

VETERINARY SATELLITE MEETING  
Rugby, England – October 23<sup>rd</sup> to 26<sup>th</sup>, 2007

Rugby, England ...the birthplace of rugby football was the host city for the Syringomyelia 2007 International Symposium with the Veterinary portion of the Symposium being held late Friday afternoon, October 26<sup>th</sup>, 2007. This Symposium was an international gathering, literally drawing delegates and speakers from around the world, and was a composite of neurosurgeons, neurologists, geneticists, scientists, pain management specialists, veterinary surgeons, mathematicians, physiotherapists, nurses, dog owners and breeders. It was an inspiring opportunity to see the magnitude of research that is being done on the conditions known as Chiari-like Malformation and Syringomyelia. Both human and veterinary medicine have collaborated together for the benefit of man, and his best friend.

Guest speakers for the Veterinary portion included: Dr. Clare Rusbridge, Dr. Graham Flint, Dr. Guy Rouleau, Dr. Sarah Blott and Dr. Dominic Marino and Dr. Bruce Fogle. The pace of the entire Veterinary segment was extremely fast and detailed... so much so that note taking at the time was impossible. Each speaker relayed important information that could only be later summarized reflecting highlighted points. Thanks to Karlin Lillington, CD's were ultimately made available for purchase. I strongly urge everyone to consider purchasing these CD's. The purchase of these productions not only educate, but proceeds also go back into research future reproductions. To order, go to:

<http://www.cafepress.com/cavaliertalk/4311456>

**CLARE RUSBRIDGE**, BVMS PhD DipECVN MRCVS  
European and RCVS Specialist in Veterinary Neurology  
Stone Lion Veterinary Centre, 41 High St. Wimbledon, London SW 19 5AU, UK

Since August, 1997, Dr. Rusbridge "has operated a neurology referral service at the Stone Lion Veterinary Referral Centre in Wimbledon gaining Royal College of Veterinary Surgeons Specialist status in 1999. She became interested in Chiari-like Malformation/ Syringomyelia in 1995 and has continued to research this disease focusing on the genetics, pathogenesis and treatment. She gained a PhD in this subject from Utrecht University in February 2007."

Dr. Rusbridge provided the initial opening greetings as Chairperson of the Veterinary Syringomyelia 2007 segment. She provided an overview regarding canine Syringomyelia, which is somewhat similar to (but revised) from the presentation she gave to us in May, 2005. Chiari-like Malformation and Syringomyelia research has evolved with regard to current treatments surgically as well as medically. More attention is being paid to discerning signs of pain/discomfort. Dr. Rusbridge reports in the October 2007 British Journal of Neurosurgery that "the Cavalier King Charles Spaniel is overwhelmingly over represented, suggesting a genetic predisposition. At least 95% of CKCS have CM and as many as 50% have Syringomyelia with the proportion of affected dogs increasing with age. "... "Other unidentified anatomical or environment factors are, however, likely to be involved."

Highlights of presentation:

- Types of pain: Neuropathic, Physiological, and Inflammatory. Neuropathic is a disease of the pain itself. Physiological pain is when you step on a nail, brain tells you to step off. Inflammatory is arthritic type pain.
- Syrinxes that are over ½ cm (.5 mm) (width) will likely experience pain
- Reference made to cavalier history and feature of first dogs having a longer nose, then a short nose, then having longer nose again
- Exceptional to find a Cavalier without CM
- Cavalier brain is size of a Labrador but contained in Toy Dog skull. Mismatch of brain size and skull.
- Risk of developing SM - just being a Cavalier.
- No clear correspondence between CM and SM. No correlation of the Caudal Fossa volume and SM
- 95% of cavaliers have CM. 50% have SM but percentage goes higher with age of dogs scanned. Not all have clinical signs. 35% of the SM dogs (syrinxes) were showing evidence of pain.

- Example discussed of a dog with SM but no CM. Question posed was “What causes SM when you don’t have Chiari malformation?” Hypothesis – CM is an important factor to develop SM but there may be other important contributory anatomical or physiological factors. Risky to make breeding recommendations based just on CM.
- Treatments are variable, depending on circumstances of individual and do a trial and error between symptoms, drugs, surgery, etc.
- Selection by skull shape – to breed for long skulls to breed away from CM/SM. An attempt was made studying head shapes to determine presence or absence of CM/SM – visually, with calliper measurements, radiographs (analysis for this still ongoing and might prove interesting) and MRI scans. Result – couldn’t look at skull shape to determine who may or may not have CM/SM.

End of Dr. C. Rusbridge’s presentation

**GRAHAM FLINT**, BSc, MB, FRCS, Consultant Neurosurgeon, Queen Elizabeth Hospital, Birmingham, UK

Dr. Graham Flint is a world-renowned expert in the human form of Chiari Malformation and Syringomyelia. His presentation provided an overview from the human perspective. According to Dr. Flint, SM remains a rare disease in the community as a whole. In contrast, post-traumatic SM is common in the population of spinal cord injury victims.

Highlights of presentation:

- Gave a mythological history of the names of Chiari, Syrinxes.
- Talked about hind brain herniation (lowest part of brain) through the Foramen Magnum (upper part of spinal canal)
- Cerebral Spinal Fluid (CSF) is formed in chambers (Ventricles) within the brain.
- Within Ventricles is a structure called Choroid Plexus which forms most of the CSF
- CSF eventually returns to bloodstream via structure called Superior Sagittal Sinus along top of the head.
- CSF has physical as well as chemical functions. Acts as a buffer.
- When CSF is obstructed, it cannot exit spinal canal as quickly as it should and may accumulate inside spinal cord forming a syrinx cavity.
- Refers to Clare Rusbridge’s theory of how syrinx is formed is a question that has exercised neurosurgeons for many years and continues to do so.
- Syrinx cavities form in centre of spinal cord, result in damaging nerve cells in centre of cord, causing weakness and wasting of muscle groups that these nerve cells supply.
- There are 4 types of Chiari – Type 1 and Type 2 most seen. Type 1 relates to a mismatch between brain size and volume of Posterior Fossa (human) or Caudal Foss (dogs). Type 2 is associated with Spina Bifida and Hydrocephalus.
- Surgical treatment not mandatory. Talks about medical treatment as long as symptoms don’t display evidence of neurological deterioration.
- Talked about differing surgical techniques
- Talks about questioning what are the mechanisms that cause fluid to accumulate inside spinal cord. Many suspect there are other mechanisms operating besides misshaped skull in development of hindbrain hernias in first place.
- Says liaison between Veterinary profession and Human profession will continue with further exchanges of knowledge.

End of Dr. G. Flint’s presentation

**GUY A. ROULEAU**, M.D. Ph.D. FRCP© Director, Centre for the Study of Brain Diseases, Montreal, Canada

Guy Rouleau is a Professor in the Department of Medicine at the University of Montreal. He heads up the Research Centre at Saint-Justine Hospital, Montreal, Quebec. Dr. Rouleau has spent the last 20 years of his

work focused on understanding the genetic basis for diseases of the brain. He has already mapped over 20 disease loci and significantly contributed to the identification of over 10 genes causing diseases.

Highlights of presentation:

- Opens presentation with discussion of Chiari Malformation (CM) and Syringomyelia (SM) in the human condition.
- Discusses origin of the name of the Chiari disease as being named after Hans Chiari, believed to be Viennese (Austrian).
- Says incidence of CM in humans is 1 in 1,200 – not very common
- Jokingly said he does not recommend people have an MRI done unless there is a good reason because they might find something you don't know you had going on in your head.
- CM in humans is associated with SM – near 60%.
- CM pathogenesis (organization and development of disease) remains largely unknown. Says disease originates, probably, from a Mesodermic problem, not a Neuroectodermic (brain derived or nervous system initial tissue) problem. This is from schematic tissue. This is an important difference because most of the other forms of Chiari are definitely Neuroectodermal and says they believe this is Mesodermal. It also gives clues as to what might be going on.
- Cause is multifactorial. As a geneticist, they are looking at evidence such as familial aggregation (family history).
- Says clearly, genes can cause Chiari Malformation and they have evidence that there is familial clustering. So, taken together, they can say there clearly are genetic factors that predispose to Chiari Malformation in humans, but what they cannot say is what is the importance of those factors relative to relevant risks. They don't have the data to be able to say that.
- Talks about a small study for heritability - suspected to be very high. Study needs to be reproduced.
- The number and identity of genes involved is unknown. Don't know if it is 1 gene, or 20 genes.
- Talks about methods used in finding linkage and positional cloning – for that, they need large families. Does not exist for human studies but it does in certain dog breeds.
- Talks about human studies, methods explored and says there is an animal model – dogs.
- 20-25,000 genes in the Human Genome. Plausible candidates in the hundreds.
- CM/SM in Cavaliers – says that CM is present, to some extent (either mild or severe) in almost 100% of dogs of this breed. SM is present in 50-70% - they also have other medical conditions.
- Talks about Genetic Diversity in dog breeds being closer than for humans with different ethnic backgrounds. The diseases we see in many breeds are probably just accidents – are traits that were in the founder individuals, often recessively therefore no apparent problem, but with inbreeding, this leads to a higher frequency of certain diseases in certain breeds. Different disease in many different breeds.
- Genome of the dog has been sequenced. There are a lot of markers that are available. Says they have the tools to study these animals
- At first, early observations seemed to indicate it would be a simple trait, but as studies were done and more information became available, it became obvious that they were dealing with something more complex than just a simple Mendelian trait.
- Clinically affected offspring often have affected (sub-clinically or clinically) parents. Worsens with each generation.
- Reinforces comments made by Dr. Clare Rusbridge and Penny Knowler regarding clinically affected cavaliers share a small number of ancestors. Again the concept of a founder population.
- Goals are to: Map Chiari Malformation and Syringomyelia (two different entities, related, but different); To identify the genes – using positional candidate approach; To characterize these genes - use information to develop a rapid and inexpensive test.
- DNA Collection is a very large project that involves many, many institutions, groups and people. Database has data on something like 10,000 dogs. They have around 1,500 DNA samples in their lab... quite a few from MRI confirmed dogs. Many are from MRI “clear” dogs – that is, cleared of SM, not CM.
- Are looking at data of the MRI cases to see if they can use this information to have other strategies to be able to identify the genes.
- Says “we” should know that, given the high rate of Chiari-like Malformation in the Cavalier means that they cannot use Cavaliers to map genes, but they can be used to identify genes for SM.

- Whole Genome was complete – 250 markers... 173 dogs and linkage was done
- Preliminary results indicate they may be on to something. Are in the process of confirming, or infirming, these linkages and then to go onto positional cloning steps.
- Talks about genes being screened and expenses involved.
- Future plans to follow up on Genome Scan. Have the DNA samples and info to do so.
- Dr. Rouleau says he thinks they have what they need to find the genes that cause SM but what about CM?
- Says Cavaliers, alone, can't help to find the genes. Says they are looking at other CM families within other breeds.
- Can do a study with other affected breeds with the assumption that, probably, the genetic basis is identical and therefore do a large scale association study. Can probably do both studies at the same time.
- Outlined breeds affected. Said most important to him at the present time was the Brussels Griffon. Says this is the best bet to map a gene for Chiari Malformation.
- Plan for the CM study is to continue with their collection, perform a Genome Scan for Brussels Griffons, follow up with fine mapping and positional cloning and to perform a dense snip association study, using cases from different breeds.
- After the mapping phase, they will know where the predisposing gene is and, using this information, there is a test which would be probability based to indicate which dogs may be carriers, which dogs may not be carriers. This information could be used by breeders. Once the gene is identified, there would be a simpler, more accurate direct mutation test.

End of Presentation

**SARAH BLOTT**, B.Sc, M.Sc, Ph.D Department of Genetics, Centre for Preventive Medicine, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk, CB8 7UU

“Dr. Sarah Blott is a Research Group Leader at the Animal Health Trust (AHT) and is interested in the development of breeding schemes for companion animals that combine state-of-the-art knowledge in quantitative genetics with molecular genetic markers. She has a M.Sc. in Animal Breeding and a PhD in Quantitative Genetics, completed at the Roslin Institute (Edinburgh).”

Highlights of presentation:

- Advises that presentation is to talk about “how to breed away from genetic diseases. Says that they believe the disease (CM/SM) has a genetic basis.
- The 2 year Project is funded by the Kennel Club Charitable Trust (UK) and intend to look at 2 breeds; the Labrador Retriever, because it has good hip dysplasia records and the Cavalier King Charles Spaniel for Syringomyelia.
- Both are examples of complex diseases, are multifactorial and that we are not going to have a single gene DNA test.
- Discusses persons she will be working with (Tom Lewis, a quantitative geneticist and Prof. John Williams, a world expert in designing breeding schemes). Says they hope to come up with recommendations and strategies to enable us to breed away from the disease (SM).
- Explains what Complex Diseases are: These are diseases caused by multiple genes and also the environment has an effect, so it is a combination of genes and environment which leads to the disease phenotype.
- Different genes can have different amounts of influence on the disease. The combined effect of the genes interacting with environment leads to disease phenotype
- When talking about MRI measurements and clinical observations, these are also phenotypes. These are things that can be measured on a dog which can be derived from this combination of the genes and environment.
- Only genes are passed on to the next generation, so this is what we have to focus on. Says we need to separate the effect of the genes from the environmental effects.
- Says they have tried to look at the genetic component of the phenotype... how much of the phenotype is genetic in origin? This is called the “heritability” of the trait. Says, how much of the variation is actually due to the genes and how much due to the environment.

- Need to think about genetic correlations between different traits. This may be different diseases that the population shows or may be between different measurements on the same disease. Need to understand whether we have the same genes acting on the different traits or if they are different genes. Says they can get that information by looking at the genetic correlations.
- Would be extremely beneficial if they could find the genes involved or have genetic markers associated with those genes.
- Need to have this information before making any sensible decisions on how to go forward with breeding strategies.
- To do this, need the “right data”. Makes reference to data collected by C. Rusbridge/P. Knowler.
- Need good phenotypical measurements, MRI scans, clinical observation on reasonable portion of the population and pedigree information.
- If they have pedigree and phenotype information, they can then estimate “heritability” of the condition. If they have information about other conditions, they can estimate genetic correlation between these traits.
- If we have Genotypes and Phenotypes on appropriate individuals, whether from same family or extended families, we can begin to map these genes and come up with genetic markers.
- Once we have that information, we can use that information to evaluate individuals in the population.
- Discussed example and said that based on genetic relationship of dogs in her example, she was able to calculate the Breeding Value for each dog in Pedigree.
- Genetic Values allow you to rank the individuals so you will know which dogs potentially have highest risk of passing on the genes for the disease. This can be a way to make selection for which dogs you want to breed from.
- Genetic markers will increase accuracy of Breeding Value prediction.
- Gives an example of parents and offspring and their resulting Breeding Value statistics which would be an average of the parents. If we had genetic markers, then you can see which genes the offspring have inherited and then each dog receives a different Breeding Value according to actual genes inherited. Increasing accuracy of prediction of whether dog will inherit or pass on disease.
- To breed away from disease, we need to apply selection to population but also need to be aware of impact of selection in population as a whole.
- Talks about importance of maintaining diversity for breed for long-term health of the breed. Maximizing diversity, you actually minimize risk of other diseases popping up.
- Must be aware of selection leading to loss of diversity.
- Discuss using Optimization Techniques. Says they can carry out selection as well as ensuring not losing diversity. Didn't want to go into too much detail on Optimization Techniques, except to say that basically, the information that goes in, such as: Breeding Value for dogs – genetic value; Pedigree relationship – for whole population; Genetic Markers. All this information combined results in an Optimal Solution which tells what the best mate combination we can come up with, giving best Breeding Value, most genetically low risk offspring. All the while, maintaining long term diversity of breed and try to maintain as many families and line and diversity while making the selection.
- In second part of project – use information to look at different breeding strategies so we can come up with recommendations.
- Starting with current population – look at different scenarios:
  - o What is time scale to diminish disease prevalence?
  - o What kind of range of Breeding Values should be used for breeding to bring disease prevalence down?
  - o What is acceptable rate of diversity loss – minimize future risks of disease
- Talks about implementing breeding plans and strategy and is dependant upon decisions taken by breeders - Plan to develop tools to help breeders.
- Says they will be contacting Breed Clubs, Kennel Clubs and individual breeders.
- Need to provide educational seminars to teach how to use these tools and understand what's going on
- One of the tools they would like to develop is a Mate Selection Program.
- Gave an example of criteria that would be entered. Would obtain Breeding Value of dog and ranking of suggested mate. Will be evaluating your dog, not just with the mates suggested, but the whole population. Can even suggest some possible mates who would give even higher Breeding Values for offspring.
- Project has just started. Expect to finish in February, 2010.

- First part of project includes making enquiries from breeders as to what they want. They also have to make an estimation of Heritability and Genetic Correlation. This will have to be done in the first 6 months of the project. This would allow them to come up with Breeding Values for the dogs.
- Says they already have Pedigree records from the UK Kennel Club and also have data from C. Rusbridge and P. Knowler.
- Need MRI scans and 5 Generation Pedigrees from anyone.
- Pedigree data will look at population structure. How related are dogs in the current population? How many dogs are used for breeding? This information will inform our modelling. Need to know where they are starting from
- The second year of the project will be taken up with this modelling where they look at different breeding strategies and what the possible outcome might be.
- At end of the 2 year project, they hope to have come up with set of recommendations.
- During project, will be developing software to do analysis with ultimate aim of delivering an internet based piece of software for breeders to use to make decisions.
- Objective is to:
  - o Avoid inherited disease in individual dogs;
  - o Reduce prevalence of the disease in breed as a whole;
  - o Maintain population diversity to assure long term health of the breed

End of Dr. S. Blott's presentation

**DR. DOMINIC MARINO**, DVM, DACVS, CCRP Chief of Staff, Long Island Veterinary Specialists (LIVS)  
 163 South Service Road  
 Plainview, NY 11803 USA

Dr. Marino is board certified by the American College of Veterinary Surgeons and is the former head of Orthopedic/Neurosurgery service at the Animal Medical Centre in New York City. He has authored many scientific articles and authored chapters in veterinary medical textbooks. He is currently at the Long Island Veterinary Specialist facility in Plainview, NY (LIVS). Dr. Marino has conducted studies regarding Chiari-like Malformation/Syringomyelia and currently has a clinical investigation underway that is of special benefit to breeders in their screening programs. (See accompanying materials).

Highlights of presentation:

- Dr. Marino defines Syringomyelia as a fluid filled cavity within the spinal cord parenchyma. It becomes a problem when it causes problems for our pets.
- Advises that 75% - 85% of dogs screened have a syrinx but percentage figure may be skewed because he sees clinically affected dogs... dogs that are not doing well. He says this figure may still be accurate for the general population. Even so, he does have research projects on dogs that are normal and are finding a fair number of dogs having CM and a fair number suffering from a syrinx (SM).
- Says Hydromyelia differs. It's a slight dilation of central canal but some believe it's the start of problems. Says it becomes a problem when fluid expands from its inner lining out of the central canal and into the substance of the grey matter in the spinal cord.
- Makes reference to a slide with syrinxes, and its relevant size. Says that if this happened all at one, the individual would experience paralysis but because it happens over time, the body compensates for a time but eventually signs occur.
- Discusses physiological function of pulses (from heart beats) causing a pulse wave of CSF flowing down. The pressure and velocity alterations that occur cause problems in the cord
- Refers to several mechanism theories have been discussed which lead to formation of syrinxes. Refers to C. Rusbridge theory of fluid jets causing pressure gradings. Other theory is mechanical fluctuations or beatings of the spinal cord cause an inflammation of the spinal cord where they drive fluid into the cord. Says there are many ways to look at this and that theories change. There is no one answer that explains everything they are seeing yet.
- Talks about the dog's lack of Cerebellar Tonsils (such as humans have). Looking at the Vermis that herniates through Foramen Magnum – the end portion of the Cerebellum.
- Talk about a mismatch between size of brain or bone being too small.

- Says there have been cases where everything looked fine, yet there was a herniation.
- Suspects some dogs have a loss of integrity of the suspensory apparatus that holds the brain within the skull.
- Says their “collagen” isn’t as strong as it should be.
- Says there are medical conditions in human and veterinary patients that cause that. Refers to Shar Pei’s and their loose skin, yet these dogs aren’t being reported as a Chiari patient or having syrinxes but admits to not having seen a lot of them.
- Goes on to say that over the years, they are seeing more and more breeds affected. He is unaware of any breed that has been looked at this extensively. It may be the more they look, the more they’ll find.
- Says Cavalier breeders were the first enthusiastic group to get organized to get the dogs scrutinized at this level.
- Says he doesn’t think this will be labelled a “Cavalier Disease”.
- Talks about conducting surgery on other breeds under 35 pounds.
- Proportion of cavaliers is dropping as more and more dogs become identified.
- Mentions latest information out of Cornell University relates to abnormalities in the front part of the brain may be associated, not necessarily cause/effect, but associated with presence of a syrinx. That is the Frontal Sinus. Says they look at front part of the skull and is this causing some abnormality that results in a syrinx formation.
- Says they divide these problems into 2 situations:
  - o 1) Is the direct compression of the cerebellum
  - o 2) The other is the fluid alterations. The fluid alterations seem to cause a mechanical problem with every heart beat. This seems to be most common reason they see clinical signs.
- Talks about clinical signs related to brain or syrinx – most are related to syrinxes.
- Says there are other reasons that dogs develop syrinxes. Chronic fractures, tumours, cysts, slipped discs.
- Says that draining a syrinx or putting in a shunt is only done as a last resort.
- Talks about CINE MRI (a moving MRI) showing CSF.
- Says that 75-80% of syrinxes are located in cervical region but that was only where they looked. Last 19 dogs showed all had a syrinx in Cervical region, ½ of them had a syrinx in the Cervical and Thoracic region and ¼ of them had it in the Cervical, Thoracic and Lumbar region. Says be careful what you look for because you will find it. Says it was interesting that they didn’t see dogs with Cervical syrinxes and then jump to Lumbar. They didn’t see syrinxes just in Lumbar or Thoracic. They seemed to all start in Cervical area and progress. Don’t know if this will bear out but it’s a start.
- Talks about anatomy of central canal being very small, almost a theoretic space in adults – really closes up and is not really present after a certain age.
- Talks about imagining that space dilating so much that it occupies 70-80% of the spinal cord.
- The substance of the spinal cord is needed for transmitting information. This is where you get your signs from.
- Talked about decompression surgery and reoperating due to scar tissue formation
- Talks about Chiari Institute being 10 minutes away from LIVS facility and meeting with human doctors about problems. Talks about techniques learned.
- Says they have operated on 50 or so cases. Results of 20 cases – 85% sustained clinical improvement. Talks about cranioplasty.
- Surgical candidates receive free follow up MRI at 6 months to see how candidate did on surgery.
- Thermography – Non-invasive. Measurement of surface skin temperatures. Under the control of the Autonomic Nervous System. Controls blood supply to the skin which influences temperature. Abnormality ANS will show up as surface temperature changes on skin. Depending where it is – e.g. syrinx in mid spine
- Using this technology to evaluate dogs in a screening program to see if dog warrants an MRI, or not, and evaluate resolution of a syrinx getting better or not. Lists diagnostics offered in his screening program. (See accompanying material).

End of Dr. D. Marino’s presentation.

VETERINARY SATELLITE MEETING  
Rugby, England – October 26<sup>th</sup>, 2007

**QUESTION AND ANSWER SESSION**

The Q & A session was chaired by: **DR. BRUCE FOGLE**, MBE, DVM MRCVS.  
Dr. Fogle has written over 50 books. He has been the invited speaker at symposia and Veterinary Facilities in 24 countries and is a professional consultant to several international pet food and insurance companies, the Encyclopaedia Britannica and Microsoft Encarta.

Questions were directed to the entire Speakers Panel of: Clare Rusbridge, Graham Flint, Guy Rouleau, Sarah Blott, Dominic Marino and B. Fogle.

CAROL FOWLER: attending

Q: Do you think that the severity of the health problems of the Cavalier breed is now so bad that a sensible way forward would be to outcross to another breed, for example, the Welsh Springer Spaniel or Brittany Spaniel? Such a combination would produce a slightly bigger, more robust dog with a more natural head and muzzle shape.

A: Sarah Blott (S.B.) replied by saying that hopefully by the conclusion of her project, they will have an idea of how bad the situation is. Says that only in extreme cases would they recommend outcrossing to other breeds because you would also have to know what the disease status is on the breed you are bringing in and even though outcrossing, it doesn't guarantee that you will eliminate the disease. Regarding seeing other breeds with CM/SM, Dominic Marino (D.M.) replied by saying that the more we look, the more we see and that we are only at our infancy stage with this. It is too premature to make any conclusions right now, other than to say that in small breed dogs, more is cropping up. To early to say cross breeding (to other breeds) will help, or not. Clare Rusbridge discusses breeding to long skulled dog but agreed with S.B. that you have to be careful what you are breeding to and also, with the dog you have bred to, you have to be concerned about what you have brought back in. Says ideally it has to be done with guidance and having the genetic markers and the computer program that S.B. hopes to design. C.R. says she would say... not yet. Guy Rouleau talks about 46% diversity within the breed. Said that there are human population studies that indicated less than that. G.R. felt that 46% diversity was enough if we can devise good breeding schemes and figure out some of the genetic basis, then he predicts it would be possible to limit the disease and keep the breed.

DEBBIE KERR: attending

Q: Now that a animal genetic specialist has been brought on board, do the panel agree to having some controlled breeding programmes set up to benefit the breed. Every mating is whether we like to call it or not an experiment to some degree. So should all experiments not have a "Control" so that we can ascertain if there has been a positive or indeed negative reaction? I refer to the "control" as being as many A to A matings as possible and collecting as much data on the progeny of these matings therefore perhaps developing some common traits which could help in finding the pattern of heritability?

A: G.R. recapped the question and posed it to S.B. S.B. says we get this information as an actual consequence from people when they send in their information and we collect enough data across the population to be able to see what's going on. Talked about comparing blood. (Sorry, difficult to understand audio).

MARGARET CARTER: attending

Q: There are litters being bred in the UK where both parents are scanned. Some of those puppies are now being MRI'd. Breeders need to know whether following the recommendations of the informal breeding guidelines is helping them to reduce the incidence of Syringomyelia in the litters they are producing. Are there any plans for the results from future generations of UK scanned cavaliers to be collected and analyzed by researchers, or is this something that breeders, groups or breed clubs should consider doing themselves?

A: C.R. responded by referring to the current breeder guidelines as being very basic and some would argue not very good but the basic principle of them is do not breed dogs with early onset Syringomyelia. This is a no-brainer because there is a strong chance this is inheritable. Discuss breeding older dogs with Syringomyelia to older clear dogs. This was because the incidence was so high, they didn't want to recommend only breed clear dogs because of the risk of breeding in something else. "We want guidelines now, "we" want results now. We're dealing with breeding capacity of the dog and the lifetime of the dog and the fact that this is an acquired disease. Emphasizes that she is providing early, early results of dogs over 2.5. No point is showing clear dogs that are less than 2.5. Discusses graph – 2 clear parents = 60% clear. 2 affected parents = no clear dogs. 1 affected parent = 4% clear. Says it is disappointing also to find that A to A doesn't produce all A's, but the proportion of getting more A's is more likely. S.B. says that even when the 2 year project is finished they expect to still gather information on current generations. Hope to come up with scheme to offer breeding tools and have the information going into the database. Breeding scheme is a dynamic thing. Not going to do the project and then just stop. We have to continue forward with each generation as well.

HELEN HOWARD: attending

"Ruth Pereira, a Griffon breeder/owner/charity doyenne in the US has persuaded the Canine Health Foundation to do research to trace a DNA marker for Syringomyelia. This is wonderful news because if a marker can be found we will all be able to afford our breeding stock to be tested. So very different from the costly MRI scans. If the problem is hereditary and the marker can be found, sensible and proper breeding programmes will be able to be planned and we can really move forward. A big thank you to Ruth for enabling this to happen." Author: Tessa Gaines.

Q: So – Helen's question is "Why can't we do that"?

A: G.R. – We are doing that. This is what I showed. The more effort the better. G.R. was asked about a time line. G.R. – afraid someone would ask. If comparing to the MRI, it's less costly and because the disease occurs with increasing age, you have to keep waiting to know if they're definitely clear of SM so, not only that it'll be much earlier in the breeding life of the dog. Many unknowns, hard to predict time... could be as quick as 1 year if things are perfect, if difficult it could be impossible... so somewhere between one year and never. Says things are much quicker than they were. Funds are important and limiting. Should have something useful within next two or three years. Maybe not the gene identified but at least the marker that can be used to help with the prediction. Can't promise anything but to try. Talk about luck. C.R. talks about funds needing to be matched.

Meg Pryor (audience) talks about the Canine Health Foundation – goal is a world-wide study. Says her group (Brussels Griffon – USA) is a small group and needs participation internationally. Test and submit information through the correct channels.

GERRI PRYOR CARTER: ROS LOADES: nominated

Q: Could the team supply us with a detailed action plan that would include goals, such as a timetable for when we can expect the DNA test to be devised, a best estimate of how much it will cost to develop the test on a timely basis and how we can make best use of reproductive tools (like semen collection and freezing) to protect and preserve the gene pool until we have the DNA market test?

A: B.F. voiced question for Gerri Pryor Carter – Asked if breeders should be organizing storing frozen semen now for the future when the testing is in place and can then use genetic material that might otherwise be lost. C.R. says yes. Should store semen. The genetic pool is small. Talks about champion sire might have useful genetic material that you want to add back. Keeps genetic pool as large as possible. Unknown female (Sophia ??) discusses Cornell University they have a gene bank, have been collecting DNA from a variety of breeds for some time. Have a large gene bank for dogs that could be useful. U/M talks about semen banks being set up in UK by breeders for their breeds. Talks about cost being 400 pounds to collect and 75 pounds to store.... not being a large amount of money.

TESSA GAINES: attending

Q: As a breeder and being with the Griffon Bruxellois for just over 50 years and with Japanese Chins for 40 years, and not having had any problems with Syringomyelia in the past, or at least none of my stock having shown symptoms as described today, I am wondering if with the flat faced, large headed breed SM

may be induced at birth. Yes, the formation of the skull may well be hereditary, but at birth when there is a breach presentation and the head/shoulders are stuck and one helps the dam with the birth, can one induce a malformation or problem at that time? One has to mention that even with a “normal” birth the head shape can be changed as it emerges through the passage and vulva. Within 48 hours the head shape has changed and one can see what it may be like. However, the head/skull goes on developing in Griffons until there are about three years of age. Can a problem be started, as with Von Perthes where it can be hereditary and also induced? At birth, the blood supply to the hip joints may be curtailed for a short while and Von Perthes may show up at a later date. Can damage be caused at birth to the head/neck region thereby causing a problem? I should just mention that the Chins give birth far more easily than the Griffons and the whelps are far more lively.

A: Graham Flint responded with human childbirth conditions. Refers to (??) theory saying birth injury was not uncommon cause of problems with hindbrain. G.F. says he thinks (??) was correct that this could occur but incorrect in the frequency of it, says he very seldom encounters it. Recites a case of a patient. Says her problem was based on scar tissue. Says he asked UF if her mother had a difficult birth. UF surprised, said how did you know? Knew because this is what used to happen when obstetrics where not as good as they are now. Talk about consequences of forceps applied for a long time, trauma to back of head would lead to scar tissue from haemorrhage inside... blood, with time, organizes into scar tissue. Discuss other breeds with high incidence of caesarean surgery. G.R. talks about humans born with deformed heads, this is normal. Talk about Cerebral Palsy children not having Chiari. Says birth injuries would be an unlikely explanation. Interesting part of the question – perhaps there is something in the birth process. Don’t know the genetic predisposition. Could be something that acts at birth. Doesn’t change the strategy and the approach. Could be that what you are saying is important but from genetic predisposition standpoint... it was an interesting question.

JEANNE BOYD: nominated

Q: Since the whole issue of SM boils down to insufficient CSF flow (which ultimately results in syrinx formation), and since CINE MRI can now accurately capture the flow rate, would CINE MRI be the best method for evaluating breeding prospects? Why or why not? If the answer is “not” and you are allowed a follow-up it would be – could we then establish precise measurement norms (modelled after the Birmingham doctor’s measurements) and assimilate those measurements into the grading system instead?

A: D.M. talks about CINE has value uses it to evaluate results of procedures they’ve done. Don’t know if it correlates to breeding mechanisms. G.F. talks about human use of CINI MRI’s but says he doesn’t use it because it’s a matter of resource utilization. In human medicine you take history and history determines what you do. B.F. talks about dog owners providing good history. G.F. – then use it selectively. UF talks about using CINI in cavalier and felt it was extremely useful. Could see obstruction and CSF flow. G.F. that depends on if you’re conducting research or a service. UF says we are demonstrating that you can use this in dogs. G.F. asks what motivation of the question was. Jeanne Boyd – curiosity and would it help in breeding (inaudible). UF – discusses study purpose. To determine is surgery appropriate to dogs or should they do something different. D.M. talks about history and categorizing patients and what is normal and how it affects data. Says there are a lot of dogs that are “normal” that aren’t normal.

DAVID HARWOOD: distant question from USA

Q: What about use CINI MRI for evaluation of CSF flow? And thermal imaging? Can these be used to reliably screen puppies and breeding dogs?

A: Part of question has been answered. Question regarding thermal imaging referred to UF says it has not been established in dogs, it has been used in human medicine, mostly research and breast exams, can be used in breast cancer. Talks about equine doctors using it for years to evaluate injury in limbs. For dogs, dogs have hair and hair is an insulator. Owners don’t want dogs shaved. Did initial study with normal dogs to see if they could prove if you could even find patterns whether shaved or not. So far with normal dogs, patterns were similar whether shaved or not. Now need to use it on dogs with the disease. Talks about cavalier study is early, still collecting data, objectively, early data shows certain patterns that they are seeing. Talk about being able to tell between mild, moderate severe, and clinical and non-clinical dogs and

it may be viable to screen cavalier first and to pick out ones that have a thermographic pattern that is suspicious for Chiari to screen for MRI. Talk about undercoats. UF doesn't know, hasn't imaged articular breeds (laughing). Don't know if it will make a difference. Discusses breeds she has done. D.M. discusses bad press that Thermography had years ago... now a days, technology has advanced. It is meant as a screening, non-invasive. It only is intended to say what is suspicious not meant to make a diagnosis.

BRIDGETTE EVANS: attending

Q: Has there been any research into the actual cell structure of the cerebellum? Is it a case that we have a similar problem as MVD where the inability of the organ to hold itself together (loses elasticity in structure) cause the blockage of the CF fluid rather than the fact that there is a malformation for the cerebellum to fall into?

A: D.M. responded that he is not aware of any histological studies. Not pointing fingers but wondered where veterinary pathologists have been with regards to picking this up. Talks about his days when he was a student, not seeing them on necropsy. Not aware anything being looked at at that level. C.R. talks about spinal cord being difficult to get out and pathologists have to be persuaded to do it. In a few years may be able to answer that because there's been a bank for cavalier tissue set up. Need to find out more. G.F. talks about not having come across any article that addresses that question. Asks again what the motivation is for the question.

B.E. makes a connection between MVD and whether the Cerebellum is "slopping into" through the malformation causing the blockage. G.F. – interesting question. Don't think anyone has looked into that. Whole question as to why hindbrain hernias form in the first place has been addressed throughout this entire Syringomyelia 2007 conference, even the Russian Federation suggesting that there might be an environmental toxicity, which is unusual. So, it may not be such a crazy question to pose but no, I'm not aware of any work that's been done. G.R. talks about separating Chiari from Syringomyelia. Chiari has more to do with occipital bone hypoplasia or early closure. When thinking of Syringomyelia, actually thinking about genes that may be important. There may be a genetic variability and susceptibility to develop syrinxes under conditions where you have abnormal, or even normal, CSF pressures. It may be related, not impossible but we don't know right now.

ELSPETH GLEN: attending

Q: The subject of dilated ventricles rears its head every now and then. I know neurologists' opinions vary on finding very full ventricles on an MRI scan. In my line, having scanned 4 generations now, I have found that dilation of the ventricles does not automatically indicate the presence or degree of severity of a syrinx. There would seem to be a "familial" trait running through my older scanned bitches. They did not demonstrate dilation of the ventricles. Although some of them have syrinxes, there was no real correlation between the severity of the SM and the size of the ventricles. However, when scanning the 3<sup>rd</sup> generation, 2 dogs and 1 bitch demonstrated varying degrees of ventricle dilation. 1 of the 3 had a very small syrinx – the bitch. Her ventricles were 2-3 times larger than normal (scanned at age 3 and age 5). I had, of course, introduced a new line via the stud dog. Further, when I mated this 3<sup>rd</sup> generation bitch, 1 of her progeny had ventricles x 4 normal size. He had no syrinx, but the scan was done a 6 months. Could it be possible that symptoms identified on an MRI scan as being an individual dog's reaction to having the Chiari Malformation, could vary familiarly? E.g. do some "family lines" react by demonstrating familial symptoms, like dilation of the ventricles and others do not? Could we study some families and find this out?

A: G.R. talks about twin studies regarding ventricle size. Don't remember details and don't know about information about the ventricles. Thinks that the ventricle question is a MV question. Not inconceivable that there is a genetic variability to have a susceptibility to have larger ventricles under similar pressure conditions between different individuals. May be same mechanism as Syringomyelia or not, don't know. Not a crazy thought that it might be related. May or may not be related to Chiari. Might be possible. G.F. said from human perspective, they do see hydrocephalus in association with Syringomyelia but not very often. Talks about treating hydrocephalus first – reduces pressure. Asks why is it we occasionally see hydrocephalus but most of the time we don't and is that telling us something? Talks about his theory and anecdotal experience. Says he can't answer the question but the question is not crazy. C.R. responds with

saying it's a difficult question to answer and D.M. referred to it earlier and that is - it is normal to see a degree of ventricle dilation in small breeds but don't know what normal is. Have to scan dogs off the street to establish that first. Are looking into it.

VERONICA HULL: attending

Q: It seems that the foramen magnum defect contributes to the CM in the Cavalier, but other breeds also have this defect, notably the Japanese Chin and the Peke, but few of them have SM or even the CM... why is that?

A: C.R. responds by saying it depends on what you are referring to when saying the foramen magnum defect. I think you are referring to occipital dysplasia which is basically the foramen magnum should be an oval shape but in most brachycephalic breeds it is a keyhole shape of varying degrees. Talk about old King Charles Spaniels skulls analyzed from Natural History Museum not having supra occipital bone at all. Just a space at the back. So something has been in these dogs since \_\_\_\_ was started. Represents a failure of membrane there to become bone. Regarded as an anatomical variant. Not meant to be associated with disease. How it influences Chiari malformation is another matter. I propose that maybe in some dogs having a membrane there might have a little bit more accommodation. If you had a genetic tendency for severe disease, your phenotype might be milder disease. G.F. says this list of questions that were terribly daunting when I first looked through them, are becoming increasingly interesting. Talks about morphometric studies on Posterior Fossa, several presented at 2207 conference. Says as far as he knows, noone has measured area of foramen magnum in humans. Interesting thought. D.M. talks about CAT scan technology. Talk about multi-slice CT scan. G.F. talks about 3-D CT construction of the skull.

SUE ROBINSON: attending

Q: The recommended breeding guidelines were revised at the Roundtable last year. I am among a few breeders who didn't and still do not feel comfortable with the re-grading and in particular Grade A. Some dogs are scanned Grade A grade with mild Chiari Malformation. Some are scanned Grade A with mild Chiari Malformation, herniation, central canal dilation and ventricular dilations. Too many breeders who are scanning say their dogs are clear. However, if one asks to see the certificate (and there a great number of breeders who will feel too intimidated to ask) one finds there is herniation and/or dilation and DV. We feel the gulf between A and D is far too wide and only wish to breed the best to the best. We are asking for Grade A to be redefined e.g. Grade A1, Grade A2, Grade A3, etc. with Grade A1 for the Chiari Malformation only.

A: C.R. responds with saying – the answer is I would love to but the trouble is if you are going to redefine it you have to know what quantities you are going to redefine it as. There doesn't seem to be a correlation between mild or severe CM and the presence of SM. Until we have some hard data, many people are looking very hard, hopefully somebody will come up with something soon, but until that time it seems inappropriate to make assessments based on the Chiari malformation when it's really the Syringomyelia that we want to prevent. Agree it's not very good but it's trying to make the best of what we have at the moment. Need KC approval. Talk about Sarah Blott's program and breeding values. Need more data and released results.

SHEENA STEVENS: CHERYL DEANS: nominated

Q: If and when a genetic marker is found for CM/SM will it be possible to correlate this with whether or not the gene will be expressed, and the degree to which it may be?

A: G.R. – Yes! (laughs) SEMINAR ENDS  
INTERESTING INFORMATION

Karlin Lillington's SM site: <http://sm.cavaliertalk.com/>

Cavalier King Charles Spaniel Club (UK) site: <http://www.thecavalierclub.co.uk/>

Cavalier SM discussion list: [Subscribe: CKCS-SM-subscribe@yahoogroups.com](mailto:Subscribe:CKCS-SM-subscribe@yahoogroups.com)