SYRINGOMYELIA NEWS

Spring 2004

A research update

By Clare Rusbridge and Penny Knowler
Stone Lion Veterinary Centre, 41 High Street, Wimbledon, London, SW19 5AU
neuro.vet@btinternet.com (CR) penny.knowler@ntlworld.com (SPK)

The DNA collection is nearing completion of the first phase. We are well on the way to having enough DNA for a genome scan so a big thank you to all of those pet owners, breeders and their veterinary surgeons that are so dedicated to the health of Cavaliers. The first phase involved collection from top bitches and stud dogs. Several of the breeders contacted have already donated from their dogs and others have promised to arrange sampling. The genetic profiles from these dogs will be compared to Cavaliers with syringomyelia, mitral valve disease and epilepsy.

We are still collecting from dogs affected with syringomyelia and their close relatives with over 150 samples to date.

The next phase of the DNA project is collection of DNA from Cavaliers with mitral valve disease. We are focusing on: dogs over 7 years of age that have clear hearts; dogs with heart failure less than 7 years of age; dogs related to dogs with heart failure less than 7 years of age. Any assistance in obtaining DNA from these groups is appreciated.

Answers to common questions

Who are the geneticists involved with this project?
Dr. Berge Minassian and team work at the centre for Applied Genomics at the Hospital for Sick Children in Toronto. This laboratory encompasses five state of the art core facilities: DNA sequencing and synthesis; genetic and statistical analysis; gene isolation and expression; genome resources; and microarray. These resources are essential for identifying disease genes.

Dr. Guy Rouleau directs the Neurogenetics laboratory at the Centre for Research in Neurosciences. Over the last 15 years, his research has focused on the genetic basis for diseases of the brain. He has mapped over 20 disease loci and has significantly contributed to the identification of over 10 disease-causing genes.

What is the geneticists' experience?
Drs. Berge A. Minassian and Guy A. Rouleau each have extensive experience in identifying disease genes in humans. Dr. Rouleau has participated in the discovery of the genetic causes of amyotrophic lateral sclerosis (ALS; Lou Gherig's disease); Juvenile Myoclonic Epilepsy; a form of muscular dystrophy; brain vascular malformations; and neurofibromatosis to name a few. Dr. Minassian has discovered two human epilepsy genes and also works on the genetics of canine epilepsy. Both researchers head large world-renowned labs with extensive resources for the identification of disease genes. They will combine their strengths to help discover the genes causing syringomyelia, mitral valve disease and epilepsy in the cavalier King Charles spaniel.

Why work with scientists in another country?
We have worked with Dr Berge Minassian successfully over a period of years in the genetics of a canine epilepsy syndrome that is inherited in 3 different breeds. He is familiar with our work on syringomyelia and provided expert advice when required. An advantage of working with scientists who are studying the human form of the disease is the availability of greater resources especially as genome scans are extremely expensive. Ultimately it will also help children with similar diseases. In a truly international spirit, Cavalier breeders from the USA, Europe and Australasia have offered to send DNA and information to Canada which will provide joint ownership of any success.

How long will it take to find a gene marker?
Many years -- the current estimate is 3 years after enough DNA has been collected.

That is too long -- I need to know what dog to use now!
We appreciate this; however we can see no other solution. Even with our knowledge of the pedigrees, we cannot tell which dog is safe to use and which is not because both syringomyelia and mitral valve disease are so widespread in all CKCS lines. The faster that DNA is collected and the more that people cooperate and work together then the quicker a blood test will be available

If my dog is providing DNA will you be able to tell if they are a carrier for a disease or not?
No. There is no way of telling this until we have a marker.

I don't want to provide DNA because I am scared that my dog will be identified as having the disease.
The information is and will remain confidential. The DNA is being used to find a marker for the disease and hundreds of samples of DNA are required, each identified by a unique number -- not the dog's pedigree name.

Do we know anything about the status of the littermates of a dog affected with SM?

The status of these dogs is unknown. There is no way of telling -- that is why a blood test would be useful. Syringomyelia has a complex inheritance like MVD, which is why it cannot be bred out in a simple Mendelian manner. It is considered best to err on the side of caution and use siblings as if a known carriers i.e. sparingly and keep track of offspring. Signs of syringomyelia are usually apparent by 3 years of age so it would be safer to delay breeding until that age.

If there is a repeat mating where the first litter were all unaffected, would the second litter also be clear
Not necessarily.

Do the dogs still scratch and have pain after surgery? How long it is before an improvement is seen?
Clare Rusbridge performs a decompression surgery where the occipital bone and part of the first cervical vertebrae are removed to create more space for the brain. The dura is also incised and resected. Most dogs are much more comfortable after surgery and

can return to the normal activities that were not possible pre surgery, for example being taken for a walk. Most continue to scratch but this may only be when very excited e.g. when greeting the owner. Most dogs take 2 weeks to get over the surgery. From then on most owners report improvement. Long term results (>3 years) are not available in significant numbers. Some surgeons prefer to place a tube in the syrinx and report excellent short term results. However the long term results for this procedure are not published yet. One of the problems with shunt placement in humans is that the tubes are prone to blockage and long term results are not as favourable.

What are the risks of surgery?
There are major blood vessels in the area and if traumatised the dog could quickly bleed to death. Although not actually operating on the brain/spinal cord, it is in close proximity and there is a risk of permanent neurological injury. In my hands this has not happened yet but it is always a serious possibility (CR)

What post surgery drug treatment would you advise?
Dogs are hospitalised until comfortable enough for morphine-like-drugs to be discontinued and then discharged on a combination of non steroidal anti-inflammatory drugs (e.g. Rimadyl) and gabapentin (Neurontin). This is withdrawn after about 2 weeks (CR).

Would prednisolone have to be continued after surgery?
I have never needed to use prednisolone in the immediate post operative period. I have one patient currently on prednisolone where the surgery failed after about 6 months. Since this patient I have modified the surgery (CR)

What if a group of breeders wanted to get their breeding dogs MRI scanned before using them? How would they go about it? Who should they approach? Where are the scanners? Could a special price be negotiated?
I would suggest approaching your nearest veterinary MRI service provider and asking. Speaking from my own perspective it should be possible however not on an individual basis. In other words a group of dogs would be done on the same day and there would not be a great deal of flexibility about the day. A special price could be negotiated (we are investigating this) but MRI is expensive -- full stop. We charge MRI routinely at £810 + VAT (including the anaesthesia etc) and make very little profit from this It is only the profit which could be discounted. There are two types of MRI service providers. The first use the facilities of local (human) hospitals -- they are less in control of the price as are being charged by the hospital. The second have their own units and are therefore more in control of the price however will have invested hundreds of thousands to millions of pounds/dollars in the technology and therefore must justify their investment and cover the running costs. It would be easiest to ask your vet where your nearest MRI service provider is. The most likely are the hospitals associated with RCVS or European Specialists in Neurology (Europe) or Diplomates of ACVIM (neurology) in the USA. (CR).

There are some MRI schemes already up and running for example the HEALEY STUDY. For details contact Joseph A. DeLucia DVM,CCRP, Valley Veterinary Rehabilitation, 1171 Valley Road, Clifton, New Jersey 07013, 973-509-5225 ext 103, Fax) 973-509-6082, www.valleyvetrehab.com, Veterinary MRI and RT Centre of New Jersey, 1071 Paulison Avenue, Clifton, New Jersey 07011 973 772-9902,(Fax)

973-772-9904, www.VetMRIRT.com

How early could you MRI screen breeding stock?
To answer this question would require a study where normal CKCS and those that will ultimately develop syringomyelia would have serial MRI to see when signs are first detectable and to relate the size of the back of the skull to the likelihood of getting the disease. This has not been done yet. Most dogs develop signs of syringomyelia by 3 years; therefore 3 years is probably the most appropriate age to scan, 2 ½ years at the earliest.

If my dog does not have syringomyelia on an MRI scan is it guaranteed not to carry the disease?
No

Finally, we should like to acknowledge Boehringer Ingelheim Limited (Vetmedin ®) and the UK DNA Archive for their vital contribution towards the DNA collection programme.