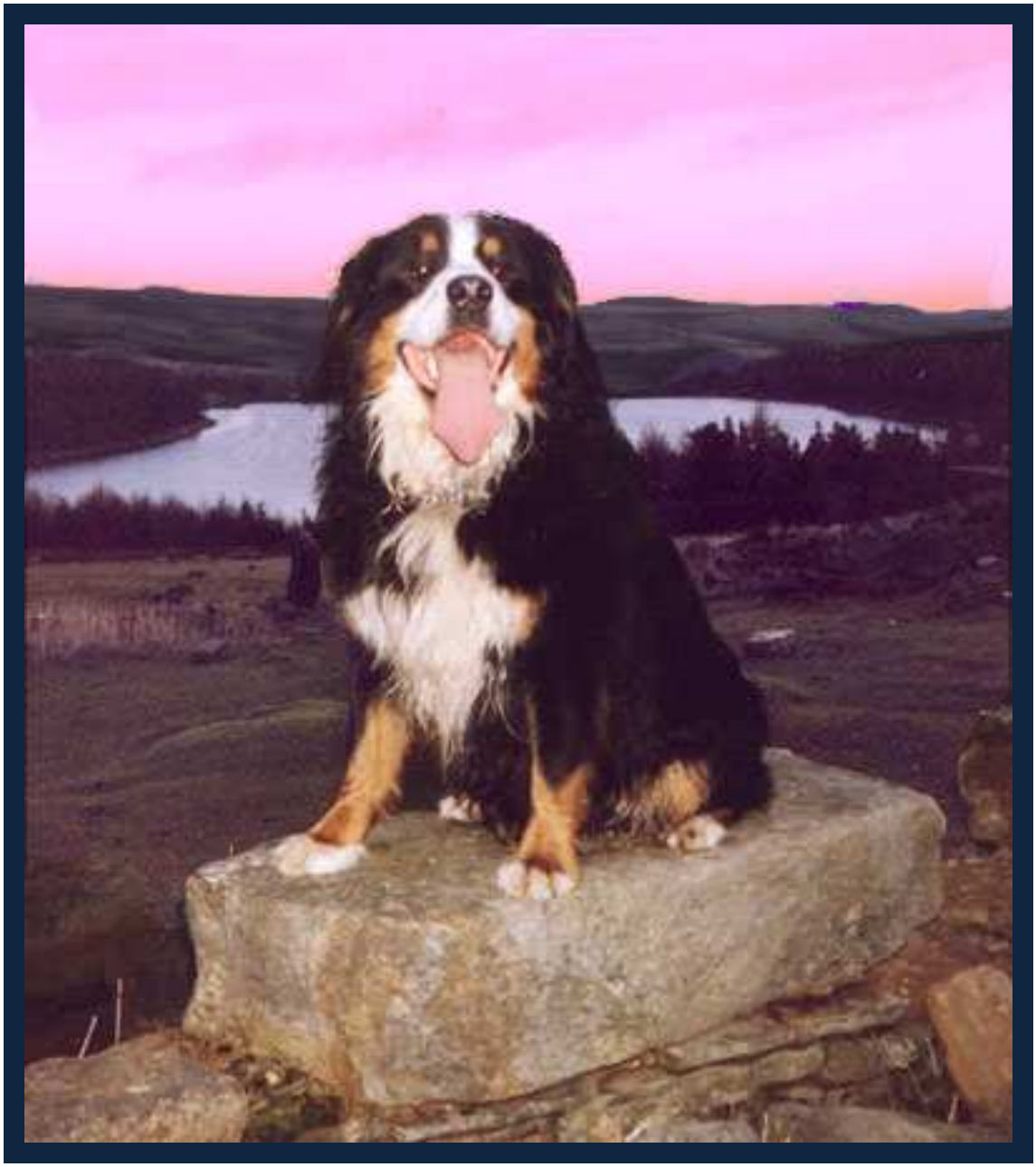
8th International Bernese Mountain Dog Health Seminar



The Woodside Hotel and Conference Centre,
Kenilworth, England
Friday 23rd September 2011

Cover Picture

Alex

Probably most breed people attending the seminar today have had an “Alex”.

Alex was the dog that first gave me my interest in the health of the Bernese Mountain Dog. Home bred in 1986 he was just 19 months old when diagnosed with Lymphosarcoma and subsequently started me on the journey where you join me today.

In those days “cancer” was a much more dreaded word than it is today right across society and dogs were often put to sleep on diagnosis. Alex was treated under Jane Dobson at Cambridge University Veterinary School and, despite the severe kidney damage the disease had already caused, he had a fantastic **normal** life for another 3½ years highlighting the progress being made at places like Cambridge and appearing at various events helping to raise, not just cash, but hopes for the future.

In truth, without Alex this seminar probably wouldn’t be taking place here today and his willingness to please and constant *“joie de vivre”* in the face of all his problems continue to give me strength over 20 years since his passing.

This seminar is dedicated to all the Alex’s of the world, may their memories stay in our hearts and inspire us to make a better, longer lasting and healthier tomorrow for our Bernese Mountain Dogs.

Steve Green
Chairman, Seminar Organising committee

Welcome

The Bernese Mountain Dog Club of Great Britain would like to welcome everyone to our seminar today and hope you have a rewarding day. We especially welcome the overseas delegates from breed clubs in other countries. This is a new experience for us organising such an event and no doubt we will be learning things throughout the week-end and I hope our inevitable mistakes don't affect things too badly.

I would like to thank the BMDC of GB committee for letting me persuade them we ought to take our turn at hosting this event. Even in this electronically connected world I feel it is important for the Bernese community to strengthen its links by getting together in the old fashioned way from time to time.
I have to thank our speakers for the time and effort they have put into preparing their presentations and delivering them today.
I also have to thank my assistants on the organising committee, Louise Harrington and Tracy Titchmarsh but especially our extremely hard working seminar secretary Jackie Green who many of you will have had dealings with.

We have tried to cram a wide variety of speakers into the day and give a good value experience for you. Most of all we hope the experience gives you some enthusiasm or ideas to energise whatever projects you are involved in to help the Bernese Mountain Dog in whatever way you can in your country.

I have tried to learn from some of the other seminars held in different countries since the year 2000 and add a few ideas of my own. One of these is to expand this booklet to include an update on Bernese Mountain Dog related projects that are not being presented here today but are still worth mentioning and recording. I wish to record my thanks to all the people around the world who have taken the time to produce these reports.

I then thought it would be a worthwhile thing to ask for the reports made to the BIWG meeting yesterday to be forwarded so they could be included as well to make the whole booklet a reflection on the state of the Bernese Mountain Dog across the world and available to people who couldn't attend the BIWG meeting.

Finally I have to thank everyone for coming today and making our seminar a success. Since we decided to organise it the economies of all our countries have taken a severe down turn so we are just glad so many people have been able to join us.

We hope to see many of you enjoying the rest of our Ruby Jubilee week-end with us but today is a day to widen our knowledge of the health of the Bernese and I wish you a rewarding day at our seminar.

Steve Green
Chairman Seminar Organising Committee
Chairman BMDC of GB
President B-IWG

Rules of the Day

Rule 1] We have included an ambitious variety of speakers and need your help for the day to go well and finish on schedule. Please observe the break times and return to the room in good time for the next session. Any changes to the programme will be announced during the day.

Rule 2] Modern courtesy- Please turn your mobile phone off or to silent, if you have to take a call please leave the room as smoothly as you can, take the call and then return quietly and fuss free.

Rule 3] Many people are discouraged from attending these events because of the technical nature of them. This cannot be helped as some of the subject matter cannot be other than incredibly detailed. However, if you are finding certain sessions heavy going do not get frustrated, just concentrate on the overall message of the presentation and don't worry if you cannot follow all the details.

Rule 4] Enjoy your day!

Grateful Thanks

The motive from the beginning was to keep the seminar as cheap as possible and we have to thank the following who have supported our efforts in one way or another. Much of the seminar's costs are underwritten by our club health fund and this has been extremely helpful in these financially turbulent and uncertain times for so many people.

Firstly, we are especially grateful for a generous donation from the estate of the late **Alberto Vittone,** an Italian lover of the Bernese Mountain Dog. His estate has made provision for much funding of health related projects for our breed, including the AV award which, over the last five years or so, has donated many tens of thousands of euros to various research projects helping the Bernese Mountain Dog.

Royal Canin as regular sponsors of our Championship Show tomorrow kindly agreed to sponsor this seminar as well.

VRCC Veterinary Referrals in Essex have helped to sponsor the printing of this booklet so our thanks go to them.

The Membership of the Bernese Mountain Dog Club of Great Britain

Finally the most important group of people to thank are our marvellous club members for their support for this seminar. For several years we have asked for health fund donations with annual subscriptions making it clear we had to fund this seminar and, as you can see from the following, lots of people have made donations to our health fund. Our heartfelt thanks go out to these people, not only for the financial difference their varied contributions

have made, but also for properly demonstrating that there truly is an interest in the health of our breed amongst our members.
Massive thank you to:

Mr & Miss	S. & R.	**Adcock & Webb**	Ms & Dr	E.M. & J.E.	**Ford & Mitchiner**
Mrs & Master	L.S.	**Allan**	Mr & Mrs	R. & J.	**Forder**
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Mesdames	V.A. & S.S.	**Annable & Spence**	Miss	D.	**Gaunt**
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Mr & Mrs	M. & B.	**Sargent**	Mr & Mrs	E. & H.	**Tupper-Vinke**
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Mrs	E. A.	**Smith**	Mr & Mrs	G. E. & G	**Williams**
Mrs	L. P.	**Smith**	Miss	S. L.	**Wilson**
Mr & Mrs	F. & H.	**Spear**			

A really big THANK YOU to all the above club members

Seminar Timetable

	Arrival – Coffee, Tea etc	8.15	8.50		Session Time
	Please be seated	8.50	9.00		
	Welcome, Introduction, housekeeping, notices	9.00	9.10		1 hr 30 mins
Dr Jane Dobson	Latest Advances in Clinical Treatments for cancers	9.10	10.30	*1 hr 20 mins*	
	Interval	10.30	11.00	*30 mins*	
Dr Bernoit Hedan	Genetic Progress in the fight against Histiocytic Sarcoma	11.00	12.30	*1 hr 30 mins*	1 hr 30 mins
	Lunch	12.30	1.30	*1 hour*	
Dr Lorna Kennedy	DLA Research and its potential in the battle against Malignant Histiocytosis	1.30	1.50	*20 mins*	1 hr 45 mins
Dr Jeff Sampson	The Kennel Club position on Breed Health and the way forward for health schemes	1.50	2.50	*1 hour*	
Samantha Goldberg	Steroid Responsive Meningitis – an emerging problem for the BMD?	2.50	3.15	*25 mins*	
	Interval	3.15	3.45	*30 mins*	
Dr Urs Geissbuehler	Study of Morbidity and Mortality in Bernese Mountain Dogs in Switzerland	3.45	4.05	*20 mins*	1 hr 10 mins
Prof Berndt Klingeborn	Results of Swedish Pet Insurance company survey into BMD Health	4.05	4.25	*20 mins*	
Pat Long	Background to and why BMD owners should all support Berner Garde	4.25	4.45	*20 mins*	
Steve Green	Berner International Working Group	4.45	4.55	*10 mins*	
	General Discussion and close *(subject to time)*				

PLEASE return to your seat promptly to allow the next session to start on time.
THANK YOU


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Don’t just bin it or file it - this booklet has a purpose!

We all live in different countries and our laws and regulations and restrictions vary completely from country to country. This applies to the way our dog worlds are structured as much as anything else. Identical practises and recommendations can never work but the important thing is that we keep working for the Bernese Mountain Dog and talk to each other in order to learn from each other. No one has a monopoly of good ideas but what works fantastically well in one country may not even be legal in another.

However, whilst our structures may differ, from experiences at these seminars over the years I know that the biggest real problems we all face are very similar. Health wise for the Bernese Mountain Dogs the biggest issues in most countries are longevity and MH, these problems will not go away or improve by themselves and are plain to see when they occur. There are people in every country who can see problems realistically and honestly and try to investigate and tackle them and find out what our breed needs to do to improve.

However, it is a fact that the breed health people in each country can do nothing without the widespread and practical support of the owners and breeders and this needs to be co-ordinated by the breed clubs There will always be people who just want to breed, show and sell puppies and our not so visible health issues are not a real consideration for them. If dogs who could develop MH in middle age had a reliable and visible sign as puppies then who knows how much funding we would have raised by now! No one would be able to ignore our biggest health problem, however, because it does not affect puppies so many people can choose to ignore it. A simple blood test that could be applied to puppies prior to selling to say whether they are likely to develop MH in later life would make people think really seriously about the breed and their breeding. The only way to get a clue as to their possible existence in any puppy is to look back at ancestors and relatives but we all know that not enough people do these kinds of things and crucially not enough people record this information anyway. In many of our countries we need to find ways of encouraging more of breeders and puppy buyers to do this.

Whatever the scientific challenges faced may be, the biggest challenge to many of us in most countries is how to get everyone involved with our breed engaging with health schemes. Compulsion through strict regulation is not always the way to go as people just leave the clubs and do their own thing with no monitoring or checks or even recording.

There has to be a balance between regulation and education but both have to work together because these two tactical approaches need to support each other. There are no easy answers for any of us. Talking to each other and sharing our experiences of different systems and initiatives can only help us. We can improve each other’s morale and learn of ideas that might work for us.

This booklet is therefore an attempt to not only record the information presented at the seminar but also spread it around the Bernese world to stimulate interest and discussion afterwards and help everyone get the most from our Bernese event. Hopefully everyone who attends our seminar will return to their own country with new energy and enthusiasm to help our breed with some new ideas how to do this. By recording the information from each country and making it easier to spread the

message of how things work so well in some countries and what sort of things are happening it is hoped to encourage others at every level to follow. Please use the booklet to prompt discussion and awareness.

Some countries have already achieved a great deal for the health of our breed. Good progressive behaviour amongst owners and breeders is common practice and no one thinks it is an effort. People openly discuss and record problems in their lines and contribute information about them for all to see. For us in the UK I feel we have a long way to go to catch up with some countries. We pride ourselves on having freedom of choice and being over regulated by either our breed clubs or our Kennel Club but with that freedom comes responsibility and many people seem reluctant to fully take on board just how much progress that could entail. We are very good at some things, hip and elbow scoring for example, but very poor at others such as recording information honestly and openly but by appreciating what is happening elsewhere with good results we can hope to progress. I hope this seminar is a step to making people in the UK and elsewhere aware of the possibilities if everyone engaged with breed health properly.

Absorbing the many progressive attitudes and successes described in this booklet can only help us all to go home from the seminar and simply encourage people do the right thing whenever they can.

The Booklet

The remainder of this booklet is split into three sections, speakers, projects and countries.

Section 1] The Speakers *(page 12)*
The first section is the synopses sent by each speaker to cover their subject.

Section 2] The Projects *(page 49)*
The second section consists of reports, updates and summaries from health projects around the world relating to Bernese Mountain Dogs. We are grateful to all the busy people who took time out of these projects to produce these reports for us.
These first two sections were left completely open to the contributors as to how large and what format their report was in.

Section 3] The Countries *(page 90)*
The third section is made up of reports from various clubs around the world outlining the current situation of Bernese Mountain Dogs in their country. Not every country that was asked was able to reply but there is still a good deal of interesting information to compare our different countries. Most of these reports formed the basis of presentations to the B-IWG at our meeting yesterday although some reports were extended from this to give more detail.

We thank all the clubs that replied to the questionnaire.

Section 1

The Speakers

1] Speaker - Dr Jane Dobson

Cancer in Dogs, new approaches to diagnosis and treatment including histiocytic disease

Dr Jane Dobson
University Reader in Veterinary Oncology, Cambridge, UK

Cancer is an important disease in pet dogs and is estimated to affect as many as one in four dogs. The past 20 years have seen many changes in the attitude and approach of both the pet-owning public and the veterinary profession to the diagnosis and treatment of cancer in cats and dogs, and the demand for both basic and specialist treatment of animals with cancer is continually increasing. However, while our knowledge of the basic disease process of cancer has advanced hugely in recent years, this has yet to make a major impact on the clinical management of cancer in pet animals and surgery, radiotherapy and chemotherapy remain the main methods of treatment. Surgery is the most effective method of treatment for many "solid" tumours such as mast cell tumours, low grade sarcomas and low grade carcinomas. The recognition that these locally invasive tumours require surgical resection of a margin of normal tissue to allow complete eradication and the development of surgical techniques to achieve this can frequently result in surgical cure. Increasing availability of radiotherapy facilities has lead to an increasing use of radiation either as a primary treatment, for example for brain and nasal tumours, or in conjunction with surgery for the more invasive mast cell tumours and sarcomas which may prove difficult to manage by surgery alone. Chemotherapy is the treatment of choice for systemic malignant diseases, particularly lymphoma, and chemotherapy protocols based on cytotoxic drugs including vincristine, cyclophosphamide, prednisolone and doxorubicin are now routinely used to treat lymphoma in veterinary practice. Chemotherapy is increasingly used as an adjunct to surgery for those tumours with a high risk of metastasis for example: in osteosarcoma the use of carboplatin following amputation has been established as a means of delaying development of metastasis and thus extending post-operative survival times.

However, new technology is having an impact on our approach to the cancer patient. In terms of diagnosis, use of monoclonal antibodies to "immunophenotype" tumours such as lymphoma and leukaemia has been shown to be of prognostic value, and immunocytochemistry has become more widely used in the diagnosis and classification of this and other forms of

cancer, including histiocytic tumours. Increased availability of advanced imaging techniques such as contrast-enhanced ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) are starting to revolutionize our ability to detect and determine the true extent of some tumours, allowing better planning for surgical approaches and radiotherapy.

In recent years much more targeted methods of cancer therapy have met with success in human medicine for example the small molecule tyrosine kinase inhibitor (TKI) imatinib (Gleevec – Novartis) that targets cells with activating mutations in KIT has revolutionised treatment of chronic myeloid leukaemia and gastro-intestinal stromal tumours (GIST). It has been shown that 20 – 30% of canine mast cell tumours have mutations in the juxtamembrane region of ckit, implicating KIT tyrosine kinase in the pathogenesis of canine MCT. Two TKIs (Masivet – AB Science and Palladia – Pfizer) have recently been licensed for treatment of non-resectable canine mast cell tumours and the use of these drugs in the treatment of other canine tumours is currently being explored.

Specific growth factor receptors are another potential target for newer therapeutic approaches: the antibody targeting the human epidermal growth factor receptor (HER-2), “Herceptin” (Trastuzumab – Genentech), has proven to be effective in the treatment of HER-2 positive breast cancer. Antibodies have also been developed to target other cell signalling pathways, CD20 is a transmembrane protein which regulates early steps in the activation of cell cycle initiation and differentiation. The antigen is expressed on most B-cell non-Hodgkin’s lymphomas but is not found on stem cells, pro-B cells, normal plasma cells or other normal tissues. Rituximab (Rituxan or MabThera – Roche- Europe) an anti-human CD20 antibody is approved for treatment of B-cell lymphoma in adults.

Breed Associations in Canine Cancer

It is well recognised that differences exist between breeds of dog and their risk of developing certain types of cancer. A study of rates and causes of death in insured dogs in Sweden, found that the Bernese mountain dog, Irish wolfhound, flat-coated retriever, boxer and St Bernard were the five breeds of dog with the highest mortality from tumour related death (Bonnett et al,1997). Bernese Mountain dogs, flat-coated retrievers, golden retriever and rottweilers were in the top 5 breeds with over 20% of deaths due to cancer in Denmark (Proschowsky et al, 2003). These population based studies provide useful indicators to breeds at risk of cancer, but should not be regarded as completely definitive because the outcome often depends on the structure of the population at risk with respect to breed.. The fact that there are undoubtedly breed-related predispositions to development of cancer has important

implications in understanding the aetiology of cancer as it infers a possible genetic, heritable component. Of the breeds listed above some have been associated with specific tumour types, for example Bernese mountain dog – systemic and malignant histiocytosis, St Bernard – osteosarcoma and others with a higher risk of tumours in general for example boxer, golden retriever, rottweiler, implicating different genetic mechanisms at play.

Histiocytic sarcoma / Malignant Histiocytosis

These tumours are a malignant neoplasm of dendritic cells (either interstitial or interdigitating dendritic cells) and are usually grouped with the other soft tissue sarcomas.

The term “Histiocytic sarcoma” (HS) has been adopted to encompass two ends of a spectrum of malignant tumors previously referred to as malignant fibrous histiocytoma (MFH) and malignant histiocytosis (MH). The term localised HS has been proposed to describe solitary lesions and disseminated HS the multifocal form, previously MH. The latter is highly breed specific especially in the Bernese Mountain Dog where it has been reported with a frequency of 25%. MH is also prevalent in rottweilers and retrievers. In contrast to the multifocal, disseminated form of HS reported in these breeds, most forms of HS or HS-like tumours reported in flat-coated retrievers have been solitary tumours arising in the deep musculature or fascia of limbs or in association with joints. However, we have documented an aggressive form of HS of the spleen in flat-coated retrievers, and in these dogs the clinical presentation and findings were consistent with a hemophagocytic form of HS described by Moore and colleagues (Dobson et al, 2006).

Diagnosis

HS have a range of histological appearances such that microscopically the diagnosis of HS can be complex and the nomenclature is confusing. Histological findings in HS include diffuse proliferation of neoplastic histiocytes, multinucleated histiocytic giant cells, spindle cells, anaplastic cells and in some cases presence of erythrophagocytic cells. Lymphocyte infiltrates in HS have also been mentioned.

Immunohistochemical staining is an increasingly important technique to accurately identify the cell of origin in poorly differentiated tumours such as HS. Identification of histiocytes can be achieved with molecules involved in antigen presentation such as MHC class II molecules and the b2 integrins CD11d/CD18. On the basis of immunohistochemistry, HS is CD18 positive, and the use of this marker has enabled HS to be differentiated from synovial sarcomas of the joint, and poorly differentiated sarcomas elsewhere in the body (Craig et al, 2002)

Management & Prognosis

Many localised histiocytic sarcomas may be managed initially by surgical excision (sometimes requiring amputation), however, in some breeds of dog, particularly the flat-coated retriever, these tumours carry a poor prognosis due to a high (50 - 70%) rate of distant metastasis, hence long term survival rates are poor. Radical surgery requiring amputation is therefore difficult to justify. There is some indication that the anticancer drug Lomustine (CCNU) may play an adjuvant role in the management of such tumours: in a small study of 16 dogs treated with aggressive local therapy and adjuvant Lomustine chemotherapy, median survival for all dogs of 568 days was reported. However, 2 dogs had local recurrence and 8 dogs developed metastatic disease and in these cases the median time to relapse was 201 days (Skorupski et al, 2009). The response rate to Lomustine in 56 dogs with gross disease was reported to be 46% (overall response) but with a median survival of 106 days (Skorupski et al, 2007). Many dogs with disseminated histiocytic sarcoma are euthanased at the time of diagnosis due to the widespread nature of the lesions and associated morbidity. Disseminated HS is generally considered to be poorly responsive to therapy. It remains to be seen whether more targeted therapies might play a role in the management of histiocytic disease in the future, first we need to identify potential targets.

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Dr Jane M Dobson

MA BVetMed, DVetMed, DipECVIM-CA&Onc MRCVS

Graduate of the Royal Veterinary College, works as houseman / registrar at the Beaumont Hospital (RVC) before studying comparative oncology at the Royal Marsden Hospital, London. In 1984, moved to Cambridge as research assistant working on hyperthermia in the treatment of cancer, leading to DVetMed in 1989. Received BSAVA Woodrow award in 1994, Diplomate of ECVIM-Ca in 1997, received BSAVA Blaine award in 2001. Founding Diplomate in the subspeciality of Oncology in ECVIM. RCVS recognized specialist in Veterinary Oncology. Currently University Reader in Veterinary Oncology, University of Cambridge. Main interests are in anti-cancer chemotherapy, radiotherapy and research into breed associated tumours in dogs. Co-author of Small Animal Oncology and co-editor of 2nd & 3rd edition of the BSAVA Manual of Canine and Feline Oncology.

Notes

2] Speaker - Dr Benoit Hedan

Genetic progress in the fight against histiocytic sarcoma

Benoit Hédan[1], Rachael Thomas[3,4], Heidi G. Parker[2], Gerard R. Rutteman[6], Catherine André[1], Elaine Ostrander[2] and Matthew Breen[3,4,5].

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[5] Cancer Genetics Program, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, USA
[6] Small Animal Clinic, Faculty of Veterinary Medicine, University of Utrecht, The Netherlands.

Histiocytic sarcoma (HS), including localised and disseminated histiocytic sarcoma (previously called Malignant Histiocytosis), are soft tissue sarcomas which are uncommon in the general dog population. However, there is a strikingly high incidence in a subset of breeds suggesting heritable predispositions, as it is the case for many canine diseases.

The pathogenesis of histiocytic malignancies is elusive. HS is highly aggressive tumour that responds poorly to therapy. Death occurs within weeks to months after diagnosis. In order to understand more about the underlying molecular causes of this cancer, an international collaboration was established, involving the laboratories of M. Breen (NCSU, USA), E. Ostrander (NIH, USA) and C. Andre (CNRS, France), each of which bring complementary skills. Thanks to the support of several American and European clubs, this collaboration has been ongoing for several years, and we have now collected blood and tissues samples, necessary for further genetic studies, on more than 650 American and 1300 European BMD

Analysis of our collective dataset gave us the opportunity to characterize the epidemiology of HS in multiple breeds, including the BMD, leading to publications that are of use for veterinarians and breeders alike (Abadie et al. 2009; Hedan et al. 2011). The work of Breen and collaborators (Hedan et al., 2011) showed that BMDs typically present with an internal or disseminated form of HS and are diagnosed at significantly younger ages than Flat Coated Retriever (FCRs), who more frequently develop a localized form of the disease that is restricted to the skin or limbs. Using tumour tissues we established primary cell cultures and used these to indentify

recurrent chromosomal aberrations associated with tumour progression. DNA from 125 HS tumor tissues was used in array comparative genomic hybridization (aCGH) analysis to identify highly recurrent DNA copy number imbalances shared between the two breeds. The chromosomal location of a subset of recurrent genomic imbalances suggested the involvement of key cancer associated genes in HS pathogenesis. Interestingly some deletions span regions that include well known tumour suppressor genes including *CDKN2A/B*, *RB1* and *PTEN*. The identification of the genes involved in the most frequent aberrations will be helpful for development of new therapies (Hedan et al., 2011).

In a parallel study, an ongoing collaboration between the Ostrander and André labs is aimed at identifying the mutations and functional changes that increase susceptibility to histiocytic sarcomas in BMD. To this goal, whole genome scans were performed on American and European populations of BMD (244 cases and 232 controls) using the 22,000 SNP markers array (Illumina). These experiments identified (1) two main loci associated with increased risk for BMD to develop HS, and (2) additional loci with potentially smaller effects. The study of the first locus by Ostrander's lab indicates that alterations in this region lead to cancer development (Shearin et al , submitted), which is concordant with the recent findings (Hedan et al., 2011). Analysis of the different loci in a French population of 900 BMDs showed the implication and interaction of these regions on the risk to develop HS and more generally on the life span of BMDs. These data are being evaluated for use in the development of genetic tests for risk of HS in the breed.

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Notes

3] Speaker - Dr Lorna Kennedy

Is the MHC a genetic risk marker for malignant histiocytosis in BMD?

Lorna Kennedy[1], Benoit Hedan[2], Catherine Andre[2]

[1] Centre for Integrated Genomic Research, University of Manchester, UK
[2] Laboratoire de Genetique et Developpement, Universte de Rennes, France

There is a group of genes in all mammals called the Major Histocompatibility Complex (MHC). These genes are involved in the immune response and have a major influence on response to infection and disease susceptibility and resistance. Most of the genes in the MHC are very variable, and the more variation there is within a population, the better that population is able to withstand immunological challenges such as disease epidemics. For individuals there is some evidence that heterozygosity provides some advantage over homozygosity.

The canine MHC is known as DLA and I have spent the last few years investigating DLA diversity in many different dog breeds. Within the canine MHC we study three different genes which are called DLA-DRB1, DQA1 and DQB1. These genes are situated close together on the same chromosome, and are inherited as sets, which we call haplotypes. We have now studied over 12,000 dogs and have identified over 150 different haplotypes. However, within a single breed we generally find only a small subset of these haplotypes. On average, a breed will have seven haplotypes: one at a frequency > 20%, two with frequencies between 10-20% and four with frequencies between 2-10%.
Towards the end of 2010 I had two different people enquire about DLA diversity in Bernese Mountain dogs, so I checked to see how many BMD we had tested. At that time we had data for 17 BMD, and these dogs had four haplotypes that were found in more than one dog. However, 17 does not really comprise a good sample size.

I was also asked if there was a DLA association with Malignant histiocytosis in BMD.
I did some googling and ascertained that the American Kennel Club was funding a study on malignant histiocytosis in BMD, and that Catherine Andre was one of the collaborators on that project. I contacted Catherine and asked if they were considering DLA typing the samples that they had collected. When she said that they were indeed wanting to DLA type the dogs, I volunteered to do this for her.
We have now DLA typed 50 cases and 44 controls and have identified six haplotypes within this breed, and these include the four haplotypes identified previously. There is one very frequent haplotype (61%), two with frequencies

between 10-20%, two with frequencies of about 6% and one rare haplotype with a frequency of 2%.
This is a typical DLA profile for a breed, and indicates that BMD have a similar DLA diversity to many other breeds. Whether this is enough diversity is another question altogether.

There is also some evidence that one haplotype is increased in controls compared to cases, suggesting that this haplotype may be protective against developing malignant histiocytosis. However, I would not recommend using this as a genetic marker at this point in time, since we do not know how much protection it provides, and there will be many other genes involved in susceptibility and resistance to this disease.

Curriculum Vitae

Dr Lorna Kennedy - After graduating from the University of Oxford in 1976, Lorna worked in human immunogenetics for 15 years, during which time she established an international reputation for the high quality of her research. In 1993, Lorna moved to the University of Manchester and began her research into canine immunogenetics. She was awarded a PhD in 2000. Since then her research has focussed on comparative immunogenetics, investigating the Major Histocompatibility Complex in dogs and many other species. Her research is centred on investigating the genetic basis of complex diseases in dogs, including autoimmune conditions, neurocognitive disorders, plus response to infection and vaccination.

Notes

4] Speaker – Dr Jeff Sampson

Breeding for Better Health

Dr Jeff Sampson
The Kennel Club Genetics Consultant

The Kennel Club (KC) and the breeding of purebred dogs generally have been under intense scrutiny in the UK since the screening of Pedigree Dogs Exposed in 2008. The programme concentrated on two broad aspects of dog breeding:

- Exaggerated breeding leading to breed conformations with associated health and welfare issues
- Inbreeding and the prevalence of inherited disease in purebred dogs

Although none of the issues raised were new, indeed the KC had been addressing both general areas for a number of years, the aftermath of the programme saw acceleration in the KC's programme to address both general issues. This talk will summarise the progress that has been made in the intervening period.

More details of all the KC initiatives covered can be found on the Kennel Club's web site www.thekennelclub.org.uk and some leaflets will be available at the show venue tomorrow.

Notes

5] Speaker - Samantha Goldberg

Steroid Responsive Meningitis

By Samantha Goldberg BVSc MRCVS
KC Health Coordinator for the UK Beagle Clubs

Steroid Responsive Meningitis (SRM) is also known as Sterile Meningitis and as the name suggest is considered to be a non-infectious disease. The condition is seen in many breeds of dog but Beagles along with Bernese Mountain Dogs, Duck Tolling Retrievers and Springer Spaniels seem to be over-represented in the canine population. In Beagles it has become colloquially known as Beagle Pain Syndrome or Stiff Beagle Syndrome/Disease because of the symptoms seen. It is primarily a disease of the younger dog, most often being seen around 6-8months of age for the first time although it has been seen as young as 10 weeks and in dogs of up to 2 years. However there is a form in older dogs more often called Granulomatous Meningo-Encephalitis or GME. SRM is more likely to be treatable with GME sometimes being refractory to treatment and more likely to frustrate the veterinary surgeon and owner.

The cause of SRM is unknown at the moment. It is known to be an immune response but the trigger has not been identified. The immune response results in an intense inflammation of the blood vessels supplying the neurological system particularly the meninges (lining around the brain) and the cervical spinal cord (neck). The body is “attacking” its own cells and suppression of this is imperative in treatment. It is also known as Arteritis in some texts but this may be a separate condition and SRM is not the same condition as Auto-immune polyarthritis. It is possible that the same genetic basis may lead to auto immune disease developing but we don’t yet know if SRM is an auto-immune disease or not.

The symptoms seen reflect the pain produced in the head and neck area and most commonly dogs present with a stiff gait, reluctance to eat and drink, lethargy and pyrexia (raised temperature). Some dogs are very stoic and as such the owner may not be able to pinpoint initially exactly what is wrong just that the puppy is out of sorts. Often this is initially attributed to an injury since puppies are generally lively and some affected dogs may cry out in pain. However the usual use of non-steroidal anti-inflammatories such as meloxicam and carprofen does not produce any improvement. There is no infectious cause so anti-biotics do not improve the situation either.

Diagnosis is most commonly based on symptoms and a spinal tap. Samples are taken under a General Anaesthetic from the fluid bathing the cervical spinal cord and they show typical changes of increased numbers of cells and protein. The recent use of the Magnetic Resonance Imaging technique (MRI) is also producing very useful information on the condition, giving an idea of the severity of the disease in an individual and helping to decide on the best treatment regime. Some dogs may have an apparently normal spinal tap but the MRI scans show abnormalities consistent with the inflammation within the brain. MRI scans have the advantage of being completely safe although expensive. The spinal tap although much cheaper runs a small risk of herniation of the hind brain into the spinal canal. This means the brain can move backwards into the space caused by removing some fluid causing pain and sometimes seizuring. Ideally both diagnostics should be carried out.

Initial treatment regimes are based on suppressing the immune response that has caused the problem. Steroids usually prednisolone at an immuno-suppressive dose are used and then the dose tapered down. The course is ideally carried on for a number of weeks with a slow tapering down and increasing the dose back up with any recurrence in symptoms. A short course of anti-biotics is usually given after the spinal tap. A new and very useful treatment is a drug known as cytarabine. More commonly used in chemotherapy this drug is proving a very effective treatment for SRM. It is an injection and initially given intravenously but can be given under the skin at a later stage. The side effects are uncommon and it can be given easily in consultations at the vet. It produces a quicker response and at the moment seems to be resulting in less relapses than using steroids alone.

Given that some breeds of dog are over represented in the population with SRM there is a possibility of a genetic predisposition that basically means some dogs may have a hereditary make up that makes them more likely to develop the disease. The availability of DNA marker tests for screening of canine disease is a major research area. The main institute in the UK that is developing these marker tests is the Animal Health Trust. The Beagle owners in the UK have been collecting DNA samples from affected dogs and their close relatives and the AHT are currently analysing these.
The first analysis run was not conclusive and we need more samples from affected beagles. The DNA is collected using a simple cheek swab brush and can be done by your vet or owner. Instructions come with the kit. It is essential that such samples include a health report on the dog in question as knowing the DNA has come from an affected dog means those are marked as ones which could show differences. This disease is not new as I have had people describe the symptoms shown by dogs in the past that suggest SRM, but I am having a larger number of reports of it

occurring in the last few years. We have a real chance with new technology to find out more. The gene pool is smaller than in the past for many dog breeds as less people keep male dogs for use at stud and people are more likely to travel to use a major sire or even use AI. The Internet means people are more aware of any issues when they buy a puppy and finding out if there is any way of avoiding breeding puppies with SRM should be a major priority in all breeds.
There seems to be a familial tendency in some cases to produce SRM and where possible matings should avoid “doubling up” on SRM.

Samantha Goldberg BVSc MRCVS
UK Beagle Clubs KC Health Co-ordinator
Member of the KC/BSAVA Scientific Advisory Group

Notes

6] Speaker - Dr Urs Geissbeuhler

Morbidity and mortality in Bernese Mountain Dogs with pedigree born in Switzerland in 2001 and 2002

Menga Corina Rossetti[1], Urs Geissbühler[2], Marcus Doherr[1]

[1]Department of Clinical Research and Veterinary Public Health and [2]
Departement for Clinical Veterinary Medicine, Vetsuisse-Faculty, University of Berne

The aim of this study was to identify the most frequent diseases and causes of death in a cohort of purebred Bernese Mountain Dogs (BMD) born in Switzerland in 2001 and 2002. In 2010, a questionnaire was sent to the owners of 921 (of 1290 registered) BMD. Information was extracted from the questionnaires of 402 owners who responded, as well as from the medical records provided by private veterinarians from 294 of the 402 dogs. The most frequent conditions identified by veterinarians were hind limb lameness (85 cases) and fore limb lameness (64 cases), followed by otitis externa, acute diarrhoea, hot spot (pyotraumatic dermatitis), conjunctivitis and cruciate ligament injuries (47–59 cases each). The most frequent specific tumour identified by veterinarians was histiocytic sarcoma (40 cases). By the end of the study (October 2010), 196/402 (49%) of BMD had died, 117 (59.7%) due to neoplasia. The most frequent neoplasms resulting in death were tumour of unknown type (55/117; 47%), histiocytic sarcoma (35/117; 30%), and lymphoma (11/117; 9.4%). Male dogs had a significantly shorter cumulative survival and a higher morbidity for histiocytic sarcoma, lymphoma and unspecified malignant tumours than female dogs. Findings of this study indicate the common occurrence of certain disorders in the BMD and, in particular, early death associated with malignancy. Further studies to identify possible risk factors and inheritance of these disorders may help breeding programmes improve breed health and longevity.

Figure 1: Cumulative survival derived from life table analysis (3 month increments, figure truncated at 96 months) of female (black, solid line) and male (grey, dashed line) Bernese mountain dogs (BMD) – Analysis of Swiss birth cohorts of 2001 & 2002. Hazard ratio (HR) male/female 1.52 (95 % CI 1.14 - 2.02)

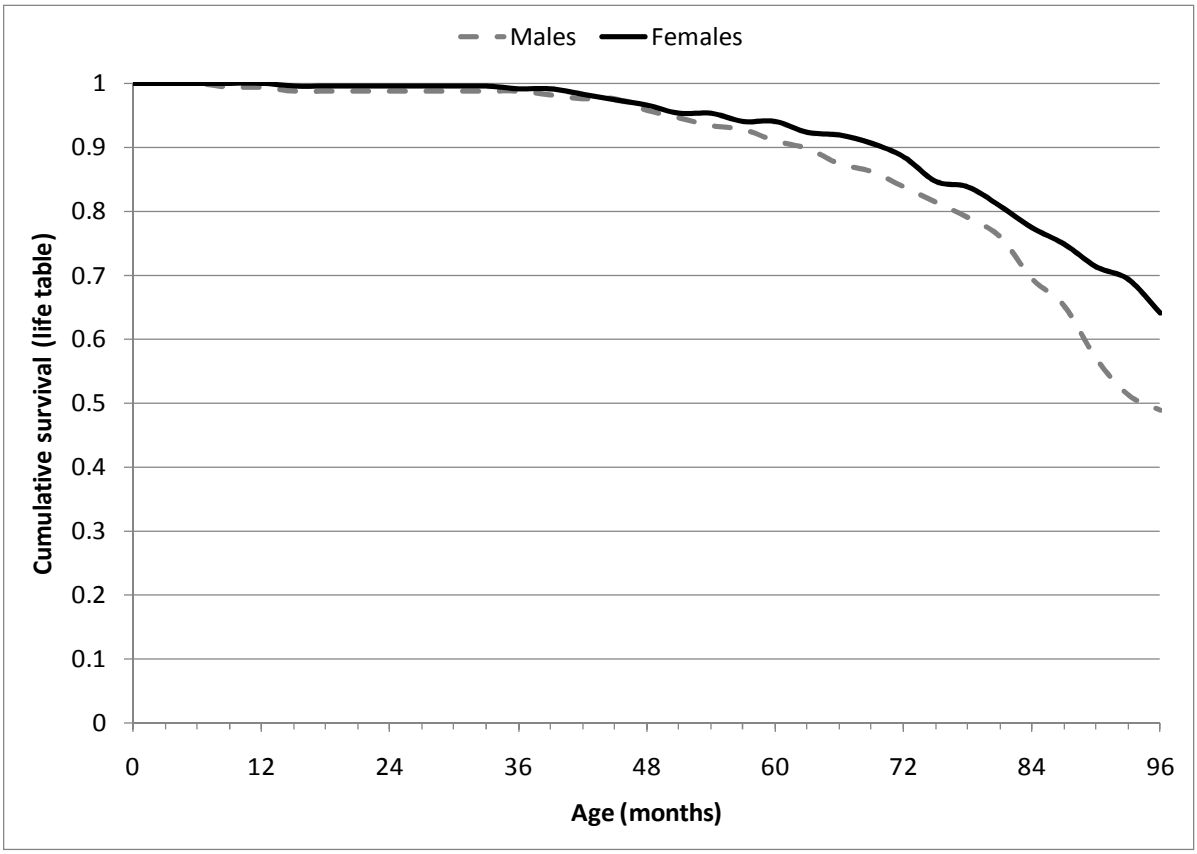
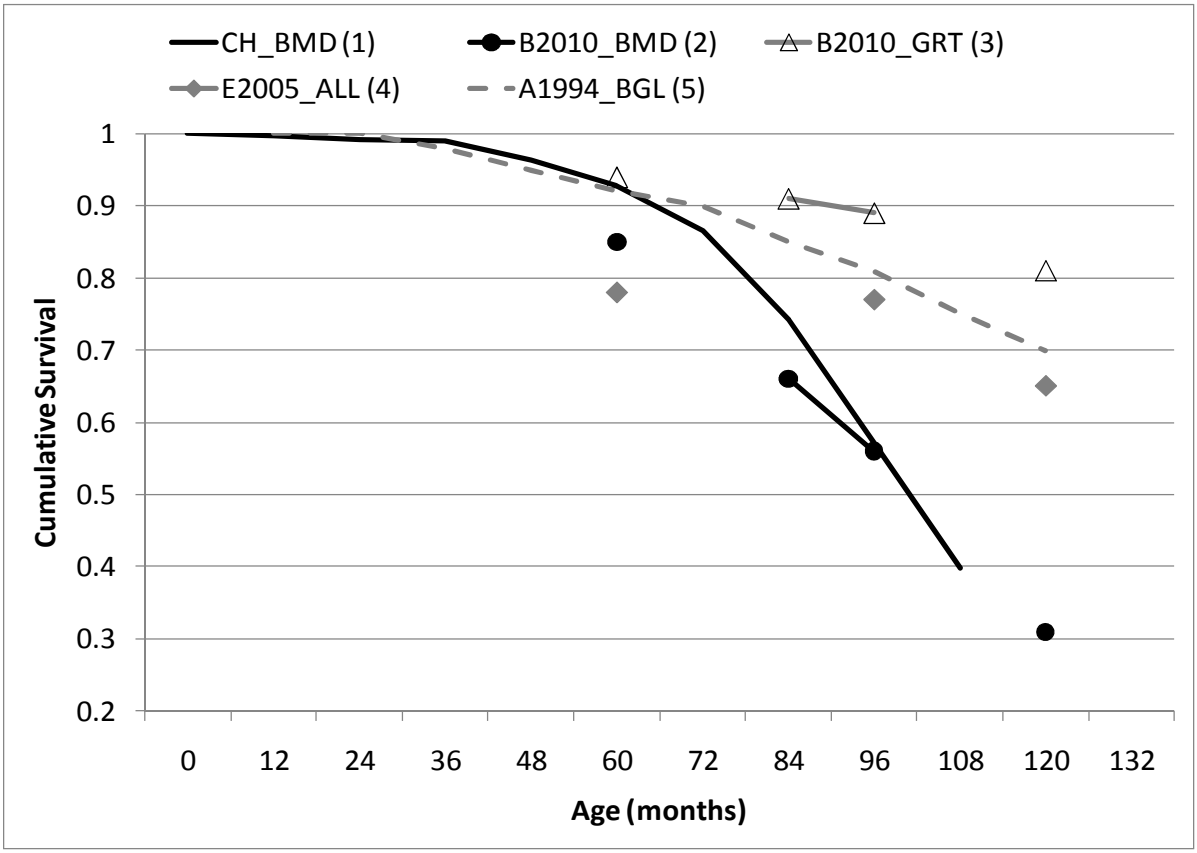


Figure 2: Comparison of cumulative survival (life table analysis, 12 month increments) of Bernese mountain dogs (BMD) from Switzerland (1; birth cohort 2001&2002) and Sweden (2; extracted from Bonnett and Egenvall (2010)), Golden Retrievers (GRT) from Sweden (3; extracted from Bonnett and Egenvall (2010)), Swedish insured dogs (4; extracted from Egenvall et. al. (2005)) and breeding colony Beagles (5; extracted from Albert et al. (1994))



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Notes

7] Speaker - Prof Berndt Klingeborn

Swedish Pet Insurance Survey of Bernese Health

Berndt Klingeborn, DVM, VMD, Professor

Chairman, The Breeding Committee, The Swedish Club of Swiss Mountain Dogs

Health problems in pedigree dogs have prompted an increased focus by veterinarians, geneticists and ethicists on several issues related to breed predispositions for canine diseases. As a complement to listing and classification of disorders known to/accepted as affecting dogs of various breeds, valid estimates of their occurrence have been requested by those trying to elucidate the extent of problems in purebred dogs. The need for statistically significant and robust prevalence data of inherited disorders is listed as a key research topic. The lack of quantification of the occurrence of disease over time precludes our knowing whether and to what extent breed specific diseases are increasing in the population.

The Swedish dog population is unique in that a large portion of the animals are covered by an insurance plan. This is mainly due to that the Consumers Law states that the breeder is responsible for a fault of the puppy up to two years of age if it is likely that the fault was present before the puppy was sold. The breeder is covered by an insurance and the puppy has to be insured by the new owner to request compensation. The Swedish insurance company Agria (Agria Animal Insurance, Stockholm, Sweden) is market leading and has 60% of the market in Sweden. This means that Agria insures approximately 40% of the entire Swedish dog population. From 1995 to the present Agria has provided data on both health care and life insurance claims for descriptive and analytical research. The database was validated and it was concluded that it was acceptable for research purposes, as well as a resource for breed clubs and breeders (Agria breed profiles) in their work on breed-specific strategies to handle health issues within their breed. The insured dog population reflects the general Swedish dog population with regard to gender distribution, breed structure and median age. The life insurance ends at 10 years of age, and veterinary care insurance at 12 years of age. The study comprises over 200,000 dogs per year from 80–133 different breeds during the period of 1995–2006 (1, 2, 3, 4, 5). A hierachial registry has been used to assigne diagnostic codes to each claim. This registry contains more than 8,000 alpha-numerical codes and is based on 14 different major organ systems (6). By presentation of relative as well as true prevalence data by breed and comparison to all breeds, breed-specific pattern

of the disease burden, presented as general mortality and morbidity, is clearly featured in the Agria breed profiles.

The study shows that the Bernese Mountain Dog (BMD) breed has serious health problems presented as true prevalence and incidence data of mortality and morbidity as well as in comparison to all breeds. The breed is presented in the database as 1,000–2,000 dogs insured yearly. Survival analysis shows that in the interval from 1995 to 2002 only 30% of BMD will be alive at 10 years of age compared to all breeds where almost 70% are alive. Of the 20 most common specific diagnoses in the BMD, lymphoma/sarcoma is in the first place. Tumours are also found as the cause to death in 7 major organ systems. Compared to all breeds 18 of the 20 common diagnoses are more prevalent in the BMD. During 1995-2002 tumours accounted for 37% of all death in the BMD compared to all breeds which accounted for 4%. An increase in incidence was seen between 1995-1998 and 1999-2002, and in 2003-2006 tumours accounted for 43.8% of all deaths in the BMD. Also in the period 1995-2002 compared to 2003-2007 the average age by year of death due to tumours was lowered from 7.1 years to 6.9 years. The ranking of breeds in population size was No 29 years 1995/2002 and No 40 2003/2006. Rank for rate claimed death was No 3 years 1995/2002 and No 2 2003/2006. The relative risk for claimed death was 3 times higher for the BMD compared to all 133 breeds.

Veterinary care risk was higher for the BMD compared to all breeds 1995-2002. At the age of one year almost 25% of the BMD had visited a veterinary clinic at least once. The figure for all 80 breeds at one year of age was 14%. The most common specific diagnoses were skin tumour followed by pyometra and lameness. Of the most common diagnoses only 2 out of 20 had a higher prevalence in all breeds than the BMD, i.e. traumatic injuries and gastroenteritis. Population rank was 36 1995/2002 and 45 2003/2006. Rank for rate for more than one veterinary care event was 6 1995/2002 and 5 2003/2006. Almost 50% of BMDs had at least one veterinary care event in each period, and up to an average 3.7 claims per claimed dog in 2003/2006.

One can argue that the results presented do not represent the BMD breed in other countries if population sub-structure of the BMD can exist, i.e. that all dogs of the breed do not not share the same level and type of genetic variation. Recently, a study presented the evaluation of the genetic relatedness of independenly bred lines of European and American dogs from the BMD, flat-coated retriever, golden retriever, and Rottweiler breeds (7). BMD, flat-coated retriever, and Rottweiler have a low genetic diversity between different geographical origins. However, golden retriever showed clear differences between US and European populations in genetic variation.

How to use the results of the surveys in practical strategies for breeding more healthy BMDs are discussed and exemplified by introducing estimated breeding values for hip dysplasi and elbow dysplasi (8), and tools such as efficient population size, breeding structure, and inbreeding statistics (9).

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Notes

8] Pat Long

Berner Garde

In the late 1960's, Barbara and Martin Packard formulated their dreams for the future of the Bernese Mountain Dog. They recognized that health in Berners could not be improved without open sharing of health information. They designed a data base to collect and maintain health information, and began to enter data on Berners that were normal or affected by diseases known or suspected to be genetic in origin.

In 1995 the Berner-Garde Foundation was established. In addition, the Packards were instrumental in founding the Institute for Genetic Disease Control (GDC), an open registry for health certification. This open sharing of information on affected, as well as normal dogs, was unique and has proved to be invaluable to the Bernese community. The GDC's open registries influenced the Orthopedic Foundation for Animals' (OFA) ultimate decision to make information available on affected as well as normal dogs when OFA agreed to absorb several of the GDC registries in 2002.

I joined the board in 1998, and the first thing I was asked to do was to design a new logo. I'm rather proud of the design, and no one has suggested that we need a new one - yet! In late 2003 I agreed to be the file manager, a role I still fill today. My background is in mainframe computers. I am not a breeder, nor do I have any medical background other than what I have learned on my own. Trying to help the database accommodate the needs of ever expanding types of data has been challenging.

Some comparative numbers:

	Nov 2006	July 2011
# People:	19.037	28.032
# Litters:	13.375	25.825
# Dogs:	39.759	77.081
# Health Records:	8.092	14.263
# Certification Records:	25.446	54.878
# Dogs indicated as deceased:	5.008	12.63
# Dogs with actual death date:	4.12	8.389

To break down the entries, dogs come from the following countries based on their primary registry:

	2009	2011
Australia:	70	483
Austria:	9	511
Belgian:		917

Canada:	1.617	9.407
Czeck:		114
Denmark:		701
Estonia:		88
Finland:		1.369
France:		493
Germany:	140	1.193
Great Britain:	90	993
Hungary:	35	534
Ireland:		15
Italy:	5	273
Norway:		1.629
Poland:		80
Portugal:		15
Russia:		116
Slovakia:		72
Slovenia:		50
Spain:		113
Sweden:	40	4.672
Switzerland:	226	2.183
The Netherlands:	19	385
United States:	14.826	42.312

For litters whelped:	**2006**	**2011**
Unknown whelp date:		2.096
before Jan 1970:	184	595
between Jan 1970 and Dec 1979:	587	991
between Jan 1980 and Dec 1989:	2.103	3.066
between Jan 1990 and Dec 1999:	5.093	7.011
between Jan 2000 and Dec 2099:	3.449	11.551
after Jan 2010:		514

Data can be submitted by the owner or breeder, or it can come from public sources of information. All health certifications are verified. Other health information can be entered without verification, but it will be designated as "anecdotal." If it has been verified by a report from a veterinarian or pathologist, it will be designated as "diagnosed."

Site operators are not assigned to us by breed clubs, they are volunteers. We try our best to select people who are meticulous and thorough. But most of all, we try to select people who are good hard workers. You can see from the numbers that a tremendous amount of work has been done by the site operators over the years. We have had far more volunteers over the years, and have taken the time to train them and work with them, only to have them drop out because life circumstances made it impossible for them to dedicate the time. We thank them for trying, it was still a lot of work to read all the material to become an operator.

One other point I like to stress. When dogs disappear off the scene, people talk. I have yet to hear any gossip that is kinder than the facts. The best way to stop gossip is to get the documented information displayed in Berner-Garde. And always remember that absence of data does not mean the absence of problems.

The Bernese Mountain Dog DNA and Tissue Repository was initiated in 2006 to facilitate study. Whole blood can be stored, as well as tumor tissue. This will help to facilitate future studies, and reduce the time needed to acquire sufficient samples for the study.

Last year we added a stud finder query to allow people to look for boys using a variety of search criteria. If owners want their boys designated as available for stud, they can submit a dog submission, or they can email any of the site operators.

In 2008 a geneticist named Dr. Bert Klei used the database to show a relationship between inbreeding and longevity. Dr. Klei found that for Berners over the age of two, each 1% increase of the coefficient of inbreeding equated to about a 3 week reduction in longevity. The average COI of Berners is probably somewhere between 15% and 20%. The average COI appears to show a declining trend over time.

This year we have added a coefficient of inbreeding calculation. It makes complete pedigrees more critical. It allows for the calculation of COI on a test pedigree as well. For those breeders who want to consider inbreeding as one aspect of their breeding decisions, Berner-Garde now has the tool available.

With the importing and exporting of dogs, can we really say that any of us are isolated from problems elsewhere? We can find the studies, we can raise the money to fund them, but we can't have any success with those studies without participants. We need to store DNA from all the Berners we possibly can, and we need health information to be openly shared.

Update on Degenerative Myelopathy

In late 2008 we had the opportunity to begin using a newly developed genetic test for Degenerative Myelopathy. IT is a mutation of the SOD1 gene that is associated with Lou Gehrig's disease (ALS) in humans. But what does this test tell us, and what do we know about the genetics of DM?

As of August 2011:

Results of the genetic test for DM

	At Risk	Carrier	Clear	Total	Allele Frequency
BMDs	179	504	429	1.112	0.39
Total	4.876	5.591	10.907	21.374	0.36

Dogs studied post mortem for DM:

	DM	At Risk	Carrier	Clear
BMDs	15	12	2	1
Total	134	127	6	1

The BMD found to have DM but clear of the SOD1 mutation was found to have a second mutation, one that has not yet been found in any other breed. The 6 dogs in 4 different breeds that had a single copy of the SOD1 mutation are the bigger question. Currently, there is no answer for this, only hypotheses. Are carriers at slight risk? Or like ALS in humans with 140 mutations on 9 genes, could the carrier status be a coincidence and there is some other mutation causing the DM in those dogs? Is there another gene that has an amplifying effect on the SOD1 mutation? I would argue based completely on my own wild speculation that the DM in the carriers (4,4% of all dogs with DM) is more likely to have been caused by a separate mutation, or a combination of mutations. But I'm not a geneticist, and my guess isn't worth a farthing.

The next question of interest is how many Berners found to be at-risk go on to get the disease? This would help us know what the rate of penetrance is. We know that not all at-risk Berners get DM, so there is incomplete penetrance. Are there other modifier genes? Is there something in the environment that plays a role? Exercise, diet, anything? Perhaps more Berners would get DM if they lived longer? This may take us years to learn, if we ever do.

The bigger question for us, however, is how do we make use of the test? We don't want to eliminate all dogs with the gene mutation out of the breeding pool. If the numbers above are an accurate sample, then we would rid ourselves of 61% of the breeding dogs just for this one trait. At a recent conference, I asked how we could best use the test, and a geneticist who is also a breeder had the most sensible suggestion that I had heard to date. Have the test done. Try to have one breeding partner be clear of the mutation. And avoid carrier to carrier matings if there is any indication in either line that relatives may have had DM.

In other words, focus on the whole dog which includes the extended family, breed from as much knowledge as possible (don't trust, verify!), and weigh the risks and benefits - just as you would with all aspects of ANY breeding dog. And having a tool such as Berner-Garde for openly sharing information is one of our best resources for striving to make improvements in the health of the breed.

Notes

9] Speaker - Steve Green

The Berner International Working Group
Steve Green (President)

The Berner-IWG (BIWG) is an international body formed to help the Bernese Mountain Dog by addressing health related issues on an international basis. This is by sharing information and details of health initiatives in different countries, involving experts from around the world and trying to co-ordinate and assist their efforts. The main function though is purely for communication.

The Berner IWG grew out of the International Health meetings which were originally strongly supported and promoted by the Swiss club who have hosted no less than three of these get togethers in 2000, 2002 and 2007. Our thanks must go to the Swiss KBS for their determination to make these events happen and get the ball rolling. From the first event in Langenthal in September 2000 through to the massive event in Burgdorf in 2007 as part of their centenary celebrations the Swiss club has been a constant strong supporter. The other events have been hosted by the SSV in Hohendra, Germany in 2003, the VSSO in Salzburg, Austria in 2005, SIBB in Como, Italy in 2006 and CIABS in Padenhe sul Garda, Italy in 2009 and now 2011 hosted by the BMDC of Great Britain.

The Berner-IWG has a stated aim of improving the average life expectancy of every Bernese to at least 10 years, we refer to this as “Objective 10”.

The Berner-IWG aims to physically meet once every few years in a different country and this is usually allied to a major Health symposium with international speakers. These meetings and seminars are also sometimes organised to coincide with the main BMD Club show of the hosting country so delegates get the chance to see some of that country’s dogs. As you would expect nowadays much activity takes place away from the meetings in the form of emails.

Although appearing formally in 2005, due to the infrequent meetings the Berner-IWG has to be considered as a fairly new group and still finding its feet to a certain extent but is slowly developing and has a strong desire to help the BMD. To keep things as unbureaucratic as possible we try to be as informal as possible. We need to have some gentle rules in order to function but we aim to keep these to a minimum. We deliberately have no powers, no funds, no bank account, no desire to sell puppies, validate breeding, organise shows, approve judges or any of the other activities often seen as power and influence in the dog world in some countries. We are absolutely no threat to the influence of any club and simply a group where the Bernese Mountain Dog clubs of the world are welcome to come together to share all kinds of

information about our beautiful breed. This will be mostly health and sometimes welfare related information but could be anything which helps the breed or even might simply be of interest to Bernese owners in other countries.

People attending the BIWG meetings do so as representatives of their club or other groups from around the world that have a purpose beneficial to the Bernese Mountain Dog. Any significant action will always be through the breed clubs so it is the clubs that should attend the meetings, not individuals in their own right. These representatives then have a responsibility to report back to their clubs. Researchers and scientists actively involved with projects to help our breed are also welcome to attend. In the interests of openness individuals can attend subject to space available but those taking active part in the meeting should be representatives of bona fide BMD breed clubs or acknowledged experts with a link to research to help the breed.

One very important point to understand is that the clubs that engage with the B-IWG have very different backgrounds in which they work. Whilst there may be some similarities from country to country there are often big differences in how the dog world is organised in different countries. The cultures, rules, regulations and even laws that affect them can be very different. For example some countries can publish all information about individual dogs and owners very easily and in other countries nothing can be made public. In some countries hip and elbow information about individual dogs is widely and freely available but in others it is classed as private and cannot be shared without specific permission. Trying to have a rigid system to accommodate all of these or impose a fixed set of recommendations on our members would be impossible as around 20 countries are now represented and this number grows every meeting. Our function can only ever be to encourage clubs to take the best steps they can in their country and share what information they can with the rest of us.

This means we cannot expect everyone to be able to contribute in exactly the same way and why we cannot expect all our members to take the same actions. What works well in one country may even be illegal in another.

So, in reality whatever our ideals we can only come together and share our experiences – both good and bad. This means some cynics will dismiss us as a pointless group because we can only talk about things and cannot enforce any actions. Some say this is a weakness but in many ways it is a strength. People can speak freely without fear of judgement or ridicule. The newer smaller clubs in countries with small BMD populations are especially welcome and they can perhaps learn from the more established breed clubs.

The world we live in is very much about communication and information and I expect all our speakers today and other people involved in projects to help our breed will say how important information is to their work. All real progress has to start with discussion and a willingness to share whatever information we can about our dogs. Pedigrees are increasingly covering more countries and the need for information sharing and knowledge being available will become greater. In our breed we are extremely fortunate to have the marvellous Berner Garde system to record information and make it available to all.

The main thing I hope breed based people like myself go away from these seminars with is enthusiasm to spread the message that something can be done to combat our biggest issues of Malignant Histiocytosis and longevity. The battle against them is progressing day to day, week by week, year by year and some of the front line troops have been speaking here today and the breed is very grateful to them and their colleagues. They are supported by lots of people and clubs within the breed by raising money, and there are some fantastic fund raisers out there who I'm sure could soon put the world money shortages to rights but we should be grateful they are gathering money for the Bernese Mountain Dog instead. They are supported by lots of people who arrange and publicise actual medical support by supporting blood sampling and other real physical support. In terms of the battle these people are providing funds for arms and provisions to support the frontline. However, there are lots more people who actually do very little, they split into two main groups. The first is the deniers, "*we have no big problems or even if we do there is nothing that can be done so just carry on regardless*". There is little hope for these people until they open their minds a little.

The second and much bigger group can be worked on to contribute a fantastic amount to breed health. These are the people who can see the real problems and experience them through their dogs and their friends. They stay in the breed and over the years loose a few dogs to MH and maybe other cancers and some of them at distressingly young ages. They may even attend a health seminar now and again and say all the right things when asked about breed health but …….

Do they consider all health and hereditary aspects of cancer when breeding?
Do they support health funds when asked?
Do they come forward with their dogs at every opportunity to donate blood and tissue samples?
When they do come forward do they bring all their dogs or just the ones they feel will be clear of whatever is being tested for?
Do they join in with all health schemes organised specifically for their breed

Do they openly admit when things have gone wrong in their breeding and try and put it right or do they let dogs disappear to pet homes out of the limelight or say they died of something random?

Many of these questions are not relevant to in some countries as things are very organised and people cannot do absolutely as they wish. However, in other less controlled countries many of these people are not consciously against breed health and may not even question themselves but the simple question people, especially breeders should ask themselves is "*Could I do more for the long term health of my breed even if there is a short term cost to myself?*"

Every time I have attended the International seminars the whilst the subjects of the presentations revolve around MH and longevity the most common subject in the bars and lounges away from the official parts of the week-end is always how to deal with lack of interest from so many owners and breeders. This is a common problem across the world of dogs in all breeds and whilst some countries seem to have a good mentality for addressing these things other do not seem to be making much progress and those of us who wish to make progress in health matters need to learn how these progressive countries manage to interest people.

Constantly lacking support and interest can be very demoralising for those trying to promote breed health but getting together at these International events can help all the health co-ordinators from different countries learn from each other and return to their countries with new enthusiasm and ideas.

The B-IWG is there for the Bernese clubs to use to help each other through communication. I ask that the message you take back to your clubs and countries is to support the B-IWG because purely and simply it is there to help the Bernese Mountain Dog. On that point we still need someone to volunteer to host our next meeting……!!

More details of the B-IWG and links to various BMD health related pages can be found on the web site at www.berner-iwg.org

Notes

Section 2

The Projects and the Contributors

1] **Longevity Project (Finland)**
Dr Katariina Mäki

2] **Histiocytic Sarcoma Project (Denmark)**
Dr Lise Nielsen

3] **Copan's Place (USA)**
Amy Baklund (*also attending seminar)*

4] **Classification of Malignant Histiocytosis Cases Project (Netherlands)**
Dr Gerhard Rutteman *(represented at seminar)*

5] **Malignant Histiocytosis at the Ostrander Lab (USA)**
Gretchen Carpintero

6] **Histiocytic Sarcoma and Links to Joint Injury (European Study)**
Lotte van Kuijk

7] **New Treatments for Malignant Histiocytosis Project (USA)**
Dr Scott Hafeman & Dr Steven Gow

The Bernese Mountain Dog Club of Great Britain is extremely grateful to all the above who took time to prepare and forward the following summaries of their work to share with the Bernese community.

Breeding for Longevity in the Bernese Mountain Dog

Interim report May 2011
Katariina Mäki, PhD (anim.sci)

Introduction

Bernese Mountain Dog (BMD) is among the dog breeds with the shortest lifespan. Reason for this is thought to be the high frequency of cancer in the breed. To survey the situation, the Swiss Mountain & Cattle Dog Club of Finland started routine gathering of data on lifespan and causes of death in 1995. In addition, the breed club has received data from Switzerland. The aim of this study is to analyse this data and to study possibilities to breed for longer life.

Materials

Three data sets were used in the study: registration data of the Finnish Kennel Club (FKC) as well as longevity data and Still Going Strong -data gathered by the breed club.

The registration data included all dogs that were registered in Finland. These data were used in statistical analyses for building pedigrees for the dogs in the other two data sets. The recorded information were date of birth, gender, breeder identification, and registration numbers of the dog and its parents. Breeder identification was not used in analyses, as it was noticed that some dogs had more than one breeder number.

The longevity data was provided in three pieces: data on Finnish, Swiss and German dogs. In May 2011, data on 1186 Finnish BMD individuals is available. Of the Swiss data set, 313 dogs could be linked to the pedigrees of the Finnish dogs and so exploited. The data on German dogs included 49 individuals that are closely linked to Finnish dogs. This data set has been gathered from SSV-Kurier, the magazine of the German breed club. The longevity data contained altogether 1548 dogs. It comprised of name, date of birth, date of death, cause of death (only for 792 Finnish dogs), gender, as well as registration numbers of the dog and its parents. The parents were recorded mainly only for dogs that were not included in the registration data of the FKC.

Still Going Strong -data included Finnish dogs that were known to be alive at the age of 8 years or older. This data set comprised of the same information as the longevity

data, but instead of the date of death, it included the date at which the dog was last known to be alive. This data set holded 276 dogs.

Foreign dogs in the longevity data that were not registered in Finland were added to the registration data. After this, a litter identification was established for each dog for which the registration numbers of the parents as well as the date of birth was known. The dogs born at the same day for the same parents were assumed to form a litter. Finally, using the registration data, gender was added for the dogs that were lacking this information in the longevity data.

The dogs in the longevity data had been born between the years 1959-2009, and they had died between 1968-2011 (Table 1). They came from 411 different sires and 704 different dams. There were 63 dogs with no sire and dam recorded, and thus lacking also the litter identification. The rest of the dogs came from 977 different litters. There were 709 female and 655 male dogs. Information on gender was missing for 184 dogs.

Table 1. Birth and death years for the dogs in the longevity data. For example, of the dogs that were born during the years 2000-2004, 221 died during 2005-2010.

Birth year	Death year				
	Before 1989	1990-1994	1995-1999	2000-2004	2005-2010
Before 1985	53	77	22		
1985-1989	4	71	151	32	
1990-1994		22	102	242	55
1995-1999			12	119	295
2000-2004				19	221
2005-2009					51

Methods

Survival analysis (software package Survival Kit by Ducrocq et al. 2010) was used to define the hazard function of each individual (i.e., its limiting probability of dying at time t, given it is still alive just prior to t). Individual hazard function is a product of a baseline hazard function and a positive (exponential) function of explanatory covariates (Ducrocq et al. 2010). The model was univariate proportional hazards model with a single response time, and both the longevity data and the Still Going Strong -dogs were included in the analysis.

Variance components and heritability of lifespan were estimated with linear mixed (animal) model using restricted maximum likelihood, REML (software package VCE4.0 by Neumaier and Groeneveld 1998). Two different data sets were used in this estimation: longevity data either including or excluding the dogs of the Still Going Strong -data set.

The statistical models included statistically significant explanatory covariates that were available in the data: gender, combination of birth and death year, litter, and country (Finland / Switzerland / Germany). Litter was a random covariate, and all the others were fixed. Significance of the fixed covariates was tested with likelihood ratio tests using Survival Kit.

Preliminary results

The most frequent lifespan of the Bernese Mountain Dogs in the longevity data was 9-10 years (Figure 1). The mean lifespan was 8.3 years. Six percent of the dogs had died at two years or younger, 13 percent at four years or younger, 26 percent at six years or younger, and 48 percent at eight years or younger. The longevity data may, however, be somewhat skewed, since the breed club has encouraged people to give information especially on dogs that live a long life. The frequency of these dogs is quite high in the data, while many dogs that have died younger may not be included in the data at all.

Using both longevity data and Still Going Strong -data, survival analysis reported the probability of a dog to be alive above nine years to be 95.3 %. However, the probability started to diminish soon after this (Figure 2). Probability to live longer than 10 years was 75.6 %, longer than 10.5 years 44.2 %, and longer than 11 years 7.9 %. These figures are positively skewed, since almost all the dogs included in the Still Going Strong -data set were old. In the future it would be useful to record also younger dogs in this data set.

The dogs that were born during 1970-1984 lived on average one year longer compared to the dogs that were born in the late 1980s and early 1990s (Table 2). Most of the dogs that were born during 2000-2009 are still alive, and their average lifespan in the Table 2 will thus rise in the future.

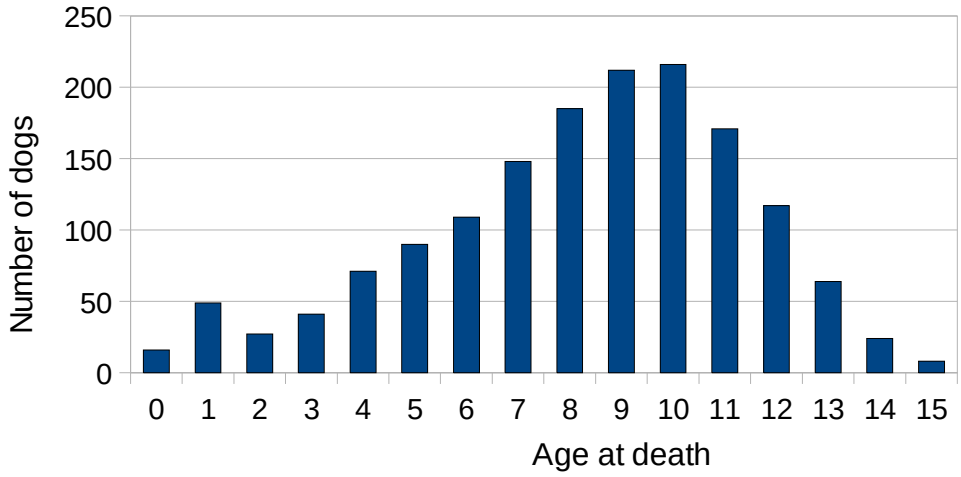

Figure 1. Distribution of the lifespan of the dogs in the longevity data.

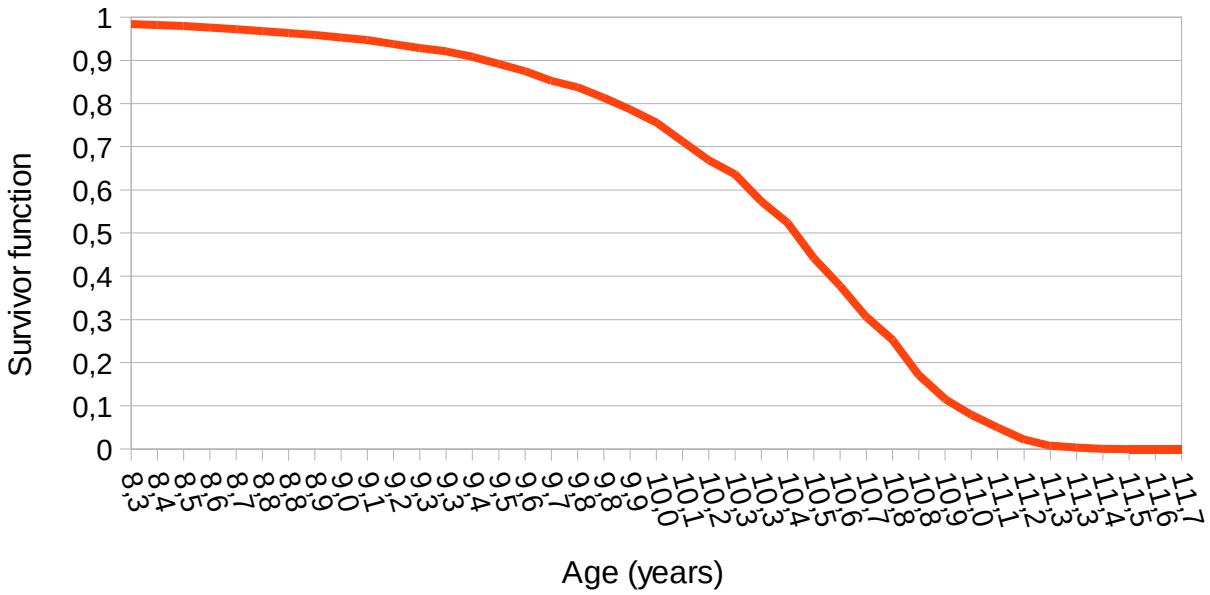

Figure 2. Probability of a Bernese Mountain Dog to be alive above certain age

Table 2. Mean and mode (most frequent) age at death for different birth periods and the proportion of dogs that died before the age of five years.

Birth year	Number of dogs	Mean	Mode	% died before 5
1959-1969	9	9.7	NA	22 %
1970-1979	57	9.5	10	12 %
1980-1984	86	9.7	10-11	3 %

1985-1989	258	8.8	11	9 %
1990-1994	421	8.8	10	9 %
1995-1999	426	8.7	10	7 %
2000-2004	240	6.5	8	20 %
2005-2009	51	1.9	1	98 %

Average age of death because of a health problem was seven years

The most frequent cause of death was cancer (332 dogs; Figure 3). In addition, problems in the immune system included 18 deaths. The next frequent cause of death was other reason (118 dogs), then came musculoskeletal problems (96 dogs), other (mainly internal organ) diseases (82 dogs), and old age problems (54 dogs).

Distribution of the causes of death has been quite uniform during the years (Figure 4). Old age as a cause of death seems to have decreased – partly because the oldest dogs that have been born in the 1990s and especially in the 2000s are still living, and partly because disease diagnostics has evolved. A dog that is being euthanized at an old age has nowadays often also a diagnosis.

Dogs whose cause of death was a disease (cancer, immunological problems, musculoskeletal problems, and other, mainly internal organ, diseases) lived approximately seven years (Table 3). Dogs that were euthanized because of behaviour problems or died in accidents or poisoning lived on average 3.5 years, and dogs that were euthanized because of old age problems lived on average 12 years.

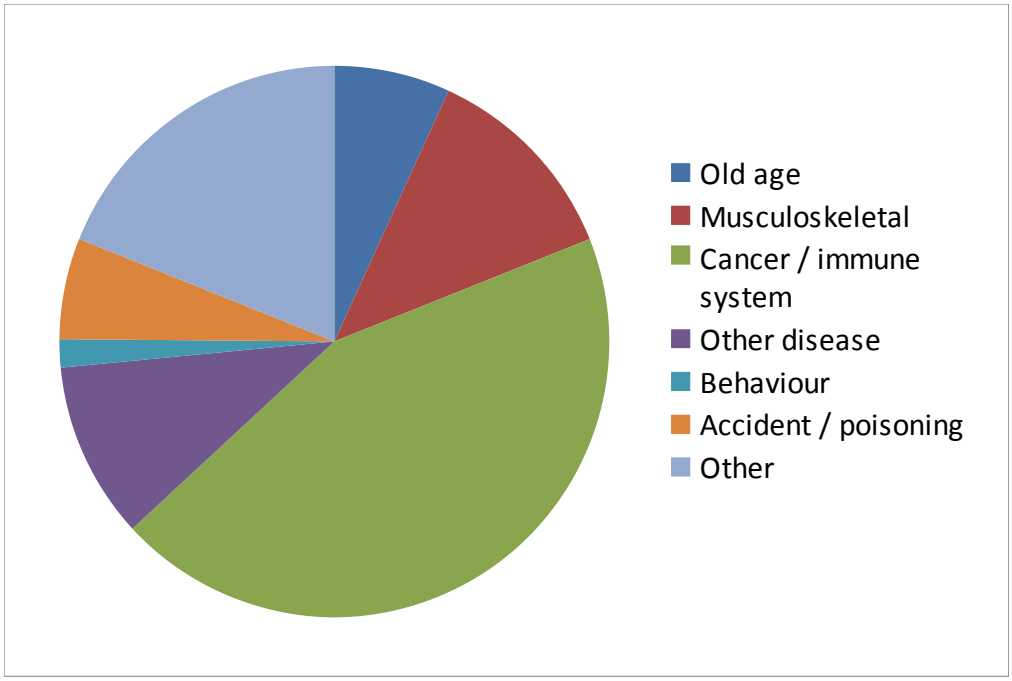

Figure 3. Causes of death in the longevity data (792 dogs).

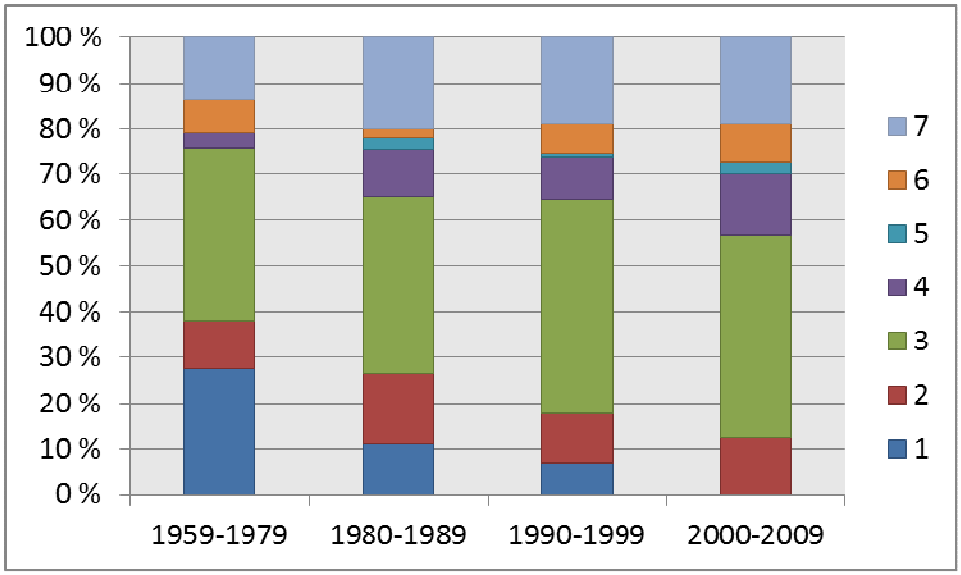

Figure 4. Distribution of the causes of death in different decades. 1 – old age, 2 – musculoskeletal, 3 – cancer / immune system, 4 – other disease, 5 – behaviour, 6 – accident / poisoning, 7 – other.

Table 3. Mean, minimum and maximum lifespan for different causes of death.

Cause of death	Number of dogs	Lifespan in years		
		Mean	Minimum	Maximum
Old age	54	12.0	7	15
Musculoskeletal	96	6.9	below 1	13
Cancer / immune system	350	7.4	1	13
Other disease	82	7.1	below 1	13
Behaviour	13	3.6	1	9
Accident / poisoning	47	3.5	below 1	11
Other	150	6.9	below 1	14

Genetic analyses

Preliminary estimates of heritability for lifespan were 0.15 (Still Going Strong -dogs included) and 0.14 (Still Going Strong -dogs excluded), with standard errors of 0.04 and 0.05, respectively. This means that 14-15 % of the variation between the dogs is due to additive genetic effects. Heritability for different traits may vary between 0 and 1, and when the value is higher than zero, it is possible to breed for the trait. The higher the heritability, the faster the possible genetic gain.

Proportion of variance accounted for by the litter effect was 35 % (Still Going Strong -dogs included) and 34 % (Still Going Strong -dogs excluded). The standard error for both these estimates was 3 %. Litter effect consists of (other than additive genetic) factors that cause differences in lifespan between litters, such as effects of dominant alleles, and interaction effects between alleles at different loci (epistacy), as well as environmental factors, such as diet.

Experimental breeding values have been estimated both with best linear unbiased prediction (BLUP) and survival analysis. The software packages PEST (Groeneveld 1990) and Survival Kit have been used for this purpose, and the statistical models have been the same as described in Methods section. Both methods are able to use all information from all the relatives of the dog in the data, and simultaneously take the environmental effects into account.

With BLUP, breeding values have been estimated both including and excluding the dogs of the Still Going Strong -data set. Breeding value estimates (EBVs) have been standardized so that the population mean is 100 and the standard deviation 10. This means that most of the dogs have an EBV that settles inside a normal distribution curve, that is between 70-130. The higher the EBV, the better is the dog's breeding value for longevity.

Breeding value estimates of survival analysis are given as risk ratios (RRs). For example, dogs with RR = 1.2 are expected, on average, to have a 20 % higher risk of death at any given age compared to dogs with an average RR (1.0).

Conclusion

Based on preliminary analyses, heritability of longevity in the Bernese Mountain Dog is decent enough to allow breeding and genetic gain in the trait. Developing a routine for breeding value estimation using the data of the breed club seems to be possible, but the best method and model cannot be clarified before more longevity data are available. Until then, the experimental estimates can be used. They have been sent to the breed club, and will be updated a few times a year.

In the next stage of the study, genetic and phenotypic correlations between lifespan and hip and elbow dysplasia will be estimated, and effect of inbreeding on lifespan studied. There are also a number of other variables that may have an effect on lifespan, but at this moment it is impossible to take all of them into account in analyses because there is no recorded data on them. In the future it may be advantageous to record for example the weight of the dog, the age of the possible spaying or neutering, and whether the household has more than this particular dog. Also it would be important to record the cause of death for each dog, since it makes a huge difference in breeding value estimation whether the dog died because of an accident or because of a disease. In addition, it would be useful to include also younger dogs in the data set of dogs that are still alive.

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Lise Nielsen

Disseminated histiocytic sarcoma in the Bernese Mountain dogs;

Characterisation of healthy animals and the search for early disease related biomarkers.

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It has been reported from several studies throughout the world that Bernese Mountain dogs have a high prevalence of cancer, and in particular of disseminated histiocytic sarcoma. In 2006, we performed a questionnaire study in Denmark where we found that most Bernese Mountain dogs had died or were euthanased by the age of 7 years old. The dogs seemed to be of increased risk of dying of cancer after the age of 5 years old and it appeared plausible that the disease was inherited similar to what had been detected in other countries.
We therefore set out to perform a screening study of Bernese Mountain dogs, which were predisposed to develop disseminated histiocytic sarcoma. In human oncology, screening programs with incorporated biomarkers are developed in an attempt to detect cancer at an early stage, thereby reducing cancer morbidity and mortality. Such screening studies in people include breast cancer studies and ovarian cancer studies where blood borne protein may be increased depending on the severity of the disease or when the disease return after therapy has been ended.
We hypothesised that biomarkers for early detection of disseminated histiocytic sarcoma exist in Bernese Mountain dogs. Danish Bernese Mountain dogs were subsequently screened every 6 months over a period of 2.5 years. At each screening visit, the dogs were examined thoroughly and all dogs had a clinical examination performed along with blood analysis, diagnostic imaging and urinalysis. In order to define possible blood borne biomarkers, breed specific reference intervals for healthy dogs were initially established for haematology, serum biochemistry and

selective haemostatic analytes. Ten analytes were found to deviate from standard laboratory reference intervals (table 1) indicating that healthy Bernese Mountain dogs appeared to differ substantially from other breeds in particular with regards to some of the liver parameters (AP, GGT). Nine out of ten analytes were considered to be breed specific variation while the tenth analyte, activated partial thromboplastin time (a blood clotting parameter), was considered an abnormality due to the presence of specific antibodies present in this subgroup of Bernese Mountain dogs for unknown reasons.

Parameter	Laboratory Reference interval	Reference interval for Bernese Mountain Dogs	Unit
White blood cell count	6.5-18.1	6.5-18.1	10^9/L
Neutrophil count	3.2-12.1	3.2-12.1	10^9/L
Lymphocyte count	1-4.8	1-4.8	10^9/L
Monocyte count	0-1.2	0-1.2	10^9/L
*Eosinophil count	0-1.2	**0-1.5**	10^9/L
Basophil count	0-0.05	0-0.05	10^9/L
MCV	60-77	60-77	Fl
*MCHC	19.23-21.09	**21.21-22.17**	nmol/l
Red Blood Cells	4.6-8.4	4.6-8.4	10^{12}/L
hæmoglobin	7.4-11.8	7.4-11.8	mmol/L
Haematocrit	0.39-0.59	0.39-0.59	L/L
Platelet count	200-500	200-500	mia/L
ALT	6-102	6-102	U/L
*AP	19.8-174	**0.0-464**	U/L
*GGT	0-6.6	**0-12.2**	U/L
Glucose	3.9-6.55	3.9-6.55	mmol/L
Urea	3.3-9.4	3.3-9.4	mmol/L
Creatinine	40-130	40-130	umol/l
*Amylase	186-798	**285-1255**	U/L
Lipase	6-498	6-498	U/L
*Cholesterol	3.50-6.99	**5.29-10.08**	mmol/L
*Total Bilirubin	1.0-5.0	**0.0-3.0**	µmol/L
Albumin	26-44	26-44	g/L
Total protein	57-82	57-82	g/L
Resting Bile acids	1-6.41	1-6.41	µmol/L
Calcium	2.2-3.3	2.2-3.3	mmol/L
Magnesium	0.63-1.05	0.63-1.05	mmol/L
Phosphate	0.91-1.96	0.91-1.96	mmol/L
Sodium	142.4-153.64	142.4-153.64	mmol/L
Potassium	3.81-5.07	3.81-5.07	mmol/L
PT	< 8	< 8	Sec
*aPTT	<12	**-100**	Sec
Fibrinogen	1-4	1-4	g/L
D-dimer	0-0.5	0-0.5	mg/L
vWf:ag	70-180	70-180	%
TEG(R)	3-9	3-9	Min
TEG(K)	2-7	2-7	Min
*TEG(MA)	39-59	**41-73**	Mm
TEG(angle(a))	28-59	28-59	Degrees
*TEG(G)	3.2-7.2	**2.7-10.9**	K

Table 1: Reference intervals for Bernese Mountain dogs and the standard laboratory reference interval. The highlighted intervals are different from the standard.

MCV: mean corpuscular volume, MCHC: mean corpuscular haemoglobin concentration, AP: alkaline phosphatase, GGT: γ- glutamyltransferase, PT: prothrombin, aPTT: activated thromboplastin time, vWf:ag: von Willebrand factor antigen, TEG: thromboelastography. * marks the analytes which had a new reference interval generated.

The screening study successfully identified all dogs with early disseminated histiocytic sarcoma using diagnostic imaging along with routine and advance blood analysis. Routine blood parameters such as haematocrit, platelet count, white blood cell count, monocytes, calcium and albumin were not useful for detection of diseased dogs. However during the screening study, the dogs with early disseminated histiocytic sarcoma had significantly higher serum ferritin concentration than healthy Bernese Mountain dogs. We therefore concluded, that a combination of imaging and blood analysis might identify early disseminated histiocytic sarcoma if performed every six months after the age of 4 years old in Bernese Mountain dogs. We are subsequently continuing to look for biomarkers of cancer but also trying to characterise the immune system in healthy and diseased Bernese Mountain dogs in more detail, as we believe that defaults in the immune system may participate and part of the basis of the histiocytic sarcoma seen in Bernese Mountain dogs.

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Notes

COPAN'S PLACE

FIGHTING CANCER, FOUR PAWS AT A TIME.

Background of Copan's Place

Copan, the Bernese Mountain Dog, did amazing things in his very short time here on Earth. Copan showed kindness and courage with everything he did. Copan loved to hike, was a therapy dog listening to children read books, and most of all just loved to be with his people. Including me.

Cancer touched Copan's life twice. He helped me through my battle against breast cancer. He was the one who would quietly lie in the room at night by my bedside when everyone else had gone home. He was always by my side to cheer me on with his happy smile and wagging tail. Through all 26 weeks of chemo he lovingly guided me on small walks to keep my spirits up and keep me smiling through those difficult days. He even said it was okay if we skipped a day now and then.

After helping cure his owner of breast cancer, Copan then had to battle cancer himself. Copan lost his battle with a histiocytosis cancer on January 7, 2008 at the age of six. Unfortunately, the cancer was too aggressive and made him too weak to survive a trip to get radiation and then the stem cell transplant. Copan lost his battle with cancer on the same day I had been diagnosed three years earlier.

Meeting Dr. Edmund Sullivan who had this leading- edge treatment for treating dogs with cancer, I knew I had to do something to make this treatment available worldwide. I couldn't watch another animal suffer so much from cancer.

After Copan's death, my wish was to help other dogs faced with cancer and build a worldwide facility where dogs could have a chance to be treated and survive. So I created Copan's Place, a non-profit 501C-3 foundation, named after such an amazing and courageous dog.

To date we have treated over 80 dogs over the total U.S. and they are in complete remission.

Amy

Amy Baklund
Founder and Executive Director

Interview with Dr. Edmund Sullivan

Q: How does this leading-edge treatment work?

A: We collect stem cells from the dog's bloodstream while using a machine similar to a dialysis machine. The dog undergoes total body irradiation without the stem cells to kill any remaining tumors, and the harvested stem cells are then re-infused into the dog so a new immune system can develop and save the dog's life, if all goes well.

Q: How did you learn the technique?

A: I contacted Dr. Rainer Storb at Fred Hutchinson and told him I had a dog with lymphoma. He told me, "I've been waiting 25 years for this phone call." He invited Theresa and I to come to Fred Hutchinson and gave us the opportunity to learn this technique (which originated when dogs were used to develop bone marrow transplant treatments for humans). Things have come full circle now, with the ability to treat dogs. Dr. Sullivan's work has been published in the JAVMA. JAVMA—05-06-0281—CR—Lupu—4fig—0tab—VLS—BGM

Q: How many dogs have you treated?

A: I've been involved in the successful treatment of about 80 dogs after helping to train doctors at North Carolina State University, Los Angeles, New York and San Diego. About 20 of the dogs are in the Seattle area.

Q: Where will Copan's Place be located?

A: We envision a centrally located area like Kirkland, Washington. We need a treatment center and linear accelerator because we've been using two other hospital facilities. The travel and stress do not create an ideal situation so we want to be close to an international airport where we can easily pick the dogs up and take them directly to Copan's Place.

Q: What are your financial needs?

A: We've raised $250,000 already and our goal is to raise $1 million to create a fully dedicated structure for Copan's Place housing the linear accelerator the key piece of equipment needed to do the transplants.

JAVMA—05-06-0281—CR—Lupu—4fig—0tab—VLS—BGM

Use of multigeneration-family molecular dog leukocyte antigen typing to select a hematopoietic cell transplant donor for a dog with T-cell lymphoma

Marilena Lupu, DVM; Edmund W. Sullivan, DVM; Theresa E. Westfall, DVM; Marie-Térèse Little, PhD; Benjamin J. Weigler, DVM, PhD, DACLAM, DACVPM; Peter F. Moore, BVSc, PhD, DACVP; Patrice A. Stroup, BS; Eustacia Zellmer, BS; Christian Kuhr, MD; Rainer Storb, MD

Case Description—A 7-year-old Golden Retriever was examined because of anorexia, lethargy, vomiting, and gradual weight loss.

Clinical Findings—Splenomegaly, pancytopenia, high serum calcium concentration, and alkaline phosphatase activity were detected. Magnetic resonance imaging revealed an enlarged mesenteric lymph node and increased signals from the bone marrow of the ilium and vertebral bodies. Histologic examination and immunophenotyping of biopsy specimens confirmed a stage V (b) T-cell malignant lymphoma.

Treatment and Outcome—Clinical remission was attained by use of 2 chemotherapy cycles, followed by an allogeneic hematopoietic cell transplant performed at 18 weeks after diagnosis. A donor was identified by molecular dog leukocyte antigen typing methods. The patient was conditioned with 2 fractions of 4 Gy total body irradiation delivered 3 hours apart at 7 cGy/min, followed by an IV infusion of recombinant canine granulocyte colony-stimulating factor mobilized leukapheresis product and postgrafting immunosuppression with cyclosporine. Chimerism analyses revealed full donor engraftment that has been maintained for at least 58 weeks after transplant. Remission has been confirmed by normal results of serum thymidine kinase assays and the absence of peripheral blood clonal T-cell receptor gene rearrangements.

Clinical Relevance—Systemic chemotherapy induces remissions; however, most dogs succumb to disease recurrence because of multidrug resistance. Outcome of allogeneic hematopoietic cell transplantation in dogs can be excellent because of improved donor-recipient selection by use of molecular dog leukocyte antigen typing, compared with early attempts, and better prevention of graft versus host disease, better supportive care, and substitution of peripheral blood mononuclear cells for bone marrow. (*J Am Vet Med Assoc* 2006;228:728–732)

A 7-year-old neutered male Golden Retriever that weighed 37.5 kg (82.5 lb) was clinically evaluated at Bellingham Veterinary & Critical Care in February 2004. The dog had a 20-day history of anorexia, lethargy, and vomiting and had 10% weight loss during the preceding 2 months.

Clinical examination revealed an enlarged spleen without peripheral lymphadenopathy. Hematologic examination revealed pancytopenia and mild anemia. No atypical cells were identified in a blood specimen. Ionized and total serum calcium concentrations were high (1.82 mmol/L and 14.9 mg/dL, respectively), and parathyroid hormone concentration (1.5 pmol/L) was low. In addition, parathyroid hormone–related protein concentration was slightly high (1.2 pmol/L). Serum alkaline phosphatase activity (205 U/L) was high, as was BUN concentration (32.1 mg/dL). Thoracic and abdominal radiography confirmed splenomegaly. Magnetic resonance imaging[a] revealed an enlarged mesenteric lymph node and generalized homogeneously increased signals from the bone marrow of the ilium and vertebral bodies. On the basis of these findings, splenectomy was performed, followed by mesenteric lymph node, liver, kidney, duodenum, and skin biopsies. In addition, bone marrow biopsy specimens were obtained from the iliac crest.

Histologic examination of the spleen and biopsy specimens confirmed multicentric lymphoma in the spleen, mesenteric lymph node, and bone marrow. Monomorphic, medium to large lymphocytes with irregular nuclear membrane contours expanded the periarterial lymphoid sheaths of the splenic white pulp and encroached on the follicular areas. The atypical cells invaded the splenic red pulp and trabeculae multifocally. Extramedullary hemopoiesis was also observed in the splenic red pulp. Infiltration of similar monomorphic lymphocytes expanded the paracortical regions of the

COAP	Cyclophosphamide, vincristine, cytosine arabinoside, prednisone
DLA	Dog leucocyte antigen
SSCP	Single-stranded conformational polymorphism
PBMC	Peripheral blood mononuclear cell
HCT	Hematopoietic cell transplantation

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Dr. Lupu is the recipient of a fellowship in Oncology and Transplantation Biology from National Institutes of Health, Bethesda, Md.

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mesenteric lymph node, compressed lymphoid follicular regions, and invaded lymph node trabeculae, but spared the capsule. In this location, the atypical lymphocytes included up to 6 mitotic figures/hpf (40X objective). The bone marrow contained isolated nests of atypical lymphocytes. Histologic examination of liver, kidney, duodenum, and skin did not reveal involvement by lymphoma.

Immunophenotyping of the splenic and mesenteric lymph node infiltrates confirmed that the lymphoma was of T-cell origin (CD3+). Genomic DNA was extracted from paraffin-embedded sections of the mesenteric lymph node and spleen for T-cell (T-cell receptor γ locus) and B-cell antigen receptor rearrangement (immunoglobulin heavy chain locus) analysis.[1] Duplicate PCR reactions were performed for each tissue analyzed and revealed consistent clonal T-cell receptor γ rearrangements in the spleen and mesenteric lymph node. Clonal immunoglobulin heavy chain rearrangements were not observed. The morphologic, immunohistochemical, and molecular clonality results confirmed that the atypical lymphoid infiltrates consisted of a clonal T-cell population. These findings, combined with the clinical signs, were consistent with a stage V (b) T-cell malignant lymphoma, according with the World Health Organization Staging System of Canine Lymphoma.[2]

Induction of remission was undertaken by administration of cyclophosphamide (50 mg/m^2, PO, q 48 h), vincristine (0.56 mg/m^2, IV, weekly), cytosine arabinoside (100 mg/m^2, SC, q 12 h), and prednisone (50 mg/m^2, PO, q 24 h; COAP protocol).[3]

After 2 weeks of COAP chemotherapy, the dog developed pancytopenia, anemia, anorexia, and acute bilateral pyoderma on the forelimbs, and transfusion support was initiated by use of dog erythrocyte antigen 1.1-negative compatible packed RBCs. In an attempt to prevent sepsis and bleeding, chemotherapy was discontinued and filgastrim[b] (5 μg/kg [2.3 μg/lb], SC, q 12 h) was administered for 5 days. Chemotherapy was then reinstituted with cyclophosphamide (50 mg/m^2, PO, once) and prednisone (20 mg/m^2, PO, q 48 h), and a 2-month remission was achieved.

Relapse was made evident by the appearance of lymphoblasts (2%) with high nuclear-to-cytoplasmic ratio in the blood, accompanied by increased serum calcium concentration (14.1 mg/dL). In addition, the dog developed anemia; lymphocytopenia (280 cells/μL); azotemia (BUN, 52 mg/dL); and increased serum activities of alkaline phosphatase (435 U/L), alanine aminotransferase (110 U/L), and aspartate aminotransferase (64 U/L). A second remission induction with cyclophosphamide (50 mg/m^2, PO) and prednisone (20 mg/m^2, PO, q 48 h) was attempted; however, after a single dose of cyclophosphamide, whole-blood transfusion was required for severe thrombocytopenia. One week later, a single dose of *Escherichia coli* L-asparaginase (20,000 U/m^2, IM) was given. A second remission was achieved; atypical lymphocytes disappeared from the blood, and hypercalcemia resolved.

To find a suitable HCT donor, DLA typing of 29 family members from 4 generations of dogs located in 3 countries was performed at the Fred Hutchinson Cancer Research Center. Blood samples from each dog were obtained for DNA extraction via standard protocols.[4] The DNA samples were tested for highly polymorphic microsatellite markers[5,6] in the DLA class I (FH 2200) and DLA class II (FH 2202) regions by use of a variable number tandem repeat-PCR method[5] and specific 2200 and 2202 primer pairs.[7,8,c] Results were analyzed by use of electrophoresis on 6% polyacrylamide gels prepared with a sequencing system kit.[d] Interpretation of the banding patterns suggested that 5 family members were DLA matched for both DLA class I and class II regions with the affected dog. For confirmation, the DLA class II

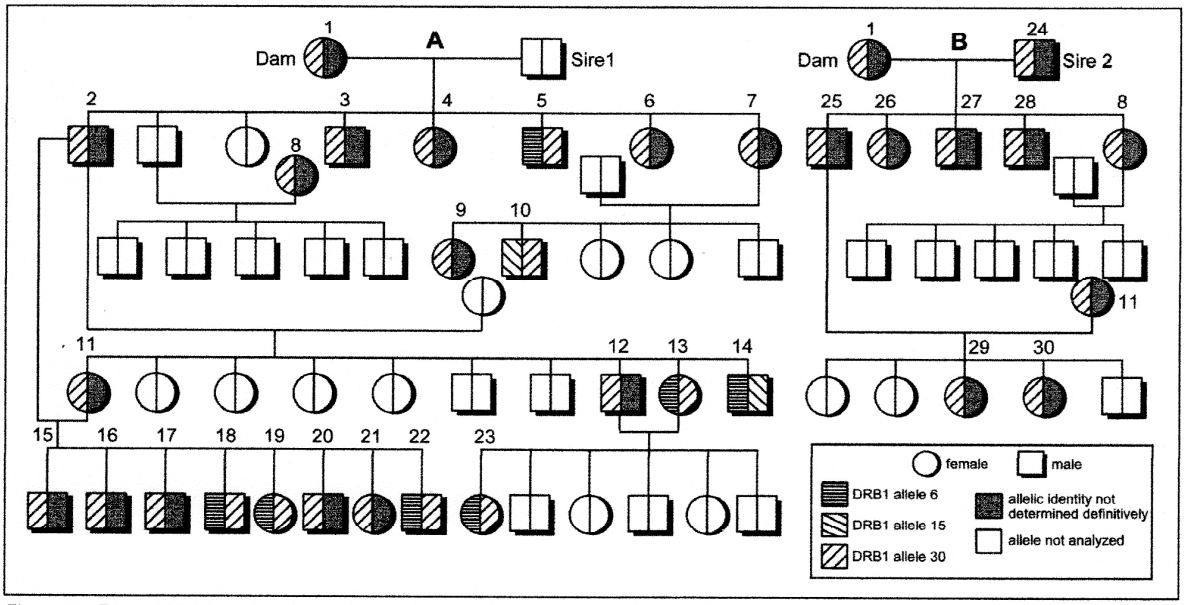

Figure 1—Four-generation genealogy and genotyping profiles of family members of a dog with T-cell lymphoma receiving an HCT from a DLA-matched related donor. A—Affected dog's dam's first litter. B—Affected dog's dam's second litter. 1-30 = Dogs for which blood samples were evaluated for highly polymorphic microsatellite markers within DLA class I and class II regions, and DLA class II DRB1 allele sequencing. A3 = Affected dog. A15, A17, A21, B29, and B30 = Dogs matched with the affected dog on the basis of results of segregation analysis of the polymorphisms and DRB1 allele sequencing. A17 = Dog selected as donor.

DRB1 hypervariable region[4,9] was amplified by use of an SSCP-PCR method[10,11] and specific IC and ID primers.[11,c] Results were analyzed by electrophoresis on 0.5% mutation detection enhancement gels[e] that revealed identical banding patterns for those dogs identified as matched by segregation analysis of microsatellite polymorphisms. The interpretation of DRB1 allele banding patterns was not sufficient for histocompatibility assessment because different DRB1 alleles could have the same size and identical banding patterns. Therefore, DRB1 allele sequencing was performed by use of a genetic analyzer[f] to identify potential allelic disparities on the basis of nucleotide alignments. Among the 30 dogs from which sequences were analyzed with the software,[g] 3 DRB1 alleles were identified: alleles 6, 15, and 30 (**Figure 1**). The affected dog shared the same DLA-DRB1 allelic sequence profile with the 5 dogs identified to be matched on the basis of the segregation analysis of microsatellite polymorphisms and SSCP gel banding patterns. Among the DLA-matched relatives, a 13-month-old male that weighed 29.5 kg (65 lb) was selected as the HCT donor. The donor's blood group was DEA1.1 negative.

The HCT was performed 18 weeks after diagnosis and 1 month after the second induction chemotherapy, while the dog was still in remission. Two weeks before transplantation, 240 mL of blood was collected from the intended donor and stored for the purpose of priming the apheresis machine. To avoid transmission of any potential blood-borne pathogens to the recipient, the donor was screened for *Dirofilaria immitis*, *Ehrlichia canis*, *Ehrlichia equi*, *Babesia canis*, *Borrelia burgdorferi*, and *Rickettsia rickettsi*.

For mobilization of PBMCs, the donor was given recombinant canine granulocyte colony–stimulating factor[h] (5 µg/kg [2.3 µg/lb], SC, q 12 h, for 5 consecutive days). Leukapheresis was performed with a 12-F, 20-cm dual-lumen central venous catheter[12,i] and a continuous flow blood separator,[j] with acid citrate dextrose solution as an anticoagulant. The PBMC collection lasted 4 hours with the donor under general anesthesia while body temperature, respiratory rate, and pulse rate were monitored. Electrolytes and the hematologic profile were evaluated every hour by use of a portable clinical analyzer.[k] To avoid anticoagulant-induced calcium depletion, 10% calcium gluconate was administered throughout the apheresis procedure via IV pump injection, at 10 mL/h. The donor's body temperature was maintained by use of microwave heating pads. The apheresis product contained 92 × 10^3 nucleated cells/µL and 0.36 × 10^3 CD34+ cells/µL. The CD34+ cell count was analyzed via flow cytometry by use of a canine anti-CD34 biotin–conjugated monoclonal antibody.[13,l] The affected dog was given 2 fractions of 4 Gy total body irradiation with an interfraction interval of 3 hours, delivered at 7 cGy/min from a 4-MV clinical linear accelerator.[m] Immediately after irradiation, the dog was given an IV infusion of 440 mL of freshly isolated PBMCs containing 3.6 × 10^6 CD34+ cells/kg (1.6 × 10^6 CD34+ cells/lb; **Figure 2**).

Post-HCT immunosuppression was attained by administration of cyclosporine (5 mg/kg, PO, q 12 h), from the day before HCT until day 35 after HCT. Cyclosporine blood concentration was evaluated twice weekly by use of a monoclonal whole-blood assay.[n] To achieve therapeutic concentrations ranging from 400 to 600 ng/mL, as measured by the monoclonal whole-blood assay, the cyclosporine dose was adjusted to 4.5 to 5.5 mg/kg (9.9 to 12.1 mg/lb). The CBC was assessed daily until the WBC concentration exceeded 1,000 cells/µL and platelet concentration exceeded 30,000 platelets/µL, when frequency of CBC was reduced to once per week. Serum biochemical analyses were performed daily to monitor liver and kidney functions.

Supportive treatment after HCT included administration of lactated Ringer's solution (13 mL/kg [5.9 mL/lb], SC, q 12 h) and 20% fat emulsion[o] in lactated Ringer's solution (6.5 mL/kg/h [3 mL/lb/h], continuous rate infusion) administered via IV catheter, which was maintained for 4 days after HCT; thereafter, the dog was given nutrition PO. Antimicrobials, consisting of neomycin sulfate (6 mg/kg [2.7 mg/lb], PO, q 8 h), polymyxin B sulfate (25,000 U/kg/d [11,364 U/lb/d], PO, q 8 h), and enrofloxacin (10 mg/kg [4.5 mg/lb], SC, q 24 h), were administered until the WBC concentration exceeded 1,000 cells/µL. *Lactobacillus* GG[p] (80 mg, PO, q 12 h) was administered as a balanced probiotic. During the first week after HCT, the dog lost 12% of baseline body weight, all of which was regained during the following month. On day 14 after HCT and hospitalization, the dog was released to its owners, with continuation of administration of the cyclosporine, enrofloxacin, and *Lactobacillus* GG.

Hematopoietic engraftment was evident as manifested by sustained increases in granulocyte and platelet counts after the postradiation nadir and detection of donor cells in the peripheral blood by use of microsatellite marker polymorphism analyses.[8,14] Granulocyte count was within reference range by day 10 and platelet count by day 22 (**Figure 3**), and the dog did not require transfusion. For analysis of donor engraftment, granulocyte and lymphocyte fractions were separated from the recipient's blood by use of a gradient method, and genomic DNA was extracted via standard protocols.[4] A PCR-based assay was performed with a 2001 primer pair.[8,14,c] The donor contribution to recipient hematopoiesis was quantified by estimating the proportion of donor-specific DNA among host DNA after autoradiography. This revealed mixed hematopoietic

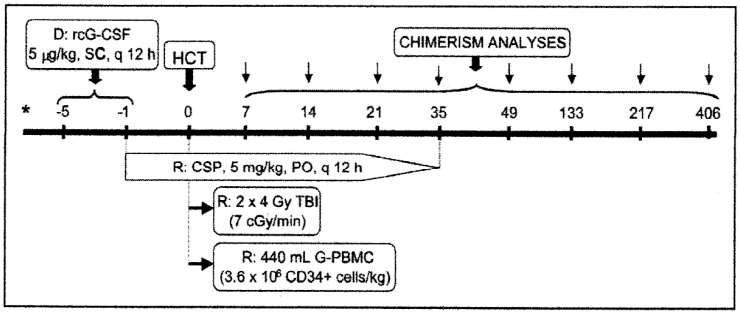

Figure 2—Myeloablative HCT schema of a dog with T-cell lymphoma. *Days before or after HCT. CSP = Cyclosporine. D = Donor. rcG-CSF = Recombinant canine granulocyte colony–stimulating factor. G-PBMC = rcG-CSF mobilized PBMCs. R = Recipient. TBI = Total body irradiation.

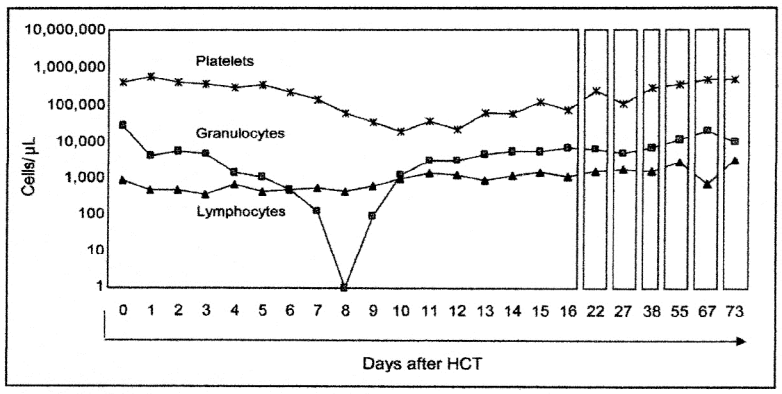

Figure 3—Blood concentrations of WBCs and platelets after HCT in a dog with T-cell lymphoma.

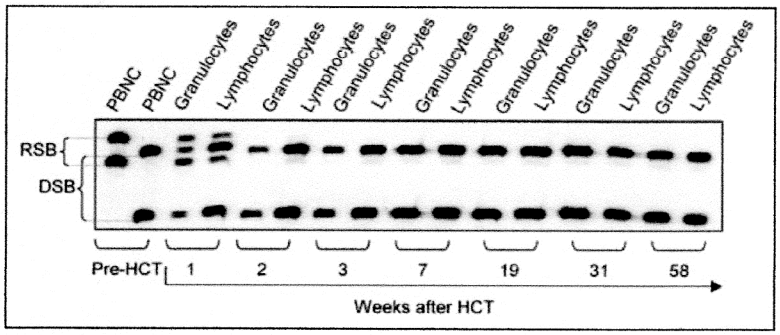

Figure 4—Chimerism analyses of blood from a dog with T-cell lymphoma receiving an HCT from a DLA-matched related donor. DSB = Donor specific bands. RSB = Recipient-specific bands.

chimerism by week 2 after transplantation and, subsequently, progression to full donor chimerism in the granulocyte and lymphocyte fractions, which has been maintained for at least 58 weeks (**Figure 4**).

On day 55 after HCT, serum activities of alanine aminotransferase (233 U/L) and aspartate aminotransferase (106 U/L) increased. At the same time, an erythematous rash developed, affecting the plantar region of the paws, periocular and perioral regions, dorsal and lateral nasal skin, pinnae of the ears, abdomen, and dorsal region of both forelimbs. Histologic examination of multiple skin biopsy specimens revealed diffuse lymphocytic infiltrates and apoptotic cells in the follicular epithelium and occasionally in the glandular epithelium, confirming graft versus host disease. Treatment was initiated with cyclosporine (7.5 mg/kg [3.4 mg/lb], PO, q 12 h) and enrofloxacin (10 mg/kg, SC, q 24 h). The skin lesions improved after 20 days of cyclosporine administration, which was continued at the same dose for 5 months and then gradually tapered by 5%/wk until month 13 after HCT, when it was discontinued. While receiving cyclosporine, the dog was without clinical signs with the exception of sporadic vomiting and diarrhea without weight loss. Clonal rearrangement studies of blood T-cell antigen receptor genes[1] and serum thymidine kinase assays[15] performed after HCT have revealed no evidence of residual lymphoma.

Discussion

Systemic chemotherapy is presently the treatment of choice for canine lymphoma, with remission rates approaching 58% to 96%.[2] However, most dogs succumb to recurrence of their disease, typically by 12 months after diagnosis[16] because of development of multidrug resistance. When the COAP protocol alone is used for the treatment of dogs with lymphoma, a median survival time of 25 weeks has been reported.[3]

The canine species has served as an excellent random-bred preclinical model for human HCT,[17–19] providing a valuable basis for many of the principles and techniques of transplantation. Increasing knowledge of the molecular immunogenetics of the canine major histocompatibility complex has provided unique tools for rapid identification of suitable DLA-matched family members, which could serve as hematopoietic donors.[4–6,8,10,11,20–23] Treatment of spontaneous lymphoma in dogs with a high dose of total body irradiation and chemotherapy followed by autologous[24–30] or allogeneic[30–32] marrow transplantation has been reported. Among dogs in chemotherapy-induced remission that were given autologous marrow grafts, approximately 25% became disease-free long-term survivors.[26,29,30] However, allogeneic grafts were complicated by high rates of fatal graft versus host disease[31] and other complications, although there was evidence of beneficial graft versus lymphoma effects.[33] Since those early studies, outcomes of allogeneic HCT have improved, in part because of improved donor-recipient selection by use of molecular DLA typing[5,11] and in part because of better prevention of graft versus host disease,[34,35] better supportive care, and substitution of PBMCs for bone marrow.[36] The dog described here has remained in remission for more than 15 months after HCT and 19 months since the initial diagnosis and has been thriving, with complete donor chimerism.

a. Northwest Radiologists, Bellingham, Wash.
b. Neupogen, Amgen, Thousand Oaks, Calif.
c. Invitrogen Corp, Carlsbad, Calif.
d. Ultra Pure Sequagel Sequencing System Kit, National Diagnostics, Atlanta, Ga.
e. MDE Gel Solution, Cambrex Bio Science Rockland Inc, Rockland, ME.
f. ABI PRISM 3100, Applied Biosystems, Foster City, Calif.
g. SeqEd, Applied Biosystems, San Jose, Calif.
h. Supplied by Amgen Corp, Thousand Oaks, Calif.
i. Arrow International, Reading, Pa.
j. COBE Spectra apheresis system, Gambro BCT, Lakewood, Colo.
k. I-STAT CG8+, I-STAT Corp, East Windsor, NJ.
l. 1H6 canine anti-CD34 antibody, Biologics Facility, Fred Hutchinson Cancer Research Center, Seattle, Wash.
m. Clinac 4/80, Varian Associates, Palo Alto, Calif.
n. Abbot Laboratories, Abbot Park, Ill.
o. Liposyn, Intralipid 20%, Baxter Healthcare Corp, Clintec Nutrition Division, Deerfield, Ill.
p. Culturelle, ConAgra Foods, Omaha, Neb.

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Allogeneic Hematopoietic Stem Cell Transplantation for Treatment of Canine Lymphoma

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation is a common treatment option for humans with hematopoietic malignancies. Much of the basic principles and techniques of transplantation was completed in canines as a preclinical large animal model, however, transplantation as a treatment option has not been routinely available to dogs with spontaneous lymphoma.1, 2 In this presentation, we discuss the recent advances that have made these transplantation techniques available to client owned dogs, and we outline the steps needed to successfully complete an allogeneic stem cell transplant.

BACKGROUND

In the late 1970's it was demonstrated that 25% of canine lymphoma cases could be cured with a combination of chemotherapy, total body irradiation, and autologous marrow recovery.3-6 Later, similar results were obtained with the use of peripheral blood mobilized stem cells as the recovery cells rather than marrow.7 Additional studies found that allogeneic stem cells from dog leukocyte antigen (DLA) matched donors could also cure lymphoma.8,9 All of these transplant procedures were hampered by significant procedure related toxicities (marrow failure, overwhelming infections, and radiation toxicity), and the allogeneic procedures were additionally plagued by potentially fatal graft versus host disease (GVHD).10 Years of intense investigation of the molecular immunogenetics of the major histocompatibility complex of dogs lead to the development of techniques to rapidly identify DLA-matched family members for use in allogeneic transplantation procedures.11-21 Subsequent advancements identified treatment regimens for controlling GVHD, and better post-transplant medical support (with broad spectrum antibiotics and transfusion support with irradiated blood products) lead to less treatment related morbidity and mortality. Collection of peripheral blood mobilized stem cells using a dual lumen central venous catheter and an automated apheresis machine further reduced morbidity to the donor by eliminating the need for marrow harvesting.22 In the last three years, these techniques have been expanded further to be available outside of the laboratory setting to include client owned dogs.23

MATTERIALS AND METHODS

Patient Staging and Induction of Remission

Standard staging should be performed to characterize the type of lymphoma before chemotherapy is initiated. Additionally, flow cytometry, immunohistochemistry, and/or gene rearrangements, should be performed to identify a molecular marker of disease for use in identifying complete remission and relapse. Standard chemotherapy protocols can be used to achieve a complete remission, and a transplant procedure is expected to be more successful if performed while the patient is in the first remission. A rest period of 3 weeks after the last dose of chemotherapy (including prednisone) is advised before the transplant. During the induction chemotherapy an effort to identify a donor is made.

Identification of a Donor-Recipient Pair

Allogeneic transplant procedures in client owned dogs are limited by the donor pool being confined to siblings of the patient with lymphoma. Additionally, a DNA sample from at least one of the parents (and in some cases both) is needed to help identify DLA matched donor-recipient pairs. Because it can sometimes be difficult to find siblings, it is important to initiate a search for a potential donor as soon as possible. We have found that breeders often keep good records on the location of littermates, and we have left the process of finding the potential donors up to the patient's owner. A good family tree is diagrammed, and a blood sample (5cc whole blood in EDTA) from the patient, the sire and dam, and as many siblings from the same or subsequent litters of the same breeding pair, are collected and sent chilled overnight to the lab where the matching techniques are performed. As blood samples are delivered to the lab, the DNA is extracted and frozen for future analysis. Once all samples are delivered to the lab the matching process is completed (25% of siblings are expected to be DLA-identical), and a donor is selected who is as big as or bigger than the patient if possible. Also, willingness of the potential donor's owner to participate is critical.

Donor Preparation

Once a donor has been identified and the patient is in confirmed remission, a time-line for the transplant day can be prepared. The transplant day is defined as day zero, and important preparations are made in reference to this day. Beginning day -30 the donor is screened for tick borne diseases, heart worms, and a CBC, chemistry, and a urinalysis are performed. A pre transplant chimerism whole blood sample (10cc whole blood in EDTA) is collected and sent to the lab for DNA extraction and cryopreservation. On day -14 a blood prime (~200cc whole blood in ACD solution) is collected from the donor for use in priming the apheresis machine on the apheresis day. This blood is kept under refrigeration until the apheresis is performed. A blood prime is not needed for dogs over 30kg. Starting on day -6 the donor is given 5ug/kg Neupogen SQ BID for five days with the apheresis scheduled for day -1. Beginning day -4 a daily CBC and peripheral blood CD34+ count are done two hours after the morning dose of Neupogen in order to document adequate

mobilization of progenitor stem cells from the marrow into the peripheral blood. CD34+ counts will range from 0.5 to 2.5% of the total nucleated cell count, and total WBC counts will range between 30,000 to 65,000 cells/uL.
On the morning of day -1 (the apheresis day), the Neupogen dose is increased to 10ug/kg SQ 2 hours before the apheresis procedure is started. The donor is placed under general anesthesia and a dual lumen central venous catheter is placed in a jugular vein (Arrow Dual Lumen Catheter—12f, 15cm). A CBC is run on the donor to help set the collection parameters on the apheresis machine. The donor's body temperature is monitored and regulated during the apheresis procedure, and serial blood calcium measurements are made every 20 min. A 10% calcium gluconate solution is administered via IV pump at a rate of 10ml/h during the apheresis to avoid hypocalcemia from anticoagulant induced calcium depletion, and adjustments to the infusion rate are made as indicated. The apheresis machine (COBE Spectra from Gambro BCT) is set to run a standard mononuclear cell cycle using a closed collection set. Half way through the apheresis procedure a sample of the harvest is evaluated with a CBC and a CD34+ cell count. The target CD34+ dose is 4 x 106cells/kg body weight of the recipient. An adjustment in the apheresis time frame can then be made based upon the harvest quantity, total white blood cell count, and % CD34+ cells. The apheresis procedure may take between two to four hours, and once complete, the central venous catheter is removed.
After completion of the apheresis, confirmation that the CD34+ target dose has been reached is made with an additional CBC and CD34+ cell count on the total apheresis harvest. The harvest is kept under refrigeration until infusion into the recipient immediately after total body irradiation.

Recipient Preparation
On day -8 (just before the mobilization of the donor is started) the recipient is evaluated for confirmation of remission using molecular markers established prior to chemotherapy. A pre transplant chimerism whole blood sample (10cc whole blood in EDTA) is collected and sent to the lab for DNA extraction and cryopreservation. In addition, a urinalysis with culture and sensitivity are performed and a dental prophylaxis is completed if needed. On day -5 oral antibiotics are initiated including neomycin sulfate (6mg/kg PO q8hrs), polymyxin B (25,000 U/kg/d PO q 8hrs), and enrofloxacin (10mg/kg SC q24hrs). These medications are continued from day -5 until the after the neutrophils recover to above 1,000cells/ul after the HCT. Lactobacillus, a probiotic (80mg PO bid), is also started on day -5 and continued until day +40. On day -1 cyclosporine (5mg/kg PO bid) is started and continued to day +35 or longer if needed to control GVHD. Cyclosporine assays are performed 2-3 times per week as needed to establish therapeutic serum concentrations from 400 to 600ng/ml. Blood samples for the cyclosporine assays are collect 12 hours after the last dose.

On day 0 the patient is prepared for total body irradiation (TBI). TBI is delivered with a linear accelerator at a total dose of 8Gy in two fractions of 4Gy with a three hour rest period between fractions. Radiation is delivered at a rate of 7cGy/min, and the patient is rotated 180 degrees after 2Gy during each fraction. Immediately following the TBI the harvested progenitor cells are administered to the recipient through a peripheral intravenous catheter.

Immediate Post Transplant Care

Beginning the night of day 0 and continuing through day 4, the patient is not allowed to take in anything PO. **All steroid use should be strictly avoided (including topical use) as this has been shown to interfere with engraftment and cause graft failure.** Fluid support is intravenous or subcutaneous (standard maintenance dose) with lactated ringer's solution or saline. Daily inspections of the skin for lesions associated with GVHD are made and noted. These lesions include a red, slightly raised, expanding pruritic dermatitis of the inside of the pinnae, the dorsal and lateral surfaces of the muzzle, the skin around the eyes, and the ventral abdominal midline. If any of these lesions are found, a chemistry profile to evaluate liver enzymes should be completed, as the primary organs affected by GVHD are the skin, liver, and gastrointestinal tract. Increases in the cyclosporine dose can be made to try to bring GVHD under control. Vomiting is controlled with antiemetics as needed, and diarrhea is controlled with Imodium as needed. Antibiotics, probiotics, and cyclosporine are continued as described above, and the body temperature is monitored twice daily. During the first 5-6 days the patient is kept in a clean, semi isolated environment. Starting on day 4 once or twice daily CBCs and serum chemistry profiles are performed. Oral food and water are allowed beginning on day 5. When the neutrophil count goes below 1000cells/uL the patient is keep in an isolation room and not allowed to leave until the count recovers to above 1000cells/uL. The neutrophil nadir (counts below 100cells/uL) occurs around day 7 and can continue for 24-48 hours. The platelet nadir (counts 10,000platelets/uL or below) occurs around day 10 and can last for 48-72 hours. During this time transfusion support may be needed using cross matched fresh whole blood or platelets. All blood products should be irradiated before use (18-25Gy) in order to prevent allo-competition and potential graft failure. Cyclosporine assays are run every 2-3 days as described above in order to keep the serum cyclosporine level between 400-600ng/ml. Adjustments in the cyclosporine dose are made according to the assay results. Once the neutrophils have recovered to above 1000cells/uL (usually by day 10) the patient is allowed outside of the isolation room. Platelet recovery to a safe level (usually by day 14) allows the patient to go home and be monitored on an out-patient basis. Cyclosporine is discontinued on day 35 if there are no signs of GVHD.

Long Term Post Transplant Care

On days 30, 60, 90, 120, and 150 whole blood samples (3cc in EDTA) are submitted to the lab for chimerism assays. With myeloablative TBI, autologous marrow recovery is not expected, however, if a state of mixed chimerism exists (the presence of both donor and host origin blood cells), then a donor lymphocyte infusion (DLI) may be performed to boost the patient into 100% donor chimerism. Identification of residual neoplastic cells is another indication for a DLI. A DLI consists of donor lymphocytes collected from the peripheral blood of the donor with a target of delivering 2 x 105 CD3 cells/kg body weight of the recipient. GVHD may develop 3-6 weeks after a DLI, which may then require medical management. A DLI can also be used as an adjunct therapy for relapse of disease. In this case the DLI is given after chemotherapy induced remission. Additional long term follow-up procedures include bone marrow and lymph node aspirates to monitor for residual disease using molecular markers identified before the HCT. Chronic low grade GVHD is associated with longer survival in humans after HCT. For this reason, low grade GVHD is desirable as it infers the presence of the beneficial effect of graft versus tumor (GVT). Indeed, GVT is likely the most important benefit of an allogeneic HCT.

CONCLUSIONS

To date, we have completed three allogeneic HCT on dogs with lymphoma. Two of these dogs had T cell lymphoma grade 5b, and one had B cell lymphoma grade 3a. All three dogs survived the transplant procedure with mild complications; however the B cell dog relapsed six months after the HCT and later succumbed to advanced lymphoma. She survived 20 months from the time of initial diagnosis until death. Both of the T cell dogs continue to thrive, one now 3 years and 4 months since the original diagnosis, and the second 18 months since the original diagnosis. Neither of these two dogs needed a DLI, nor have they been on any transplant related medications.

All of the steps needed to perform a successful HCT are well described and repeatable. Additionally, many motivated pet owners are aware of the idea of a bone marrow stem cell transplant, and even though the costs and risks associated with this procedure are substantial, informed pet owners are capable of making the decision to pursue a transplant in the hope of achieving a long term treatment for lymphoma.

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KEYWORDS

Bone Marrow, Autologous, Apheresis, Dog Leukocyte Antigen, Graft-versus-host disease, Graft-versus-tumor, Chimerism, Donor Lymphocyte Infusion.

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Notes

(Mis)led by (im)proper classification of cases and controls the cause of histiocytic sarcomas can(not) be determined

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The about 500-fold increased risk in the Bernese Mountain Dog (BMD) has led to an international effort to find the genetic cause of the deadly Histiocytic Sarcoma (HS) / Malignant Histiocytosis (MH). Significant contributions of cases and controls - from which DNA is available - has come from Utrecht-based collection efforts (150 versus 100) since 2003, and this number is steadily increasing. At this symposium more on the DNA-based genetic analysis will be told by Dr. Benoit Hedan .
Starting in 2008 we have in a separate study collected and revised cytology/pathology data from over 700 BMD with HS/MH, other sarcomas and other hematological malignancies, originating from several laboratories. After reclassification, an overview will be produced of clinical and pathological data from all of the confirmed HS/MH cases. This group of cases with HS/MH will be compared with healthy controls (see below) and analyzed with tests for hereditary transmission pattern by use of pedigree data. Within the group of BMDs with HS/MH, other factors such as age of onset and localization (single = HS, multiple = MH) are analyzed for possible familial influences.
Over the years, information on healthy controls - often accompanied by blood for DNA-isolation, has been gathered. Yet, only from 9.5 years of age, such controls are effective in the genome analysis. And regular follow up led to expulsion of a large number of controls from the healthy veteran group, in cases in which solid proof, or if significant suspicion was raised of the development of a malignant tumour.
A parallel study focuses on HS/MH in Flat-Coated Retrievers.

A proper classification of tumours

Several breed societies have organized the feedback from owners on the cause of death of their dog, enabling a central registration that can alert on the occurrence of certain new or epidemic types of disease, including tumours.
Yet, often the declaration of death gives only the opinion of the practitioner, without solid proof of the final diagnosis. As such, severe doubt can arise if bone cancer (in science: osteosarcoma) is given as cause of death in BMD, in which breed this type of cancer is not frequent, whereas histiocytic sarcomas may give similar symptoms. In addition, if a BMD develops dyspnoea and on thorax radiographs a mass is seen,

many practitioners will tell the owner, that the dog must be affected by malignant histiocytosis. At autopsy, done in about 30% of such affected animals, it might have turned out, that the mass was in fact a lung-carcinoma, or even granuloma. Both conditions can be bad for the dog, although not as bad as histiocytic sarcoma. If the true diagnosis had been made in a living dog, an operation might have been successful. For genetic studies, a wrong classification can severely disturb the analysis. Furthermore, veterinary laboratories are primarily based upon providing a diagnosis as guide for the practitioner, and often stop by stating that a malignant neoplasm of soft tissue origin is a "sarcoma". For the management of the patient, this is often good enough, although specialized oncological treatment may ask for more detail. Lack of immunohistochemical analysis of such "sarcomas" hampers, again, genetic studies that target special types of sarcomas, such as HS in BMDs.
Our current study in Utrecht gathers data from BMDs from several laboratories and clinics, in which a diagnosis of (or suspicion of) HS / MH was given, plus data from dogs with tumours that have some similarity to HS/MH and that might - at thorough revision - lead to reclassification into HS/MH. But the reverse can also occur. As such, a diagnosis of malignant lymphoma or malignant round cell tumour, amelanotic melanoma, anaplastic carcinoma, but also any type of sarcoma leads to entry in our investigation. This includes a registration of clinical data, plus full, central revision of cytology slides, and/or a revision of pathology slides, with addition of selected immune markers, to obtain a high-quality diagnosis.
For HS/MH, presence of the markerCD18 by immune-staining appears specific. Still, one must acknowledge that lack of staining for this CD18 marker may happen in some cases of HS / MH. Some tumours may ‘hide’ by loss of expression of this marker for histiocytes. We experienced a few cases in which a first tumour sample was negative for CD18, whilst a later sample turned out to be positive. "*"Tumours are not simple creatures".*
A few words about systemic histiocytosis (SH). In essence, this is seen as an immune disorder and not a tumour, albeit it, that it can be lethal. Some practitioners if confronted with this diagnosis, may err and tell the owner (and via the owner the breed society) that the dog suffered from MH. Even more complicating is the possibility, that some cases of diagnosed with SH may in fact have been MH cases. The better the quality of diagnostic data, the better the genetic study is.

A good follow-up of healthy veterans

A good and complete of the health development in healthy veterans is of extreme importance both for the study of DNA as compared between cases and controls to define causative genes, but also the use of data for studies, such as our investigation by use of pedigree data.
All dogs (and people) will eventually die. For our investigations and the breed - alert system, knowledge of the certain or likely cause is vital.

If the veteran turns ill, be it unexpected weight loss, loss of appetite, anaemia, or lameness, all these symptoms may (but need not be) a sign of an underlying malignancy. Inform your veterinarian about the importance of the final diagnosis, even if made post-mortem. Some breed societies compensate (part) of costs made by the owners for post-mortem examination of this special group of veterans.
A precise diagnosis in case of problems is important for your dog, but may also be important for the health status of the breed and thus for future Bernese Mountain Dogs.

Acknowledgement

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Histiocytic Sarcoma Research in the Bernese Mountain Dog

The Ostrander Laboratory at the National Human Genome Research Institute at NIH in collaboration with Dr. Catherine Andre at the University of Rennes in France, have been working for several years to discover the genetic causes of Malignant Histiocytosis (MH)/ Histiocytic Sarcoma (HS). This is a devastating disease with genetic underpinnings, which affects the Bernese Mountain Dog (BMD), at a higher incidence than most other dogs. Our ultimate goal is to identify the genetic variants responsible for susceptibility to the disease

While rare in the general canine population, histiocytic cancers occur at a high incidence in a small number of breeds, most notably Bernese mountain dogs (BMD). Through the generosity of grants funded by the AKC-CHF and the cooperation of the breeds clubs, we have been able to identify multiple regions of the genome that are associated with histiocytic cancer in the BMD. We have also been able to narrow our focus down to only a few genes which we are currently searching for causative mutations. This finding represents a major step forward in our understanding of the disease which is likely to improve diagnosis and treatment options for dogs affected with the disease.

Critical to the next stage of the study will be our efforts to pinpoint the exact mutations that cause the disease in this breed, and to make that work available to the public as quickly as possible. From our studies a clearer understanding of the gene families involved in developing histiocytic cancers as well as the underlying pathology, will evolve. In addition, we hope to better understand the tissue specificity of the disease. That is, why do dogs with specific mutations get histiocytic cancers as opposed to other kinds of cancer? We have also collected a large pedigree and surveyed large litters of BMD. This epidemiological analysis indicates that Bernese Mountain dogs are affected by many types of cancers. The work that we are doing on histiocytic sarcoma will help in understanding additional cancer susceptibilities such as lymphomas or mast cell tumors which arise from related cell types. Finally, we hope that genetic tests will eventually develop from the foundations laid by this work so that healthier, more long-lived dogs can be bred.

This has been an exciting year for HS research and we feel very optimistic about the direction that the research is taking. None of this would have been possible without your dedication to this wonderful breed and its health. We hope our work will determine the genetic cause of HS so that steps can be taken toward the prevention of this terrible disease. With your continued participation and enthusiasm, we are making great strides in that direction.

If your dog would like to participate in the HS study and you need information or a sampling kit, please contact:

Gretchen Carpintero
Ostrander Lab Samples Manager
Phone: 301-451-9390
Fax: 301-594-0023
Email: dog_genome@mail.nih.gov
National Institutes of Health / NHGRI
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Bethesda, MD 20892-8000

As always, your participation in the study and any information you provide us will remain confidential.

Thank you for your help!

Peri-articular histiocytic sarcoma and synovial cell sarcoma in Bernese Mountain Dogs: a retrospective investigation of the prevalence of these tumors in association with previously diseased joints.

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Introduction: Histiocytic sarcoma complex (HSC) is commonly found in Bernese Mountain dogs (BMD). Peri-articular histiocytic sarcoma (PAHS) is a sub-entity of HSC. PAHS may be confused with synovial cell sarcoma (SCS) on histology. The hypothesis of this study is that PAHS/SCS in BMD will be more frequently encountered around previously diseased joints compared to normal joints.

Material & Methods: Data were obtained through a European internet questionnaire (www.bmdhealthsurvey.eu), and medical records of two pathology labs. Statistical analysis was performed by Pearson Chi-square and Fisher Exact tests. Effect Size was analyzed by Nagelkerke R^2. 4 PAHS and 4 SCS were immunolabeled with CD18 and pancytokeratin in an attempt to differentiate these tumor types.

Results:
All PAHS and SCS stained positive for CD18 and negative for pancytokeratin. 830 European BMD were included in the study. 199 dogs had previous joint disease, of whom 15 developed PAHS/SCS around a previously diseased joint; 3 dogs had PAHS/SCS in another joint. Of the 631 BMD without joint disease, 9 developed PAHS/SCS. A significant association between previous joint disease and PAHS/SCS of the same joint was demonstrated for the left and right elbow (p-value left elbow = 0.001, p-value right elbow<0,009), and left and right stifle (p<0.001), with Effect Sizes of 0.155, 0.174, 0.228, and 0.211 respectively.

Conclusions: Significant association with reasonably high Effect Sizes indicate a causal relation of previous joint disease and the development of PAHS/SCS in the same joint of European Bernese Mountain dogs, although the power of the statistical analysis is low due to the small sample size. CD18 and pancytokeratin staining was not able to differentiate peri-articular histiocytic sarcoma from synovial cell sarcoma SCS.

New Treatments for Malignant Histiocytosis

Scott Hafeman DVM and Steve Dow DVM PhD

Malignant histiocytosis (MH), also known as disseminated histiocytic sarcoma, is characterized clinically by a poorly demarcated and infiltrative tumor that develops in a variety of sites, especially the lungs, spleen, lymph nodes and bone and effects Bernese Mountain Dogs at a rate higher than that of any other dog breed [2-7]. The biological behavior of the tumor is very aggressive and survival times are typically two to four months following diagnosis [8, 9]. The tumor is typically refractory to most chemotherapeutics, including lomustine, carboplatin, and doxorubicin. Of these, the most studied chemotherapeutic agent is lomustine (CCNU). If complete surgical excision can be achieved, as in the case of localized histiocytic sarcoma, adjuvant treatment with CCNU can lead to increased survival times [10]. Unfortunately, in the vast majority of cases local control is not possible. In these disseminated cases, the complete response rate to CCNU alone is less than 10%, with a response time of only 96 days [9]. Use of other chemotherapeutics is largely anectodal and has been on the whole unrewarding.

Malignant histiocytosis is thought to be derived from specific white blood cells known as myeloid cells, including either macrophages or dendritic cells (DC) [11-13]. MH cells express a variety of markers also expressed by normal macrophages, whose normal function in the body is to phagocytize or eat bacteria that are causing an infection [8, 14]. Functionally, MH cells express Fc receptors and are also actively phagocytic, both of which are hallmarks of macrophages. A canine MH cell line known as DH82 was established and found to express many features typical of macrophages [15]. Our lab speculated that the ability of MH cells to eat bacteria could be exploited as a way to kill these tumor cells in MH patients. We have worked at development of a drug called liposomal clodronate, which consists of a drug encapsulated in a lipid bilayer that mimics a bacteria. The macrophages eat the liposome and release the drug which kills the cells from the inside out.

Through extensive in vitro studies we were able to determine that liposomal clodronate has a direct killing effect on MH cells. The cells phagocytize the liposomes as they would a bacteria, and the efficiency of uptake of the liposomes dictates the degree of cell killing achieved due to induction of apoptosis [17]. In clinical trials using single agent liposomal clodronate against MH, the drug was very well tolerated and showed effectiveness similar to treatment with CCNU. While the direct effect of the drug on MH tumor cells likely contributes to disease response, this may not be the only mechanism of action.

Our lab and others have shown that the use of liposomal clodronate is able to decrease tumor growth in a wide variety of tumors, despite the drug having no direct effects on those types of tumor cells in vitro [18-21]. The likely reason for this effect is the depletion of myeloid suppressor cells and tumor associated macrophages, which are phagocytic cells that have many pro-tumor properties. These include but are not limited to increased

immunosuppression, increased angiogenesis, and increased metastasis of tumor cells [22-26]. Interestingly, recent work has also shown that tumor associated macrophages directly protect multiple myeloma cells from the apoptosis inducing effects of chemotherapy [27]. Therefore, the depletion of these tumor associated macrophages prior to treatment with conventional chemotherapy may reverse apparent chemoresistance of tumor cells and may greatly enhance the tumor response to chemotherapy. Previous studies in our lab have shown that LC is capable of killing normal canine macrophages as well as MH cells [17].

We have conducted a series of investigations to assess the ability of LC to kill canine macrophages in vitro. We did a series of tests using LC against MH cells and normal canine macrophages grown in the lab. The results of these tests are described below.

Incubation of monocyte-derived macrophages (obtained from blood of healthy dogs) with LC elicited dose-dependent killing (**Figure 1**). This drug was also able to kill all 3 MH cell lines studied (**Figure 2).** Uptake of the drug via phagocytosis was required for cell killing. Non-phagocytic tumor cells were unaffected by the drug (**Figure 2**).

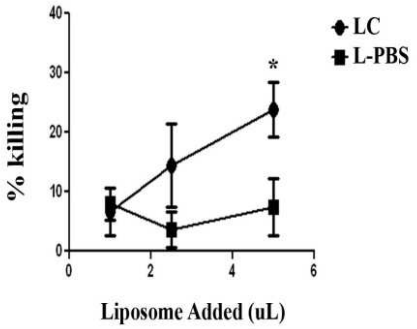

Fig 1. Liposomal clodronate effectively induces killing of canine macrophages. Monocyte derived macrophages from normal dogs were incubated with increasing doses of liposomal clodronate (LC) or liposomal PBS (L-PBS) and analyzed via MTT assay 72 hours later (* = $p < 0.05$)

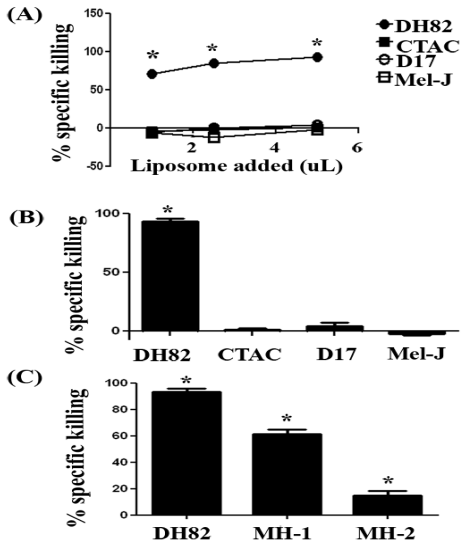

Fig 2: Susceptibility of phagocytic and non-phagocytic tumors to killing by LC. Killing of canine MH cell lines (DH82, MH-1, MH-2) by LC was compared to killing of three non-phagocytic canine tumor cell lines (thyroid carcinoma {CTAC}, malignant melanoma {Mel-J} and osteosarcoma {D17}). In (a), dose response curves of LC percentage specific killing were determined for the DH82 cell line and three nonphagocytic tumor cell lines (CTAC, D17, Mel-J). In (b), the percentage specific killing elicited by 5% LC was plotted for MH cells (DH82) and three non-MH tumor cell lines. Specific killing was significantly greater (*, p\0.05) for DH82 cells than for the other three tumor cell lines. In (c), **LC-specific killing of three different MH cell lines was compared, using LC at a concentration of 5%. Killing was significantly greater (*, p\0.05) for DH82 cells than for the other two MH cell lines.**

Results like this in vitro have caused our laboratory to embark on clinical trials of LC treatment in dogs with MH. We observed significant anti-tumor activity in canine cancer studies using LC as a single agent therapy. Patients were treated with 0.5 mL/kg of LC administered every 14 days for up to 6 treatment cycles. While tumor response was the primary endpoint, the dogs also had several biopsies of their tumors when possible. We also performed analyses of blood and tumor draining lymph node samples. These tests were done to determine changes in immune cell populations and angiogenesis that could help to explain the anti-tumor effects seen with liposomal clodronate.

The results of biopsy samples are shown for three canine patients after two treatment cycles (**Figure 3**). This data shows that tumor associated macrophages can be depleted in canine patients using LC. Therefore, we have shown that macrophages can be depleted in vitro, and in dogs receiving LC treatment for MH

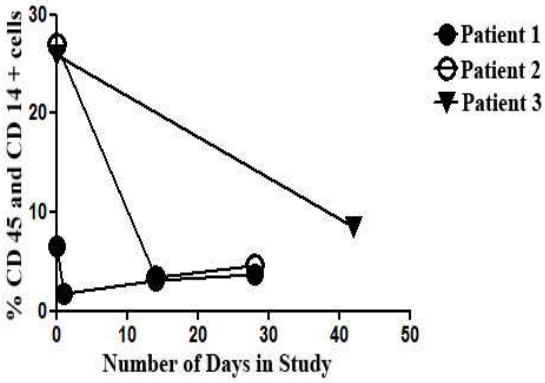

Fig 3. Liposomal clodronate depletes tumor associated macrophages in canine patients. Dogs with spontaneous tumors were treated with 0.5mL/kg of liposomal clodronate i.v. and evaluated for tumor response. Serial tumor biopsies and fine needle aspiration were used to measure tumor macrophage percentages, determined as the percentage of CD 45 and CD 14 double positive cells in the tumor. Data shown is from 3 separate patients.

While these results showed us that we were able to kill MH cells in vitro and deplete macrophages in vivo, the end result most important to our lab is showing the ability to help patients afflicted with this terrible disease. To date we have treated over 25 dogs afflicted with MH of a variety of breeds, including Bernese Mountain Dogs. As a single agent, LC is similar to CCNU which is the chemotherapy drug of choice for this disease. Clodronate treatment is well tolerated in dogs with minimal side effects. Nearly 40% of our treated patients have at least some response to clodronate. As shown in figure 4 and figure 5, some of our best results to date have come with combination chemotherapy. These figures both show complete resolution of the tumor burden in these respective patients. When clodronate is combined with drugs such as CCNU, doxorubicin, or carboplatin it seems to enhance the effects of both drugs without causing an increase in toxicity from the chemotherapy agents. These initial results have led us to conduct a currently ongoing study looking at the combination of CCNU and LC in MH dogs. This study is currently ongoing. We have treated dogs all over the United States with clodronate and have recently enrolled our first patient in the United Kingdom. We are able to treat our patients free of charge as our study is fully funded by a grant from the Canine Health Foundation, the health services arm of the American Kennel Club.

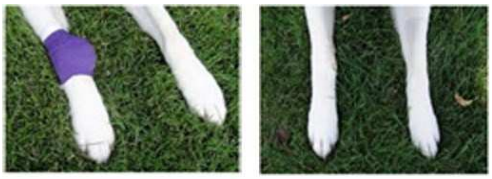

Fig 4. Tumor regression after combination therapy. Pre (left) and post (right) treatment photographs of a patient with MH. The patient also had regression of disease in the prescapular lymph node and spleen after treament with LC and CCNU.

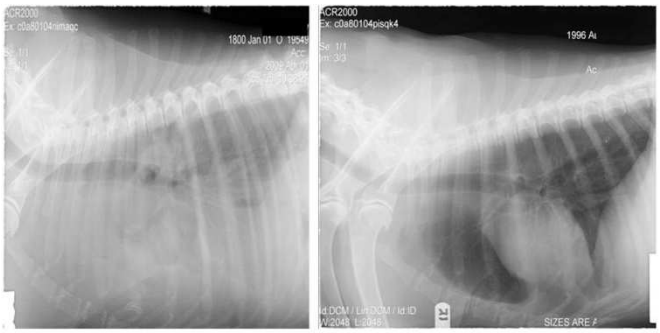

Fig. 5. Tumor regression after combination therapy. Pre (left) and post (right) chest radiographs of a patient treated with LC and carboplatin showing complete resolution of pleural effusion and pulmonary disease. This patient also had resolution of splenic and hepatic lesions.

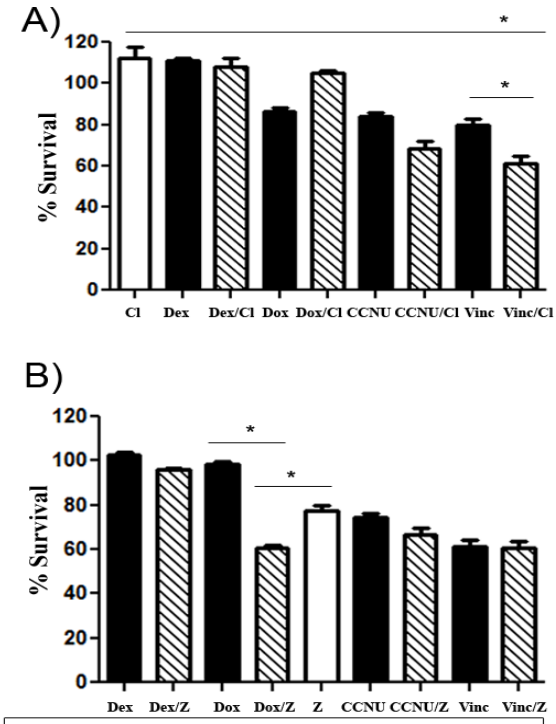

Fig 6: Certain bisphosphonate and chemotherapy combinations elicit significantly increased killing of canine MH cells in vitro. In (A), the effects of clodronate on chemotherapy-induced killing of canine DH82 MH cells was assessed, using an MTT assay to assess tumor cell viability. Cells were treated with chemotherapy drug alone (black), clodronate alone (white), or with the combination of clodronate and chemotherapy drug (cross-hatch). In these assays, only the combination of clodronate and vincristine demonstrated a significant positive interaction (* = $p < 0.05$), as assessed by 1 way ANOVA with Tukey's post test. In (B), the effects of zoledronate on MH-1 MH cell sensitivity to killing with chemotherapy drugs were assessed, using a similar approach as for (A). Cells were treated with chemotherapy drugs alone (black), zoledronate alone (white), or the two in combination (cross-hatch). The combination of zoledronate with doxorubicin showed a significant positive interaction(* = $p < 0.05$), as assessed by 1 way ANOVA with Tukey's post test . Cl = clodronate (5 µg/mL), Dex = dexamethasone (15 µg/mL), Dox = doxorubicin (0.2 µg/mL), CCNU = lomustine (1.5 µg/mL), vinc = vincristine (0.25 µg/mL), z = zoledronate (0.2 µg/mL).

In addition to our clinical trials, we continue to search for new treatments that may be effective against this disease. As shown in Figure 6 we have recently published in vitro data that shows that the combination of bisphosphonates with traditional chemotherapy drugs have synergistic interactions that lead to increased cell killing. Studies like this will hopefully spawn more clinical trials to combat malignant histiocytosis. Our lab will continue to work to find a cure for this terrible disease of Bernese Mountain Dogs.

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Section 3

The Countries and Clubs

The following summaries are from the countries that replied to a request for information Each BMD breed club was sent a suggested format for to respond to but it was made clear they could add things to this or tell us exactly what they wanted about Bernese in their country.

As you will see, some country's health initiatives are very advanced and fantastically well supported and organised whilst others are still developing and face more difficult times.

1] Argentina Boyero de Berna Club Argentino
2] Austria Verein für Schweizer Sennenhunde in Österreich
3] Belgium Belgische Club voor Zwitserse Sennenhonden
4] Canada Bernese Mountain Dog Club of Canada
5] Finland Suomen Sveitsinpaimenkoirat – Finlands Sennenhundar ry
6] Great Britain Bernese Mountain Dog Club of Great Britain
7] Ireland Bernese Mountain Dog Club of Ireland
8] Italy Club Italiano Amatori Bovari Svizzeri
9] The Netherlands Vereniging de Berner SennenHond
10] Russia Russian National Club for BMD
11] Slovenia Slovenski klub za bernske planšarske pse)
12] Spain Club Espanol De Boyeros Suizos
13] Sweden The Swedish Club of Swiss Mountain Dogs
14] Switzerland Schweizerischer Klub für Bernersennenhunde
15] USA Bernese Mountain Dog Club of America

The Bernese Mountain Dog Club of Great Britain is extremely grateful to all the above clubs who took time to prepare and forward the following summaries of the Bernese Mountain Dog in their country.

Country **Argentina**
Club Boyero de Berna Club Argentino
Name of person submitting information Rubén Hugo Somoza
Email infobbca@yahoo.com.ar

1] Your Club

A] How old is your club? The club was founded 4 years ago and the FCA approved the definitive affiliation 2 month ago.
B] How many members/addresses does your club have?180 members
C] Which month is your biggest show normally held ? It's in November
D] Approximately how many entries of BMD do you have at this? 45
E] How many official BMD breed clubs are there in your country? 1.

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 787 puppies per year
B] Is this number rising or falling or about the same over the last few years ? Rising
C] Any other comments
.

3] Breeding Controls

A] Are there any quality/health controls in place? Recommendations but not enforcable
B] Are these compulsory or only recommended? Recommended but not enforcable
C] Do these controls apply to everyone breeding or only club members? EVERYONE
D] Do dogs have to be hip scored before mating? Recommended but not enforced
E] Do dogs have to be elbow scored before mating? Recommended but not enforced
F] Do dogs have to be Character Assessed before mating? Recommended but not enforced
G] Do dogs have to have a confirmation or exterior assessment before mating? Recommended but not enforcable

H] Does the club have any control over mating selection? Recommended but not enforced

I] Are there any controls on the number of puppies a dog can sire? Recommended but not enforced

J] Are there any controls on the age a dog can sire his first litter? Recommended but not enforced
K] Are there any limits on the number of litters a bitch can have? Recommended but not enforced
L] Are there any controls on the age of bitches used for breeding? Recommended but not enforced

Any other comments Being a brand new Club; we consider a priority to educate both our members and other breeders on important issues concerning health and after that demand for them the accomplishment of the normative procedures approved by the that the institution. For us this a learning as well as a consolidation stage.

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling? NO
C] How many blood samples have been taken or are taken per year? ---
D] Would you say you get a good response from owners to this scheme? ---
E] What diseases or conditions are being looked at by your health testing? ---
F] What, if anything , do you have in place to encourage people to take part in this health testing?
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese mountain dog.
We are working and studying how to make our member aware of the importance of these kinds of tests and studies. We are very much interested in keeping ourselves informed and also exchanging experiencies and receiving advice from Clubs all over the world that are more developed and consolidated than us.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?
I graduated as a Veterinarian Doctor 27 years ago, and have been a breeder since 1996. In our hospital we treat 1200 Bernese Mountain dogs, most of which were bred in our farm.
A few years ago I started registering illnesses as well as age and cause of death in my patients.
Some colleagues also provided me with information about age and cause of death of their patients. I registered frequency and importance in the appearance of illnesses related to osteoarticular, endocrinology and oncology, among others.
The results in general coincide with the international bibliography on those subjects.
In case you find it necessary I am willing to provide you with that information

Country …AUSTRIA
Club ……Verein für Schweizer Sennenhunde in Österreich (Club for Swiss Mountain Dogs in Austria)
Name of person submitting information …Gerhard Kunz - Club President
Email vorsitz1@sennenhunde.org gerhard.kunz@gmx.at

1] Your Club

A] How old is your club? 50 years – was founded in 1961
B] How many members/addresses does your club have? …450 members
C] Which month is your biggest show normally held ? … one in Spring and one in Autumn
D] Approximately how many entries of BMD do you have at this? Since we started having club shows the number of entries has varied from 60 – 230
E] How many official BMD breed clubs are there in your country? Only one – it is for all 4 breeds of Swiss Mountain Dogs

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? …175
B] Is this number rising or falling or about the same over the last few years? ……fairly stable
C] Any other comments …In the last 10 years we have had between 130 pups born in 2001 and 197 in 2002

3] Breeding Controls

A] Are there any quality/health controls in place? YES - both
B] Are these compulsory or only recommended? Compulsory
C] Do these controls apply to everyone breeding or only club members? Only club members (see comment below)
D] Do dogs have to be hip scored before mating? YES
E] Do dogs have to be elbow scored before mating? YES
F] Do dogs have to be Character Assessed before mating? YES
G] Do dogs have to have a confirmation or exterior assessment before mating? YES
H] Does the club have any control over mating selection? YES
I] Are there any controls on the number of puppies a dog can sire? YES
J] Are there any controls on the age a dog can sire his first litter? YES
K] Are there any limits on the number of litters a bitch can have? YES

L] Are there any controls on the age of bitches used for breeding? YES

Any other comments: All dogs used in breeding have to be approved at a breeding approval test organized by the club, Only breeders abiding by the rules of the Austrian Club are able to get FCI pedigrees which are recognized by the Kennel Club. It is not absolutely necessary for these breeders to be a member of the club but in fact they all are.

4] Health Testing

A] Does your club undertake any health testing? YES
B] Does any of this involve blood sampling? YES
C] If yes, how many blood samples have been taken per year? 3 last year
D] Would you say you get a good response from owners to this scheme? NO!
E] What diseases or conditions are being looked at by your health testing? Histiotic sarcoma
F] What, if anything, do you have in place to encourage people to take part in this health testing?
Begging, pleading, information in Club Magazine, informative meetings and educational courses offered by the club, information on the club website
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog. We have very strict breeding rules and every mating has to be approved by a breed warden.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members and other Bernese clubs around the world. Are there any particular problems that you face in your country?
In 2005 a contract was signed with the SSV in Germany about the sharing information in the data bank „Dogbase“ and in that same year an cooperation agreement was signed between the KBS (Switzerland), DCBS (Germany) and the SSV (Germany) about mutual exchange of data concerning Bernese Mountain Dogs. Because of these contracts information necessary to approve a mating by the breed wardens can be found more quickly.
The main problem in Austria is that there are a lot of people in this country breeding outside the club and although these people are not getting FCI pedigrees for their puppies, the puppy buyers do not seem to be able to discriminate between pups from controlled breeding within the club, and the other people who are selling Bernese puppies. There is an enormous difference in quality.
We are also not getting information about age of death from all breeders and do not have the names and addresses of the puppy buyers

Breeding in the VSSÖ (Original mit zusätzliches in Blau)

When the VSSÖ was founded 50 years ago, and the controlled breeding of the Swiss Mountain Dogs in Austria began, nobody had any idea that the breed would ever attain the level of popularity it has today. At the beginning the appearance of the individual dog was the main criterion for the choice of the breeding animals.
Health factors did not play a great role at this time. Because of the increasing number of animals in breeding, health problems started to arise and new breeding

strategies had to be considered which have been continually adapted over the years up to the present time.

In 1996 the HD and ED X-Ray was made compulsory. From 1997 on, all prospective breeding animals had to undergo a temperament test. In order that new breeders be better prepared for their job with bringing up puppies, they have had to attend a special training course for new breeders since 2000. These courses are also compulsory for the owners of stud dogs. In addition to this, it is necessary for all breeders to attend informative meetings and educational courses regularly. The temperament test was replaced in 2002 by the more comprehensive breeding evaluation test in which a commission consisting of 2 conformation judges and one temperament judge, assess the suitability for breeding of the dog.

Over the years the requirements for the breeding evaluation test have often been changed in order to promote the controlled breeding of healthy dogs with good characters in all four breeds of Swiss Mountain Dog in Austria. Any dog over the age of 18 months of age can be entered in the breed evaluation test if it has the necessary documents. The breeding evaluation test can only be repeated once.

The dogs which are to be evaluated must have got at least the grade “very good” from a recognized FCI judge at special Austrian shows or at a Club Specialty of the VSSÖ, whereby this show result can only have been obtained at the earliest at the age of 15 months.

Bernese Mountain Dog: HD-A, HD-B or HD- C (only under certain conditions), ED- 0 or ED-1. Only one of the parents can have HD-C, and then only if the HD score of this specific mating according to Dogbase, is under 100. Only one of the parents can have an elbow-grading of ED-1.
Owners of approved Bernese Mountain Dogs must submit a full veterinary report to the Breed Commission if the dog dies before it reaches the age of 8.

Great Swiss Mountain Dog: HD-A, HD-B or HD- C, ED-0 or ED-1 (under certain conditions), OCD (shoulder) free, negative findings in regard to Cataracts, Progressive Retina Atrophy (PRA)und Glaucoma

Entlebucher Sennenhund: HD-A, HD-B oder HD-C, negative eye tests in regard to cataracts and Glaucoma. PRA-gene test by means of a blood sample or buccal smear with puppies, with the results A (homozygous free) or B (heterozygous), examination for ectopic ureter whereby only A (free) or B (bladder neck) are accepted into the breeding programme. In any mating only one of the parents can have an official HD-C report, and one of the parents must be PRA-A and as well, have a normal ureter report.

Appenzeller Sennenhund: HD-A, HD-B or HD-C, ED- 0 or ED-1. In any mating only one of the parents can have an official HD-C report

The relevant breed warden has to be informed in advance about every planned mating in order that the requirements for that breed can be checked in advance,

particularly in regard to health and club rules, but also to encourage matings with the lowest possible incest coefficient. Cross-border cooperation is necessary for this work. International cooperation and exchange of data is very important for the VSSÖ and everything is done to achieve this goal. In 2005 a contract was signed with the SSV in Germany about the sharing information in the data bank „Dogbase“ and in that same year an cooperation agreement was signed between the KBS (Switzerland), DCBS (Germany) and the SSV (Germany) about mutual exchange of data concerning Bernese Mountain Dogs. Because of these contracts information necessary to approve a mating by the breed wardens can be found more quickly.

In order to combat the problems which have arisen over the years, a Breed Commission was formed in 2007, consisting of the Breed Manager and their deputy, as well as the breed wardens of each separate breed. The Breed Commission has the task of developing health promoting measures and together with the committee of the VSSÖ, to put these into effect.

In line with this, breeders of Entlebuchers, Appenzellers and Great Swiss Mountain Dogs who import pups from interesting and sound lines, are subsidized by the Health Fund to help them bring these dogs into the breeding programme. Further the VSSÖ participates in studies on the genetic causes of histiotic sarcoma (previously called malign

histiocytosis) in Bernese Mountain Dogs and also the research programme of the University of Rennes in France on epilepsy in Great Swiss Mountain Dogs. Every blood or tissue sample sent for one of these projects is subsidized with € 30,-- In order to get a higher quota in the HD and ED X-Ray evaluations, the costs involved are paid for the evaluations of the two dogs from each litter randomly selected as puppies.
Stud dogs have a limit of 4 litters a year but if these involves less than 20 puppies, a fifth mating may be approved by the Breed Commission.
The Breed Commission also deals with all concerns the breeders may approach them with.

A working group was formed in 2010 for the Entlebucher Mountain Dogs which focuses intensively on health problems and can thus facilitate the work of the Breed Commission Homepage: http://www.entlebucher-zucht.com

Members of the Breed Commission regularly take part in international Symposiums and working groups, because improvements in breeding can only be brought about by an intensive collaboration with the neighbouring countries.

Before pups go to their new homes each litter is checked by a veterinarian when they are chipped and a health report containing information about each puppy is given to the new owners. Also each new puppy owner receives a brochure with important information about puppies and their appropriate upbringing, feeding, care and health precautions.

In all these matters the present Breed Commission wishes to thank all the breed wardens and breed managers of the past who have worked for the good of the Swiss

Mountain Dogs, and particularly Frau Dietlind Stingl who was breed manager for the VSSÖ for over 20 years and was invaluable for her help and advice and is still very active as breed warden for the Bernese Mountain Dogs.

And so we hope that together we will continue the positive work for the Swiss Mountain Dogs in the future.

Isabella Kraft
Breed Manager

Georg Woschitz
Deputy Breed manager

Country **BELGIUM**

Club BELGIAN CLUB FOR SWISS MOUNTAIN DOGS officially:
BKZS Belgische Club voor Zwitserse Sennenhonden – CBBS Club Belge des Bouviers Suisses

Name of person submitting information Carla Van Assche
Email carla@berner-mh.be

1] Your Club

A] How old is your club? 32 years
B] How many members/addresses does your club have? …approx. 250 members / …200 addresses
C] Which month is your biggest show normally held ? no month fixed; depends: this year June, last year March. Before once February & has been September for years
D] Approximately how many entries of BMD do you have at this 50
E] How many official BMD breed clubs are there in your country? 2

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? In 2010: 708 new pedigrees issued. This puts the Bernese on the 5th place
B] Is this number rising or falling or about the same over the last few years ? about the same with a little decrease. In 2008 f.e. 803 pedigrees were issued (BMD 6th place) – in 2007: 764 new borns with pedigree (BMD 5th in the ranking)
C] Any other comments …
- The registered population is supposed to be about 10% of the total population . So what are we talking about?
- The breeding commission of our club has the impression there are nowadays more matings without result or small litters. Does this explain the slight falling?

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? YES
C] Do these controls apply to everyone breeding or only club members? KMSH: EVERYONE-/ breeding clubs: ONLY CLUB MEMBERS
D] Do dogs have to be hip scored before mating? YES – scoring from 18 months on. Hips A & B can be used freely – C can only be used if combined with A or B – no breeding with hips D & E (KMSH + BKZS + BBSC)

E] Do dogs have to be elbow scored before mating? YES by breeding clubs. BKZS: only elbows 0 & I can be used. I has to be mated with 0 BBSC: only 3 is not allowed to breed / Recommended but not enforced by KMSH

F] Do dogs have to be Character Assessed before mating? YES BKZS: selection in Belgium or in other country - or test of social behavior (the latest obliged for dogs born after 01.01.2007) / Recommended but not enforced by KMSH or BBSC

G] Do dogs have to have a confirmation or exterior assessment before mating? YES an exterior assessment:

- KMSH at least one qualification 'Good' in a Belgian show (open – CAC – CACIB) with a Belgian judge or in a specialty OR pass the KMSH certificate day OR have a selection -
- BKZS at least twive 'very good' on a CAC(IB) show (1 in youth class & 1 in intermediate or open class or both in intermediate or open class) OR BKZS selection OR FCI selection
- BBSC at least twive 'very good' on a CAC(IB) show (at least one in a class that competes for the CAC) OR a selection. For Belgian dogs they only accept the BBSC selection

H] Does the club have any control over mating selection? NO

I] Are there any controls on the number of puppies a dog can sire? "YES"-: KMSH no litters after 10 years - BKZS added: max 40 litters a year but there is no maximum per litter

J] Are there any controls on the age a dog can sire his first litter? YES he has to wait until he has his hips & elbows scored at 18 months

K] Are there any limits on the number of litters a bitch can have? YES

- KMSH: best is 1 litter a year - maximum 3 litters per 2 years (maximum at 10 years old so does not really apply for BMD) but there is no maximum per litter— BBSC: absolute maximum : 6

L] Are there any controls on the age of bitches used for breeding? YES not before 18 months (scoring hips & elbows) – not after 10 years of age

Any other comments The situation is a little complex: in Belgium you have 3 different breeding guidelines.

1. SRSH – KMSH (Société Royale St Hubert – Koninklijke Maatschappij St Hubertus) the official FCI-kennel club. If you don't follow their breeding rules, you don't get a pedigree, so they apply to everyone. What do they ask?
   - hips: A & B can be used freely – C can only be used if combined with A or B – no breeding with hips D & E
   - elbows: no demands
   - at least one qualification 'Good' in a Belgian show (open – CAC – CACIB) with a Belgian judge or in a specialty OR pass the KMSH certificate day OR have a selection
   - DNA has to be known before breeding

2. BKZS – BCSM (our club) - rules only apply to members – has the most severe rules on elbows and asks for character assessment for every dog born after 01.01.2007

3. BBSC – CBBB (the other breeding club) - - rules only apply to members – character assessment only if the dog has a selection; if no selection, no character assessment needed

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling? NO
C] How many blood samples have been taken or are taken per year? N/A
D] Would you say you get a good response from owners to this scheme? N/A
E] What diseases or conditions are being looked at by your health testing? N/A
F] What, if anything , do you have in place to encourage people to take part in this health testing?
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
We didn't organise surveys. What do we try?

- We try to get information on dogs dying (date & reason) but we hardly get 20 dogs a year.

- We informed on the B-IWG, we published summaries of the speakers at the symposium (one report per club magazine), had updates from Dr Rutteman (university of Utrecht) , got news from the online questionnaire (AVA award winning project) and have been a few times in touch with Rennes university (Cathérine André & Benoit Hedan)

- Every year we ask the BMDs that become 4 years old (or elder & haven't donated yet) to donate blood to the blood bank in Rennes or Utrecht when they get their annual vaccination (costs of sending can be reimbursed so only cost = making a copy of the pedigree) This year we had exactly one reaction

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?
Nothing happens. The problem is still the same as 2 years ago: nobody is interested in this negative aspect and does not want to hear the word cancer.

Country **Canada**
Club Bernese Mountain Dog Club of Canada
Name of person submitting information Ronald Smith
Email rfrsmith@eagle.ca

1] Your Club

A] How old is your club? 32 years
B] How many members/addresses does your club have? 444 members / 316 addresses
C] Which month is your biggest show normally held ? Our National Specialty is typically our biggest entry of Bernese and is typically held in the Spring or Summer months, but sometimes in the Fall. It depends on the availability of the hosting region group's venue.
D] Approximately how many entries of BMD do you have at this? 30-200
E] How many official BMD breed clubs are there in your country? We have 1 National club and 3 Regional clubs, so 4 clubs in total.

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 1440 born with 1200 registered (there are also many unregistered litters that can not be accounted for)
B] Is this number rising or falling or about the same over the last few years ? … staying about the same
C] Any other comments One of our biggest problems is that 70% of the BMD historically are produced in one province and many of those puppies are unregistered and come from large volume breeders who act outside of the club without heath testing.

3] Breeding Controls

A] Are there any quality/health controls in place? Recommendations but not enforcable
B] Are these compulsory or only recommended? Recommended but not enforcable

C] Do these controls apply to everyone breeding or only club members? ONLY CLUB MEMBERS
D] Do dogs have to be hip scored before mating? Recommended but not enforced
E] Do dogs have to be elbow scored before mating? Recommended but not enforced
F] Do dogs have to be Character Assessed before mating? YNO not enforced
G] Do dogs have to have a confirmation or exterior assessment before mating? NO
H] Does the club have any control over mating selection? NO
I] Are there any controls on the number of puppies a dog can sire? NO
J] Are there any controls on the age a dog can sire his first litter? Recommended but not enforced
K] Are there any limits on the number of litters a bitch can have? NO
L] Are there any controls on the age of bitches used for breeding? Recommended but not enforced

Any other comments …The BMDCC has breeder guidelines for members of the club. http://www.bmdcc.ca/BMDCC%20Breeder%20Guidelines%20Draft%20Final.pdf But we have no authority to enforce these breeding recommendations nor do we have any input on non-club members breeding decisions. The Canadian Kennel Club is a registration body only and not involved with breeding decisions.

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling? NO
C] How many blood samples have been taken or are taken per year? N/A
D] Would you say you get a good response from owners to this scheme? ? N/A
E] What diseases or conditions are being looked at by your health testing? ? N/A
F] What, if anything , do you have in place to encourage people to take part in this health testing? ? N/A
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
In North America breeders are not forced to do any health testing by any registration body; however, due to peer pressure and interest in the well being of the breed we test for many things. Including but not limited to the following:
- Hip scoring through OFA or OVC or Pennhip systems
- Elbow scoring through OFA or OVC
- Some do optional Shoulder testing looking for OCD
- Heart testing by cardiologists
- Annual eye testing by CERF (Canine Eye Registration Foundation)
- Von Willebrands Disease DNA testing
- Degenerative Myleopathy DNA testing
- Thyroid screening optional

- DNA screening for parentage if showing in the US
- Some also do temperament testing by Temperament Test Associates (Canada), and also through performance event competitions such as Canine Good Neighbor test, Obedience trialing, Draft tests, Therapy Dogs International testing, and other bodies who do general temperament testing.

All of the above clearances are then listed on the public database Berner Garde. www.bernergarde.org

The BMDCC totally supports Berner-Garde both in information gathering and financial assistance and encourages other clubs to participate.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

Mass producers act outside the club and often get dogs from overseas from unsuspecting breeders on open/breeding contracts and then breed them every season and sell puppies throughout North America in Pet Stores. This is a huge problem and terrible living conditions for the dogs. People need to check with other reputable sources before sending puppies to Canada or anywhere in North America to know where your puppies are going and what they are being used for. The latest phenomenon in Canada is the “designer dog”. There are many breeders that are crossing Bernese with other breeds like Goldens, Labradors, Poodles, etc to name a few and creating Bernadoodles, Labernese, etc.

SUOMEN SVEITSINPAIMENKOIRAT
FINLANDS SENNENHUNDAR ry.

Country **Finland**
Club Suomen Sveitsinpaimenkoirat – Finlands Sennenhundar ry (SSFS)
Name of person submitting information Tarja Ekman
Email tarja.ekman@netikka.fi

1] Your Club

A] How old is your club 46 years
B] How many members/addresses does your club have? 1400 members / 1350 addresses
C] Which month is your biggest show normally held ? varies, summertime normally
D] Approximately how many entries of BMD do you have at this? 150 -180, shorthaired Sennen dog breeds 30-50
E] How many official BMD breed clubs are there in your country? 1

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 400 – 500
B] Is this number rising or falling or about the same over the last few years ? about the same
C] Any other comments

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? YES
C] Do these controls apply to everyone breeding or only club members? EVERYONE
D] Do dogs have to be hip scored before mating? YES
E] Do dogs have to be elbow scored before mating? YES
F] Do dogs have to be Character Assessed before mating? / Recommended but not enforced
G] Do dogs have to have a confirmation or exterior assessment before mating? Recommended but not enforceable
club organizes official character testing yearly, 20-30 BMDs tested every year
H] Does the club have any control over mating selection? YES

This rises from regulation of the Finnish Kennel Club. Our club has made a compulsory breeding plan for every 5 years that has been accepted by FKC and there are enforceable regulations connected to registration of puppies. Our breeding commission has made proposals and the club has accepted these in the general meeting and Kennel Club has accepted them.
HD E and ED 3 are not accepted for breeding. HD C or HD D (according to the lower hip score of the individual) must have a partner HD A or HD B. ED 1 or ED 2 (according to the "worse" elbow, so all between ED 0/1 – 2/2) must have a partner ED 0/0. Recommended that the breeding index of the combination [(sire + dam)/2] for both hips and elbows to be 100 or better (in our BLUP-system "better" is over 100).

I] Are there any controls on the number of puppies a dog can sire? YES 60 puppies and the last litter as a whole

J] Are there any controls on the age a dog can sire his first litter? Recommended but not enforced: in order to get the litter into the puppy referral of our club, the sire must be at least 18 months old. Otherwise the male must be over 1 year old to be officially x-rayed and have got the official results also before mating.

K] Are there any limits on the number of litters a bitch can have? YES 5 litters maximum**.**

L] Are there any controls on the age of bitches used for breeding? YES/ Recommended but not enforced: when over 8 years old, a veterinary certificate needed (enforceable). For our own puppy referral, the dam must be at least 24 months old, but such litters can still be registered.

Any other comments

4] Health Testing

A] Does your club undertake any health testing? **YES**
B] Does any of this involve blood sampling? **YES**
C] How many blood samples have been taken or are taken per year? **A few**
D] Would you say you get a good response from owners to this scheme? **YES** / **MIXED RESPONSE**
E] What diseases or conditions are being looked at by your health testing?

- participating in a study about heritability of epilepsy (blood samples from carriers and dogs that have diagnosis, Health Fund pays costs for taking the sample and provides materials and posting for those who have given their diagnosis public, and for the parents and full sisters of the epileptic dog); the researcher is Dr. Hannes Lohi, Finland

- a project of the Health Fund in which cheek cell samples were taken and gene tested for DM (degenerative myelopathy), samples taken in club show and Health Fund paid the testing: 7-8 BMD:s participated, was offered for 20 dogs without any limits (in 2010)

- a project of the Health Fund in which official eye inspections were made in three cities around Finland, 65 BMDs tested. Payment in co-operation with Club itself and Health Fund (2007-2008)
- all autopsies and biopsies are paid when results are given public for the club (death cause survey). Owners have to apply for the payment afterwards. Payment in co-operation with Club itself and Health Fund

F] What, if anything , do you have in place to encourage people to take part in this health testing?
- testing for free if the results are public
- informing about problems in the newsletter, motivating

G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
- collecting death and death cause data since 1995, later extended to health information during the lifetime; public in the homepage of the club, sometimes also in the newsletter
- collecting death data of elderly (8 years or older) Berneses since 2003, later extended to all deaths (Passed away-list); public in the homepage of the club, oldest 30 also in the newsletter;
- collecting data about living, elderly Berneses since 2003 (Still Going Strong-list); public in the homepage of the club, also in the newsletter, updated 4 times a year
- age research by Dr. Katariina Mäki (article in the booklet of the symposium 2011) made about all the information above and also Swiss death date information. Started in 2010, continuing. Funded by our club and Health Fund together.
- participating in epilepsy research (Dr. Hannes Lohi) and keeping and updating a public list of BMDs that have been diagnosed epilepsy
- public list of BMDs that have been diagnosed kidney dysplacia (so far only one case)

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

There is a new donation in Finland of an insurance company Tapiola for a breed club that has made remarkable steps in order to get healthier dogs. Our club was the first to receive the donation (2500 euros) in December 2010.

We have breeding indexes for hips and elbows in full use for Berneses and they are public and available in the Internet: http://jalostus.kennelliitto.fi/frmEtusivu.aspx . Recommended that the breeding index of the combination [(sire + dam)/2] for both hips and elbows to be 100 or better, since in our BLUP-system “better” is over 100.

We also have preliminary age indexes, but they are not yet public (in the beginning of July 2011) and we still need more information, testing and research in this area. In this connection we want express special gratitude to Swiss breeding commission for the help and information we have received.

Country **Great Britain**
Club Bernese Mountain Dog Club of Great Britain
Name of person submitting information Steve Green
Email chair@bernese.co.uk

1] Your Club

A] How old is your club **40 years!!**

B] How many members/addresses does your club have? 1,314 members at 872 addresses, this figure is slowly falling from a peak of around 1650 members at 1120 addresses.

C] Which month is your biggest show normally held ? September

D] Approximately how many entries of BMD do you have at this? Up to 200

E] How many official BMD breed clubs are there in your country? 6

We are the largest and oldest British club but there are 5 other Kennel Club registered clubs who, unlike some countries, have the same status as us at the Kennel Club.

The other clubs are:

Southern Bernese Mountain Dog Club (based around the South of England)
Northern Bernese Mountain Dog Club (based around the North of England)
Bernese Mountain Dog Club of Scotland
Central Bernese Mountain Dog Club (based in the middle of England)
Bernese Mountain Dog Club of Wales *(very recently recognised)*

The clubs come together under an official umbrella organisation recognised by the Kennel Club and called The Bernese Mountain Dog Breed Council.

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 2010 - 613 registered at the Kennel Club

B] Is this number rising or falling or about the same over the last few years ? Falling – previously averaged around 750

C] Any other comments

Bernese are the 56th most popular breed in the UK. (To put us into context Labradors registered over 44,000 last year).

3] Breeding Controls

A] Are there any quality/health controls in place? YES

B] Are these compulsory or only recommended? Compulsory

C] Do these controls apply to everyone breeding or only club members? Club members have some compulsory controls and some recommended

D] Do dogs have to be hip scored before mating? YES

E] Do dogs have to be elbow scored before mating? YES

F] Do dogs have to be Character Assessed before mating? Recommended but not yet compulsory. Character Testing available at some club events.

G] Do dogs have to have a confirmation or exterior assessment before mating? No

H] Does the club have any control over mating selection? No

I] Are there any controls on the number of puppies a dog can sire? No

J] Are there any controls on the age a dog can sire his first litter? Yes

K] Are there any limits on the number of litters a bitch can have? Yes

L] Are there any controls on the age of bitches used for breeding? Yes

Any other comments

The landscape in this area is changing over the last few years and clubs are responding to this. The Kennel Club is also making more information and analysis tools available but generally promotes education and persuasion over compulsory actions.

4] Health Testing

A] Does your club undertake any health testing? No

B] Does any of this involve blood sampling? N/A

C] How many blood samples have been taken or are taken per year? N/A

D] Would you say you get a good response from owners to this scheme? N/A

E] What diseases or conditions are being looked at by your health testing? N/A

F] What, if anything , do you have in place to encourage people to take part in this health testing? N/A

G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.

We of course support our Kennel Club's Hip and Elbow scoring and all members must X ray their breeding stock. Apart from this we have had numerous schemes and surveys over the years.. We had a foreleg lameness survey in the eighties, a cancer tissue collecting scheme in the early nineties in conjunction with Cambridge Veterinary School, a blood collecting scheme in the late nineties in conjunction with

AHT, Several health surveys of different types. Currently we have no schemes in place but things are changing generally in the UK as outlined below.
We do maintain a Veteran's List of older Bernese to stimulate awareness and interest of longevity.

4] Health Testing

A] Does your club undertake any health testing? Not currently but Hip and Elbow scoring is processed by the Kennel Club.
B] Does any of this involve blood sampling? No – blood sampling is actually illegal in our country and although there are ways around it, this this law does not help matters for our breed.
C] How many blood samples have been taken or are taken per year? N/A
D] Would you say you get a good response from owners to this scheme? In the past schemes have had a disappointing response when actual actions such as blood or tissue samples have been required. However, other requests only for information have often been very well supported.
E] What diseases or conditions are being looked at by your health testing?
F] What, if anything , do you have in place to encourage people to take part in this health testing?
In the past we had financial support and made the testing free with free collection at club events but this did not get the response we hoped for.
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
Several surveys over the years with varying results.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

As you will hear at the seminar from Dr Sampson there has been much activity at our Kennel Club over the last few years in the area of canine health. Whilst things were always happening the speed of developments has increased and the Kennel Club is much more proactive and looking to involve the breed clubs more. At the moment this has not directly affected the Bernese Mountain Dog because of the lack of specific recordable actions we can take.

However, the breed clubs will become more involved over the next period of time and I feel the Kennel Club will be expecting us to become more active in doi whatever we can to support health in our breed.

Country Ireland
Club Bernese Mountain Dog Club of Ireland
Name of person submitting information Valerie Hughes
Email carraigbern@gmail.com

1] Your Club
A] How old is your club? 31 years
B] How many members/addresses does your club have? 310 members /132 addresses
C] Which month is your biggest show normally held ? September
D] Approximately how many entries of BMD do you have at this? 55 - 70.
E] How many official BMD breed clubs are there in your country? One

2] Size of Bernese Population in Your Country
A] Approximately how many BMD are registered per year in your country? 317.
B] Is this number rising or falling or about the same over the last few years ? Rising
C] Any other comments

3] Breeding Controls
A] Are there any quality/health controls in place? Recommendations but not enforcable
B] Are these compulsory or only recommended? / Recommended but not enforcable
C] Do these controls apply to everyone breeding or only club members? ONLY CLUB MEMBERS
D] Do dogs have to be hip scored before mating? Recommended but not enforced
E] Do dogs have to be elbow scored before mating? Recommended but not enforced
F] Do dogs have to be Character Assessed before mating? NO
G] Do dogs have to have a confirmation or exterior assessment before mating? NO

H] Does the club have any control over mating selection? NO

I] Are there any controls on the number of puppies a dog can sire? NO

J] Are there any controls on the age a dog can sire his first litter? Recommended but not enforced
K] Are there any limits on the number of litters a bitch can have? Recommended but not enforced

L] Are there any controls on the age of bitches used for breeding? Recommended but not enforced

Any other comments

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling? N/A
C] If yes, how many blood samples have been taken or are taken per year?
…… / ……. per year
D] Would you say you get a good response from owners to this scheme? N/A
E] What diseases or conditions are being looked at by your health testing? N/A
F] What, if anything , do you have in place to encourage people to take part in this health testing? N/A
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
The Bernese Mountain Dog Club of Ireland undertook a health survey in conjunction with Cambridge University to study the health of the Bernese Mountain Dog and in particular the incidence of cancer. This study was carried out over a five year period and relied on members submitting relevant information on a yearly basis. Regretfully uptake was poor and the survey was never completed.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members and other Bernese clubs around the world. Are there any particular problems that you face in your country?
There is a particular problem with litters being advertised on a website called Done Deal. This website is well known and popular for the sale and purchase of items. The website is a regular conduit for puppy farmers selling their litters. Due to an upsurge in litters over the last 24 months the quantity of puppies available has driven the asking price down and resulted in a number of puppies being unsold at 12 weeks and older. It is hoped that, should this trend continue, many breeders will desist from breeding larger breeds. The Bernese Mountain Dog Club of Ireland regularly runs an advert on this site advising potential buyers to contact the Club for a list of reputable breeders and sends out information sheets on the breed to all enquirers. We actively encourage the public to contact us with any concerns they have regarding the breed as we strongly believe the way forward with the breed in Ireland is to educate.

Country **Italy**
Club Club Italiano Amatori Bovari Svizzeri (C.I.A.B.S.)
Name of person submitting information Silvana Vogel Tedeschi
Email Silvana.vogel@ciabs.it

1] Your Club

A] How old is your club? 23 years
B] How many members/addresses does your club have? 450 members
C] Which month is your biggest show normally held ? April
D] Approximately how many entries of BMD do you have at this? Between 140-160.
E] How many official BMD breed clubs are there in your country 1

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 1299 in year 2010
B] Is this number rising or falling or about the same over the last few years ? It's rising
C] Any other comments

3] Breeding Controls

A] Are there any quality/health controls in place? Partly YES
B] Are these compulsory or only recommended? Recommended and Enforced
C] Do these controls apply to everyone breeding or only club members? They apply to all breeders having a recognised ENCI-FCI kennel, whether they are members of the CIABS or not.
They are recommended to the other breeders (CIABS members or not)

D] Do dogs have to be hip scored before mating? Recommended but not enforced
E] Do dogs have to be elbow scored before mating? Recommended but not enforced
F] Do dogs have to be Character Assessed before mating? No
G] Do dogs have to have a confirmation or exterior assessment before mating? No
H] Does the club have any control over mating selection? Recommended but not enforced
I] Are there any controls on the number of puppies a dog can sire? NO
J] Are there any controls on the age a dog can sire his first litter? YES
K] Are there any limits on the number of litters a bitch can have? YES
L] Are there any controls on the age of bitches used for breeding? YES

Any other comments The Italian Kennel Club, ENCI, has breeding regulations which apply to breeders having a kennel recognised by the ENCI and FCI. The CIABS has its own breeding regulations which are more restrictive but they are not compulsory because the ENCI does not recognise the breeding regulations issued by the breed clubs.

4] Health Testing

A] Does your club undertake any health testing? YES
B] Does any of this involve blood sampling? No, only samples for the histiocytic sarcoma
C] How many blood samples have been taken or are taken per year? About 50 for the histiocytic sarcoma
D] Would you say you get a good response from owners to this scheme? Mixed response.
E] What diseases or conditions are being looked at by your health testing? See G
F] What, if anything , do you have in place to encourage people to take part in this health testing?
See G
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.

Research Project EBV (Estimated Breeding Values) for HD and ED – University of Padova

This project concerns 3 breeds: Boxer, Bernese Mountain Dog and German Shepherd Dogs for the joint diseases and it involves the breed clubs, the ENCI and both the certifying panels for skeletal disorders. In addition to the University of Padova there will be other universities involved. The first step of the project has already started: the EVB is being calculated for HD and ED in all BMDs. The European BMD clubs were aksed to give HD and ED data in order to get more significant data from a statistical point of view.

One more goal of the project is to consider the possible effect of inbreeding, estimated with the COI, on the onset of skeletal diseases.

Blood samples from the X-rayed dogs will soon be collected with the purpose of starting a survey on the genome. The genetic variability will be checked by genomic markers in 100 dogs of each breed. As soon as the number of samples Is enough (at least a thousand), additional molecular studies will be made. It will be possible in the future to breed using various selecting methods.

Project RDS Raccolta Dati Salute = Health Data Collection)

This has started in June and it involves the members of the CIABS, (breeders and owners), who participate on a voluntary basis. This means accepting the ENCI and CIABS breeding regulations and being willing to take part in studies, research and data collection organised by the club.

At present the project includes:

- The study of the University of Padova
- The study about longevity: data collection also through the veterinarians, to calculate an EBV for longevity.
- Fertility: data collection through specialised centres

The members who join the project have a “Quality certification” and their names are listed on the club web site.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

See 4]

Control and management of breeding is made complicated by the difference between regulations. Therefore we believe that the involvement in the project on a voluntary basis and the ”Quality certification” might be an excellent solution.

Country **Netherlands**
Club Vereniging de Berner SennenHond (VBSH)
Name of person submitting information Jessica van de Poll/ Iris van Deur, veterinarian
Email…secretariaat@bernersennen.nl / gezondheid@bernersennen.nl

1] Your Club

A] How old is your club? 33 years
B] How many members/addresses does your club have? 1599 members
C] Which month is your biggest show normally held ? October/ November
D] Approximately how many entries of BMD do you have at this? Between 250 and 150.
E] How many official BMD breed clubs are there in your country 2

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? ?? (see below)
B] Is this number rising or falling or about the same over the last few years ? ??
C] Any other comments There is no reliable number for the total population of BMD's in the Netherlands. Quite a lot are bred without a pedigree.

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? YES, compulsory (HD/ED) and recommended (Livershunt)

C] Do these controls apply to everyone breeding or only club members?
EVERYONE that breeds with a pedigree (HD/ED) and for members in the club (Livershunt also).
D] Do dogs have to be hip scored before mating? YES
E] Do dogs have to be elbow scored before mating? YES
F] Do dogs have to be Character Assessed before mating? YES but only club members
G] Do dogs have to have a confirmation or exterior assessment before mating? YES but only club members.
H] Does the club have any control over mating selection? NO
I] Are there any controls on the number of puppies a dog can sire? NO
J] Are there any controls on the age a dog can sire his first litter? YES
K] Are there any limits on the number of litters a bitch can have? YES
L] Are there any controls on the age of bitches used for breeding? YES

Any other comments Question J to L: there are differences between club members and breeding with only a pedigree. We recommend some breeders to test on Livershunt when we know that a sire or a bitch has the gene for Livershunt.

4] Health Testing

A] Does your club undertake any health testing? YES
B] Does any of this involve blood sampling? YES
C] How many blood samples have been taken or are taken per year? Approximately 150 per year
D] Would you say you get a good response from owners to this scheme? YES within the club it is an obligation.
E] What diseases or conditions are being looked at by your health testing?
At this moment just sampling for DNA tests. When there is a test for Malignant Histiocytosis and Livershunt all the breeding dogs are tested.
F] What, if anything , do you have in place to encourage people to take part in this health testing?
We have 2 showevents every year and 4 breeding test weekends. People can come with their dog with a pedigree where a vet can take blood of the dog for sampling DNA.
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
At the moment we recommend to register deceased dogs with information of the vet. We note every illness when people give us the information. We are actively helping in the research for the genes involved with Malignant Histiocytosis and we give information to the researchers of Livershunt.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

More and more we see problems with the kidneys, Acute and chronic kidney failure in young (2 to 4 years old) BMD's. Also are there more BMD's with skin problems that are allergies to all kinds of allergenes.

Hip and Elbow problems are still there but only the breeding population has to be researched. That tells us that the best material is sorted out for breeding but there are still problems with hips and elbows.

Two orthopaedic problems that are rising are the OCD problems in the shoulder and problems with the crossbands. We will have to follow these problems.

The following report was gratefully received from Russia

We are expressing our gratitude to the Bernese Mountain Dog of Great Britain for the invitation to celebrate the occasion of 40th anniversary of the breed and for the opportunity to tell about our Club in the pages of your seminar booklet.

Russian National Club of BMD was founded in 1994. By that time there had already been about a hundred of dogs, from who the breeding of BMD was started in our country. At that time nobody recognized a tri-colored nice dog in Moscow streets and gave them different names from collie to spaniel.

Much work has been done by the National Club of BMD for popularization and making the breed in our country. To work this out we used all the possible ways. Such as television (as the most powerful information channel) we took part in popular shows about animals. Among them: "My champion", "Stories about animals", "Dog show" etc. Participation in different shows took much time for filming and preparing dogs for it. Then we decided to make a film about the breed and called it " About a Bernese Mountain Dog". After we showed our film on TV, it became popular and our nationals liked it as the film showed all advantages and beauty of the Bernese Mountain Dog.

At the end of 20th century internet did not help to find information about the breed but at the same time we received lots of questions in our club. To answer them all we wrote a book which is called "About a Bernese Mountain Dog with Love". As a result a thousand copies were printed. The work with the book was hard, but thanks to some powerful desire and realising that it must be done, the book came into the world. The number of copies was not big

and very soon was over while the demand was increasing. So we edited our second book about BMD which is called "Intra vitam with BMD" which disappeared from bookstalls very fast as well. After a long discussion we made a decision to publish our own magazine and called it "Bernese Mountain Dogs in Russia". The magazine is an informative collection and covers all the aspects in the life of BMD. Fortunately creative publishing work did not detract from our main business to unite the owners of BMD and to do the breeding of this amazing dog.

We tried to bring dogs from the best kennels from all over the world to our country. No doubt we had difficulties but in general the total number of dogs in Russia is worthy. Victories of the dogs from Russia at World and National dog shows are the evidence of that.

So we have got Sennenhund Rossii **Teddy Bear Charmel** – Champion of Europe -2009, Intrechampion, Vice champion of Europe 2008, Grandchampion of Russia, Prize winner of the dog show devoted to one-hundredth anniversary of the breed in Switzerland in 2007, BOB at the at championship of Central and Eastern Europe in Germany in 2008, champion of Germany, Ireland, Hungary, Finland, Sweden, Croatia, Ukrane. BOB in Switzerland (CAC, CACIB, BOB x 2 Switzerland) etc.

Junior Champion of the world 2010 – ***Sennenhund Rossii Ganel***

The results of the last years encourage us to further development in the breed.

The duration of life of BMD in Russia vary from 8 to 11 years. We've got some lines whose duration of life comes to 12-15 years. Also we would like to assign that hard diseases don't have the mass character.

Our National Club organizes special seminars three times a year on different subjects. The subject is usually chosen by the specialists in the breed who come to judge our dog show. Some of them were extremely interesting. For example:

- F. Schweizer (Switzerland) «Standard of BMD»;
- Sharon C. Smith(USA) «What makes BMD a BMD»;
- Juhasz Istvanne (Hungary) "The expert's view on the breed in Hungary and in the world";
- Maria Amelia Martinho De Magalhaes Taborda (Portugal) "The expert's view on BMD in Europe".

Work with BMD is a very interesting, difficult and noble task as Bernese themselves help in it so much.

Once more we would like to thank the organisers for the invitation and for the opportunity to take part in this booklet. We wish us all long and fruitful work with such a smart and beautiful dog BMD.

We invite everybody to Moscow. Our traditional breed show takes place every year on the last Sunday of May.

We wish all good luck!

President of the National Club "Bernese mountain Dog" Eugunia Fedorovitcheva, vice president Lubov Shevirova.

+79037702211 +7 903 590 90 08

Country **SLOVENIA**
Club BMDC OF SLOVENIA (Slovenski klub za bernske planšarske pse)
Name of person submitting information MOJCA SAJOVIC, Club President
Email bernski.klub@gmail.com or astra10@siol.net

1] Your Club

A] How old is your club? 11,5. years
B] How many members/addresses does your club have? 86. members /70 addresses
C] Which month is your biggest show normally held? January
D] Approximately how many entries of BMD do you have at this? 50.
E] How many official BMD breed clubs are there in your country? 2

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 2010: 12 litters, 71 puppies, 2 imported; 2009: 17 litters, 105 puppies, 1 imported (imported dogs are all in the statistics)
B] Is this number rising or falling or about the same over the last few years ? Falling
C] Any other comments The number of imported dogs is rising

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? COMPULSORY
C] Do these controls apply to everyone breeding or only club members? EVERYONE
D] Do dogs have to be hip scored before mating? YES
E] Do dogs have to be elbow scored before mating? YES
F] Do dogs have to be Character Assessed before mating? YES
G] Do dogs have to have a confirmation or exterior assessment before mating? YES
H] Does the club have any control over mating selection? NO

I] Are there any controls on the number of puppies a dog can sire? NO

J] Are there any controls on the age a dog can sire his first litter? YES (15 months)
K] Are there any limits on the number of litters a bitch can have? NO (mating is allowed from 20 months until 8 years fulfilled)
L] Are there any controls on the age of bitches used for breeding? YES

Any other comments :

Recently, **new (milder) breeding rules** have been adopted: HD A, B, C allowed, ED: 1 allowed, OCD: 1 allowed

4] Health Testing

A] Does your club undertake any health testing? NO

B] Does any of this involve blood sampling? NO

C] How many blood samples have been taken or are taken per year? N/A

D] Would you say you get a good response from owners to this scheme? YES / NO / MIXED RESPONSE

E] What diseases or conditions are being looked at by your health testing?

Health testing was carried out by several owners on their own initiative. Mostly these are tests for borreliosis, ehrlichiosis and other tick-borne diseases.

F] What, if anything , do you have in place to encourage people to take part in this health testing?

G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.

In 2002 and 2003 we offered our members to have their BMDs examined by a veterinarian free of charge. We also took blood samples for biochemical analysis. As the examinations took place only in one veterinary clinic, the response of our members was not encouraging.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

The BMD Club of Slovenia held exclusive breeding competence for BMDs from 2000 until 2011, conferred to it by the national Kennel Club (Kinoloska zveza Slovenije). The Club developed high-quality breeding rules that protected the breed in terms of both health and character. Owing to divergent interests, in 2009 individual members left the Club to form a second BMD club in Slovenia. The original Club nevertheless maintained the national breeding licence. In late 2010, however, the national Kennel Club – influenced by certain BMD breeders – imposed milder breeding rules (see above) for BMDs which the Club could not agree with, finding them too permissive to ensure a quality BMD population. Thus, in February this year, the Club's Assembly decided to give up the breeding competence since it had no influence on the breeding rules and was unable to establish a constructive dialogue with the breeding committee. Keen on preserving a healthy breed with stable character and temperament, the Club adopted and invited its members to adhere to the Club's own breeding recommendations that are stricter and primarily committed to "breeding excellence".

Country **SPAIN**
Club Club Espanol De Boyeros Suizos
Name of person submitting information Arturo Fernando Ortega
Email garbin777@gmail.com

1] Your Club

A] How old is your club? 4 years
B] How many members/addresses does your club have? 140. members / 63 addresses
C] Which month is your biggest show normally held? May
D] Approximately how many entries of BMD do you have at this? 25.
E] How many official BMD breed clubs are there in your country? 1

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? 25-30
B] Is this number rising or falling or about the same over the last few years ? About same
C] Any other comments In the last two years nearly 20 puppies were imported

3] Breeding Controls

A] Are there any quality/health controls in place? Recommended but not enforcable
B] Are these compulsory or only recommended? Recommended but not enforceable
C] Do these controls apply to everyone breeding or only club members? Only Club Members
D] Do dogs have to be hip scored before mating? Recommended but not enforcable
E] Do dogs have to be elbow scored before mating? Recommended but not enforcable
F] Do dogs have to be Character Assessed before mating? Recommended but not enforcable
G] Do dogs have to have a confirmation or exterior assessment before mating? Recommended but not enforcable
H] Does the club have any control over mating selection? Recommended but not enforcable
I] Are there any controls on the number of puppies a dog can sire? Recommended but not enforcable
J] Are there any controls on the age a dog can sire his first litter? Recommended but not enforcable
K] Are there any limits on the number of litters a bitch can have? Recommended but not enforcable

L] Are there any controls on the age of bitches used for breeding? Recommended but not enforcable

M] Any other comments :

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling? YES
C] How many blood samples have been taken or are taken per year? 50
D] Would you say you get a good response from owners to this scheme? Mixed Response
E] What diseases or conditions are being looked at by your health testing?
F] What, if anything , do you have in place to encourage people to take part in this health testing? We try to spread the message that it is very important health screening and to make people aware especially breeders.
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
In accordance with Berner-Garde we send blood to Reims Iniversity and we try to get samples of Tumours and causes of death etc.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?
We cal some meetings each year in which we spread Berner values. We try to make breeders aware of health and character and also owner ethics.
In our country our numbers are definitely growing and we believe that every day our Bernese are more well known for carting, showing, character test and generally our working dogs.

Country **Sweden**
Club The Swedish Club of Swiss Mountain Dogs.
Name of person submitting information Berndt Klingeborn
Email klingeborn@tele2.se

1] Your Club

A] How old is your club? 43 years
B] How many members/addresses does your club have 1500 members
C] Which month is your biggest show normally held ? June
D] Approximately how many entries of BMD do you have at this? 200–250
E] How many official BMD breed clubs are there in your country? One

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? ca 650
B] Is this number rising or falling or about the same over the last few years ? The same
C] Any other comments

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? YES and Recommended but not enforcable
C] Do these controls apply to everyone breeding or only club members? EVERYONE
D] Do dogs have to be hip scored before mating? YES
E] Do dogs have to be elbow scored before mating? YES
F] Do dogs have to be Character Assessed before mating? NO

G] Do dogs have to have a confirmation or exterior assessment before mating?
Recommended but not enforcable

H] Does the club have any control over mating selection? NO

I] Are there any controls on the number of puppies a dog can sire? YES

J] Are there any controls on the age a dog can sire his first litter? YES
K] Are there any limits on the number of litters a bitch can have? YES
L] Are there any controls on the age of bitches used for breeding? YES

Any other comments
B) Some programs are compulsory, others recommended

4] Health Testing

A] Does your club undertake any health testing? NO
B] Does any of this involve blood sampling?
C] How many blood samples have been taken or are taken per year?
D] Would you say you get a good response from owners to this scheme?
E] What diseases or conditions are being looked at by your health testing?
F] What, if anything , do you have in place to encourage people to take part in this health testing?
G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.
Breeding indices will be introduced för hip dysplasia and elbow dysplasia January 1, 2012
Research program for renal dysplasia
Registration of cases of familiar nephropathy

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

Country **Switzerland**
Club Schweizerischer Klub für Bernersennenhunde KBS
Name of persons submitting information Martha Cehrs and Urs Geissbühler
Email marthacehrs@bluewin.ch

1] Your Club

A] How old is your club? 104 years
B] How many members/addresses does your club have?approx 1400 members
C] Which month is your biggest show normally held ? September of every year
D] Approximately how many entries of BMD do you have at this? 180-220
E] How many official BMD breed clubs are there in your country? One

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country? Between four hundred and four hundred and fifty (last year 420)
B] Is this number rising or falling or about the same over the last few years ? Falling
C] Any other comments The reason for falling numbers of puppies registered per year are mainly two-fold: the demand has fallen due to economical reasons but also because more stringent legislation regarding owning large size dogs has been introduced in Switzerland over the past couple of years. The other reason is the fact that the club has continuously increased the minimum requirements with regards to the condition puppies are raised in and drastically raised the expectation of the breeders to assist in tracking the health information of all the puppies they raised/sold through out their life

3] Breeding Controls

A] Are there any quality/health controls in place? YES
B] Are these compulsory or only recommended? YES compulsory
C] Do these controls apply to everyone breeding or only club members? EVERYONE who wants to breed dogs with a pedigree
D] Do dogs have to be hip scored before mating? YES enforced
E] Do dogs have to be elbow scored before mating? YES enforced
F] Do dogs have to be Character Assessed before mating? YES enforced
G] Do dogs have to have a confirmation or exterior assessment before mating? YES enforced

H] Does the club have any control over mating selection? NO with the exception of the fact that stud and dam have to conform to the enforced breeding rules
I] Are there any controls on the number of puppies a dog can sire? NO – however, there is a restriction of the number of litters a stud can sire per year
J] Are there any controls on the age a dog can sire his first litter? YES enforced
K] Are there any limits on the number of litters a bitch can have? NO - however the age of starting to breed and the age when a bitch must stop to be bred as well as the intervals between litters are regulated and enforced.
L] Are there any controls on the age of bitches used for breeding? YES enforced

Any other

4] Health Testing

A] Does your club undertake any health testing? NO – with the exception of encouraging dog owners to
support Dr. C. André/B.Hedan/M. Breen studies
B] Does any of this involve blood sampling? YES blood is sent to Dr. C. André
C] If yes, how many blood samples have been taken or are taken per year? …very few (under ten) per year
D] Would you say you get a good response from owners to this scheme? NO / or MIXED RESPONSE
E] What diseases or conditions are being looked at by your health testing? MH or HS
F] What, if anything , do you have in place to encourage people to take part in this health testing? Informing individual dog owners/or their veterinary at the time their dog is diagnosed with MH/HS of the steps to to take to supply blood and tissue to Dr. C. André

Country: **USA**

Club: Bernese Mountain Dog Club of America

Name of person submitting information: Julie Jackson, BMDCA health committee chair

Email jjackbcop@aol.com

1] Your Club

A] How old is your club? 53 years

B] How many members/addresses does your club have? 1296 members / 1106 addresses

C] Which month is your biggest show normally held ? April/May

D] Approximately how many entries of BMD do you have at this? (from Nancy VanHorne, nat. specialty coordinator)

2010: 724.

Note that in addition to conformation we had these performance entries:

20-herding, 108- obedience, 8- tracking, 110-agility, 166-rally obedience, 72- draft ,

In the last few years entries have been:

Rhode Island/2008: 587

Kentucky, Louisville/2007: 532

Frankenmuth/2006: 730

Largest entry to date, Gettysburg/2005, : 926

E] How many official BMD breed clubs are there in your country? 30 regional clubs

2] Size of Bernese Population in Your Country

A] Approximately how many BMD are registered per year in your country?

	2008	2009	2010
Litters:	1193	1160	1122
Dogs:	3338	3243	3120

B] Is this number rising or falling or about the same over the last few years ?

In 2000, BMD's were # 49 of all breeds. In 2010, they are no #38. There is an overall trend in popularity of large breeds.

And # of BMD's in AKC conformation shows is much larger than breeds with much more popularity.
C] Any other comments Cannot know bernese litters produced outside AKC registration, many from breeders on the internet. Based on increasing # of dogs coming into rescue, this number is rising too.

3] Breeding Controls

A] Are there any quality/health controls in place? Recommendations but not enforcable
B] Are these compulsory or only recommended? Recommended but not enforcable
C] Do these controls apply to everyone breeding or only club members? ONLY CLUB MEMBERS
D] Do dogs have to be hip scored before mating? Recommended but not enforced
E] Do dogs have to be elbow scored before mating? Recommended but not enforced
F] Do dogs have to be Character Assessed before mating? Recommended but not enforced. This is an area of breeding that we lack proper testing. Many believe this is an area for improvement
G] Do dogs have to have a confirmation or exterior assessment before mating? Recommended but not enforcable
H] Does the club have any control over mating selection? NO
I] Are there any controls on the number of puppies a dog can sire? NO
J] Are there any controls on the age a dog can sire his first litter? 12 months minimum is Recommended but not enforced (note that some regional clubs recommend 18 months minimum)
K] Are there any limits on the number of litters a bitch can have? NO
L] Are there any controls on the age of bitches used for breeding? NO
Any other comments Many regional clubs require a minimum of 2 years old for minimum breeding age in their code of ethics.

4] Health Testing

A] Does your club undertake any health testing? YES, at the National Specialty and some Regional BMD clubs will sponsor health clinics to provide access to vet specialists and DNA tests at reduced pricing.
B] Does any of this involve blood sampling? YES , for the BMD repository for research database.
C] How many blood samples have been taken or are taken per year? for repository in 2010: 259. Now have a total of 927 submissions in storage, collected from 2007 to 2010.
D] Would you say you get a good response from owners to this scheme? MIXED RESPONSE; regional clubs are getting on board and participating more. Some breeders are beginning to submit all their puppies to the respository with DNA cheek

swabs before they're sold. Then later following up with blood submission when older.

E] What diseases or conditions are being looked at by your health testing?

Hips and elbow dysplasia by X ray evaluated by OFA, von Willebrands (DNA test), AKC DNA (to confirm parentage), CERF for eyes by opthamologist, OFA heart exams by cardiologist (note that Sub aortic stenosis is best diagnosed by Doppler, in addition to current test), and more recently, DNA test for degenerative myelopathy.

F] What, if anything , do you have in place to encourage people to take part in this health testing?

- Recently have added CHIC testing requirements to qualify for the new AKC Breeder of Merit Program, which has become very popular. This may encourage breeders outside the BMDCA to participate in CHIC.
- Public education through the Alpenhorn, AKC Gazette, elists.
- Berner University at the National Specialty provides a wide variety of subjects in a classroom setting. Experts from both within and outside the club, speak on a variety of subjects to improve the health and advocacy of BMD's and their owners.*

For submitting to the repository for research samples, people seem to be eager to participate in these studies, we have a history of owners willing to pay for necropsies, participating in BernerGarde, and a desiring to help improve the overall health of the breed

G] Please outline any health related surveys, projects or other initiatives your club has organised for the Bernese Mountain Dog.

1) The last survey was done in 2005, and a new one is past due. We are in discussions to implement a survey for 2012 or 2013, and are researching methods, i.e., through a website or other electronic data collection methods to minimize the very manual, time consuming entries done by hand in the past.

5] General

Please tell us about anything else that happens in your country or your club is involved in that you think may be relevant or that you wish to tell us about for the interest of the BIWG members. Are there any particular problems that you face in your country?

A primary function of the BMDCA and the health committee are fundraising to support health research and identifying appropriate research grants to support. Fund raising is accomplished through:

- Auction at the national specialty. Items are donated by members, then auctioned in an evening social event. This is the primary fundraiser of the year, and goes to a donor advised fund. 2009: $46000; 2010: $21800.

- Berner Lover Donor Advised Fund, by Joye Neff. She utilizes email lists to get donations from around the world for a variety of raffles. Since 1999, she has raised over $700000! Note that with 2000+ people on the email lists, only 10% are participating—so this is a big opportunity for growth.

Primary research grants supported are through:

- AKC Canine Health Foundation (CHF) and Morris Animal Foundation (MAF). An extraordinary organization creating opportunities for researchers on all canine health issues. Monies donated from BMD clubs and owners are often 'matched' from $1,000,000/year from AKC, and Morris Animal Foundation (about 1/3 of grants $'s are supported by MAF). This means for every $1 donated by BMD donations, CHF and MAF match the donations, and on occasions we have received double or triple matches from the CHF. This is a powerful tool to leverage $'s raised. *

- Attached is a list of grants supported by the BMDCA, through the CHF and MAF, in 2009-2010. *

Other primary tools for health and database is:

- Berner-Garde health database. Now has 75000+ dogs with health information and pedigrees from around the world. *

- Bernese Mt Dog Repository, in partnership with Berner-Garde and Michigan State University. *

- Utilize Berner-Garde website for list of researchers seeking samples for research. This includes a variety of cancer tumor samples, blood, and spinal tissue (at time of humane euthanasia)

- A resource guide for health testing, created by the HC, to be published on the BMDCA website.*

- General update on the BMDCA website and health information

Other:

- Many new DNA tests are coming to market and are difficult to assess validity. There is no governing body overseeing or regulating these tests. So understanding importance of peer-reviewed publications, and support and collaboration within the research communities has been challenging. Currently AKC or OFA will not regulate these tests, yet, may now offer some of them on their websites. A confusing message. An example is the Renal Dysplasia DNA test.

- Renal Dysplasia DNA test through OFA raised concerns from other researchers on the 'science' used and the validity of the BMD samples

submitted. Thank you to Professor Berndt Klingeborn (Sweden) for the information he provided to us. We do not support the validity of the test.

- Histio Therapeutics Action Task force has accomplished their goal of collecting samples of 50 dogs with confirmed diagnosis of malignant histiocytosis, and health information on at least one littermate (live or dead, with or without histio) . An analysis of the data is underway with a biostatistician for a 'matched case-control analysis'.
- Degenerative Myelopathy DNA task force update was published in 2011. *
- The BMDCA Board is now working more closely with the BMDCA health committee, whereas in past years they (both the board and health committee)made decisions more independently.
- Working with the Regional Club Council to get a 'health liaison' volunteer from each regional club, to:
    - Assist their members at the difficult time during their BMD's pending end of life, to help with the process of sending tumor samples.
    - Assist members in understanding other research programs needing submissions.
    - Answer general health questions, and updates on new developments.
- The HC is open to questions/input from members, and available through the BMDCA website or a direct email address: bmdhealthcommittee@gmail.com
- The Canine Health Information Center (CHIC)was created by AKC to encourage open sharing of health data, including affected dogs. This collaborates with AKC and OFA.
    - The BMDCA recommended to AKC and CHIC that the following tests be required for BMD's: OFA hips and elbow xrays, DNA test with Vetgen for vonWillebrands (a bleeding disorder), AKC DNA # (to assure accurate parentage—also required at BMDCA national specialties), OFA Heart exam, CERF (Canine eye registry foundation) for eyes.
    - BMDCA members helped to found GDC (the Institute for Genetic Disease Control),
      which was one of the first open health test registries. When OFA agreed to merge GDC data, it was directly responsible for the change to OFA's policy on open sharing of all health test results, not just the clearances. In essence, the BMDCA community laid the groundwork

for the creation of CHIC - which was created by OFA to help motivate everyone to test and to share all results of those tests. This was something that the BMDCA members had been doing for years with GDC and with Berner-Garde. For information on CHIC, see: www.caninehealthinfo.org

- The requirements for CHIC are under review with the health committee for an update.
- *Additional information supplied separately

Appendices

I –IV

Appendix I

This report was received too late to go in the correct section

Health adjustment in The Danish Bernese Mountain Dog Club.

For the past two years the Danish club has worked hard to collect material regarding the health and the diseases of the breed.
This is to give a real general view over the health condition in general and see, if specific diseases are represented in the breed.
The aim is to work out a Breed strategy, and from this give recommendations for the future breeding.
On the long view the intentions are that the material can be used for the breeders to avoid combinations of two breeding lines, which are carriers of the same diseases.
We can see, that cancer is over represented, but otherwise it seems very scattered as to which diseases are fatal.
It seems, we are having a very stable process regarding a lower number to have elbow dysplasia after dogs with ED 3 are excluded from breeding, and we have restrictions for the breeding with ED 1 and 2.
It seems that our breeding rules here are alright.
For many years we have frequently changed the restrictions for breeding with HD, and it is therefore very difficult to see, if the adjustments has worked. There is no clear tendency of less dogs with HD D and E.
Before the club can bring some real breeding-recommendations, we still need a comprehensive collecting and preparation.
In 2010 there have been considerably less puppies bred than in the previous years, and this tendency obviously continues.
The quota of males from foreign countries used for mating with Danish females is slightly falling and this can on the long view appear to influence on the health conditions in the population.
The Danish Bernese Mountain Dog Club has supported the Cancer project for the breed in KU-life very considerably. See the article by Lise Nielsen. And we still work to collect money for further research concerning healthy, typical dogs with good vitality and stable temperaments and a long lifetime for the future.

Appendix II

This was recently widely circulated around the Bernese Community

Dr. Matthew Breen asked me to share this note with Berner Lovers:

Dear BMD community,

I am delighted that the AKC-CHF have approved funding of my latest proposal, "High-resolution cytogenetic analysis of histiocytic malignancies and development of a targeted quantitative nuclease protection assay to screen for changes in expression levels in archival samples". Although we are faced with a $25,000 budget cut, I can assure you that I will do all I can to minimize the impact that this will have on the goals of the study. I would like to express my sincere gratitude to all in the BMD community for your continued support of this project and your confidence in what we are doing. I believe that without your overwhelming support this project would not have been funded. Thank you very much.

The lay abstract for this study and the scientific abstract are pasted below for your information. This is an exciting project and I am very optimistic about the outcome. I look forward to sharing the results with you.

Best wishes,
Matthew Breen

Lay summary: In a previous study (CHF-760) we demonstrated that canine histiocytic malignancies (HMs) present with a high degree of DNA copy number alterations. We identified several aberrant regions of the genome that are highly recurrent between cases, suggesting that such regions are associated causally with the malignant process. Understanding the biology of genes within such regions is key to developing ways to halt the cancer and prolong life in patients whom otherwise have a poor prognosis. We now have an approach to identify DNA copy number changes that allows us to zoom in on regions of the genome with ~75-fold greater resolution than was possible even just one year ago. Using this technology we will refine the genome regions of interest defined in CHF-760 and identify additional, smaller aberrations. Within these regions we will identify a series of candidate genes for functional analysis. We have developed an assay for use with archival canine tumor samples that allows us to rapidly determine the level of activity of multiple genes with higher sensitivity than was possible previously. Once we have identified the key genes of interest, we will use this assay to screen HM cases for the extent of gene deregulation. In this study we also will identify DNA copy number changes that are shared with human HMs. Combining these approaches, we will narrow down the search for genes playing a key role in HMs and thus move a step closer to developing targeted therapies for canine patients diagnosed with this devastating cancer.

Scientific summary: Cancers are associated with numerous somatic changes to the genome that may disrupt the delicate machinery of the cell. A common consequence of such changes is the presence of specific structural and numerical alterations to genome organization. We have developed a series of molecular cytogenetics reagents and techniques to assess canine tumor specimens for such changes. In CHF-760 we demonstrated that histiocytic malignancies (HMs) of Bernese Mountain Dog and Flat-Coated Retriever present with a high degree of genome reorganization. We identified several aberrant regions that are highly recurrent, suggesting that these are associated causally with the malignant process. Understanding the biology of genes within such regions is key to developing improved therapies for patients whom otherwise have a poor prognosis. Using high-resolution oligo-aCGH we now can identify DNA copy number changes with ~75-fold

greater resolution, refining the size and boundaries of known aberrant regions and identifying smaller changes. We also will assess HMs in additional dog breeds and human patients, to determine regions of potentially broader significance. To assess expression levels of genes within these regions we have developed a multiplex quantitative nuclease protection assay to determine the level of activity of up to 100 genes. This process provides higher sensitivity than was possible previously, and uses archival samples usually unsuitable for analyses of this kind. Combining these two approaches, we will narrow down the search for genes playing a key role in HMs, moving a step closer to developing targeted therapies for canine patients diagnosed with these devastating cancers.

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Matthew Breen PhD CBiol FSB
Professor of Genomics
Dept. of Molecular Biomedical Sciences
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College of Veterinary Medicine

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Thank you to all of the individuals and clubs who helped make our recent 2011 Willem Wijnberg Cancer Fundraiser such a huge success.
Through your generosity we were able to raise $58,616.46 for Dr. Breen's histio research studies. I still have a few pledges to receive from people, and also need to hear from some of the lucky winners that they did receive their prizes. Thank you to the people who have sent money to cover the cost of the postage from their prizes. That is a big help! I will send the money that is due for Dr. Breen's research study as soon as the AKC CHF notifies me of the amount that we owe - and that amount will most likely be matched by the AKC CHF!
The remaining money in the 2011 Willem Wijnberg Cancer Fundraiser account will remain in the account for further research studies by Dr. Breen.

We ARE going to conquer histiocytic sarcoma (formerly called malignant histiocytoma) in our lifetimes thanks to everyone's support!!!

BERNER LOVERS ROCK!!!

Please feel free to share this note with your Berner friends, lists and clubs.

Appendix III

Bernese Mountain Dog Club of Great Britain
8th International BMD Health Seminar
Delegate List

Speakers			
Dobson Dr Jane *(UK)*			
Geissbuhler Dr Urs *(Switzerland)*	KBS	President Health Committee	
Goldberg Samantha *(UK)*			
Green Steve *(UK)*	BMDCGB	Chairman & B-IWG President	waldershelfbernese@doglovers.co.uk
Hedan Dr Benoit *(France)*			
Kennedy Dr Lorna *(UK)*			
Klingeborn Professor Berndt *(Sweden)*	SSHK	President Health Committee	
Long Pat *(USA)*	BMDCA	File Manager - Berner Garde Foundation	pat@bmdinfo.com
Sampson Dr Jeff *(UK)*	The Kennel Club	KC Genetics Consultant	
Austria			
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Nilsson Lisa	SSHK		bernerdalens.kennel@telia.com
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Gerrard Anne	BMDC of Scotland	Committee	
Green Jackie	BMDCGB	Seminar Secretary	jackie@bernese-mountain-dog.co.uk
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Titchmarsh Tracy	BMDCGB		
Trevett Aileen	BMDCGB		neelia@fsmail.net
Veitch Angela	BMDC of Scotland	angela.veitch@dial.pipex.com	
Venables Sophie	BMDCGB		clairvalcuts@jerseymail.co.uk
Wells Deborah	BMDCGB		
U.S.A.			
Cuellar Celia	BMDCA	Member	berner@frontiernet.net
Ebnet Lisa	BMDCA	Member	ebnetbmd@yahoo.com
Jackson Julie	BMDCA	Health Representative	jjackbcop@aol.com
Other Breeds			
Jeans-Brown Pamela		Bullmastiffs	Pamela@bourgueil.co.uk
Miller Deborah		Flatcoat Retrievers	millreed@waitrose.com

Appendix IV

Late Additions to the delegate List

Belgium

Andre Verschueren	info@klaverhoeve.be
Maria Verschueren	info@klaverhoeve.be

UK Veterinary Surgeons

Louise Mallinson
Meg Noble