purdue University talked about the safety and efficacy of canine vaccines.
- The number of animal vaccines has increased over the last 20 to 30 years.
  - Now the focus is shifting from vaccine access to prevention of vaccine-associated adverse events.
  - It's also important to maintain awareness and consistency: When vaccination rates drop, preventable diseases begin to spread. Example: A recent outbreak of canine distemper in Chicago.
- Adverse event studies have to follow large populations over long time spans.
  - Dr. Moore's team conducted a two-year study involving 3.5 million doses of vaccine administered to 1.2 million dogs.
  - The study identified just under 4,700 adverse events.
  - Adverse events were most prevalent in Dachshunds, Pugs, Boston Terriers, Miniature Pinschers, and Chihuahuas.
  - And the researchers found that adverse events increased by 25% for each additional vaccine given on a single occasion. This was particularly important for smaller dogs.
- Future research will focus on:
  - Vaccines supplied by more than one manufacturer
  - Adverse events more than three days after vaccine is administered
  - The importance of past vaccination records

## Major Findings

### ***How Far Do We Go??***

- Health conditions may be genetically linked to desirable or necessary traits
- Breed clubs may not recognize dogs with important characteristics removed
- Alternative: For recessive traits, breed dogs with abnormal genes to normal, cleared dogs



- Genetic research gives us the opportunity to breed undesirable or dangerous conditions out of our dogs. But a number of the researchers at the Parent Club Conference called for caution.
- From his experience as a soybean geneticist, Dr. Karl Lark argued against eliminating abnormal chromosomes after they're isolated.
  - We have no idea how different genes may be linked.
  - Run the risk of throwing out the baby with the bathwater: A target gene may affect the dog's shape or behavior, or give it the most beautiful coat you've ever seen.
  - Alternative is to make sure any dogs that carry an abnormal gene are bred with normal, cleared dogs.
- Dr. Charles Garvin talked about the controversy around the Dalmatian-Pointer Backcross Project at the University of Indiana.
  - Dalmatians are prone to high uric acid levels that lead to painful and potentially life-threatening bladder stones.
  - There is some concern that the gene responsible for high uric acid levels may be linked to the spotting pattern that is included in the breed standard.
  - After nine generations, the breeders felt the backcrossed dogs "looked reasonable," and they had normal uric acid levels.
  - Arguments over their eligibility for registration continue to this day.
- Dr. Keith Murphy said the same chromosomal abnormality that causes dermatomyositis in Shetland Sheepdogs is related to merle coloring in some Shelties.
- Expect continuing debates over the integrity of breed standards, the availability of genetic methods to prevent and cure canine disease, and the risk that important breed characteristics may be lost as we struggle to protect our dogs and keep them healthy.



## What's Next?

### **A World of Opportunities**

- Health committees
- Health surveys
- DNA testing
- *Fundraising*



## What's Next?

- The overall message from the Parent Club Conference was that we have a lot of work ahead of us to build on our tremendous successes so far.
- A lot of that work involves the parent clubs themselves, and the CHF programs that support them.

## What's Next?

### Health Committees

- Independent structure
- Close relationship with Parent Club
- Committee activities
  - Educational seminars and publications
  - DNA clinics
  - Fundraising
  - Research support
- Parent Clubs and breed foundations: *'The backbone of disease-specific research'*



- Conference attendees heard a great deal about the role and function of health committees.
- The committees are generally set up as independent structures that maintain a close working relationship with their parent club boards and officers.
- Their activities range from education and publications, to DNA clinics, to fundraising.
- And, of course, they fund their own research.
- The Canine Health Foundation has really come to see the Parent Clubs themselves and the breed foundations as the backbone of disease-specific research, helping us to identify and prioritize diseases for specific breeds.

## What's Next?

# Health Surveys

- Basic principles for survey design
  - Set goals and stick to them
  - Define acceptable proof
  - Anticipate barriers and build in solutions
  - Choose a method
  - Include healthy dogs
  - Test forms for accuracy, ease of use



- Many of you have been involved in health surveys, through your parent clubs and breed foundations.
- Here are some of the basic principles for designing an effective health survey:
  - Set your goals at the beginning, and stick to them.
  - Decide in advance what level of proof you will consider acceptable.
  - Anticipate the barriers you might encounter, and build solutions into your survey design.
  - Choose an appropriate survey method.
  - Include healthy dogs in the survey, and
  - Pre-test your forms to make sure they're accurate and easy to use.

## What's Next?

### Health Surveys

- Barriers to a successful survey: People, not technology
  - Confidentiality
  - Breed reputation
  - Low participation rates
  - Inclusion of pet population in addition to “fancy”
  - Complexity of online surveys
- Club leadership is essential
- CHF is here to help



•We’ve learned in recent years that the barriers to a successful survey are all about people, not technology.

•Confidentiality can be a problem when in-house volunteers gather the data. The alternative is to bring in outside researchers who are not associated with the breed.

•Negative health results may raise concerns about a breed’s reputation.

•...and attendees heard about a number of other challenges that have to be addressed before a survey can be conducted.

•Designing a health survey is a presentation topic in itself. But parent clubs play a leading role...and the Canine Health Foundation is here to help.



## What's Next?

# DNA and the American Kennel Club

- AKC department formed in 1997
- Compliance audit
  - 83,000 DNA samples during routine inspections
  - Compliance up from 87% to >95%
- Voluntary DNA certification
  - Owner collects cheek swab
  - Lab processes results
  - AKC provides DNA certificate
- Conditional registration



- The AKC collects DNA to verify dogs' parentage and genetic identity. This database is not used for research.
- The AKC has two DNA programs: a compliance audit, and DNA certification.
- Since 1998, 15 AKC inspectors have collected 83,000 DNA samples during routine kennel inspections across the United States.
  - In early 1998, DNA tests showed that 87% of litters had correct parentage listed.
  - By the end of 1998, the rate had increased to 89%.
  - Today, it stands at more than 95%.
  - When incorrect parentage is discovered, the AKC notifies breeders and owners. Registrations are corrected if accurate information is available, and about half are cancelled.
- The voluntary DNA certification program began in 1998.
  - The owner uses a cheek swab to collect the sample.
  - A lab processes the sample, and sends results to the AKC.
  - The AKC forwards a DNA certificate to the owner and adds the dog's DNA profile number to its registration record to appear on pedigrees.
- Since 1998, the AKC has required DNA certification of stud dogs if fresh or frozen semen is to be shipped or stored.
- The Club uses DNA testing to register multiple sired litters, and recently introduced a conditional registration program for registered dogs with parentage issues.



## What's Next?

### **AKC-CHF Fundraising MEETING THE CHALLENGE**

- We need your support
  - Contributions
  - Volunteers to tell the story

#### ■ **CALL US TODAY!**

**Jeff Sossamon**  
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•Man's best friend has no better friends than the American Kennel Club Canine Health Foundation—and our founder, the American Kennel Club. Together, we are committed to helping dogs live longer, healthier lives.

•In 10 short years, the Foundation has breathed new life into the fight against canine diseases - funding over 275 research studies (to the tune of \$15 million) that have unlocked secrets of canine genomics, identified genes that cause inherited diseases and explored causes and cures for medical conditions from cancer to cataracts. Our worldwide team of funded researchers constantly amazes us. AND, since dogs and humans share much of the same genetic makeup (and often the same physical environment), canine research is leading to advancements in human health research, as well.

•We're pleased to announce that the **canine genome sequence has been completed** and was funded in part by the Foundation. Now, the canine sequence takes its place alongside the human and mouse genomes as one of five premier tools that researchers worldwide will have at their fingertips – leading to the promise of quicker results, faster tests, and definitive therapies in the fight against canine and human disease.

•We need your financial support to continue this good work!

•There are so many great stories that the Canine Health Foundation can share. If you would agree to help us tell the story, I'd like to invite you to contact Jeff Sossamon toll free at (888) 682-9696.

•Thanks for your time.