Understanding LPN in Leonbergers

LPN or Leonberger Polyneuropathy refers to certain breed-specific forms of inherited neuromuscular disease found in our breed. It is a group of genetically based diseases that was first identified and named in August 1999 by Diane Shelton, DVM, PhD, DACVIM, a neuropathologist at the University of California, San Diego School of Medicine. LPN is considered a serious disorder with cases reported throughout the world-wide Leonberger community. It can be completely debilitating and in some cases is fatal.

Teams of scientists on both sides of the Atlantic have identified one form of the disease linked to the LPN1 gene that is located on CFA16 (or the 16th pair of chromosomes in the canine karyotype). They further provided a DNA test for the LPN1 form of the disease. This finding opens the door to effectively reducing the incidence and impact of this one type of polyneuropathy. Using the latest canine genetic research technology, single nucleotide polymorphism (SNP) arrays containing 170,000 SNPs (each a unique DNA marker in the genome), the research teams have also established a link between a segment of DNA on CFA7 that suggests the presence of another causal mutation that is probably responsible for another form of the disease.
The International Leonberger Union has urged all member nations to take action. The test is now a breeding requirement in several major European member countries, and others are currently developing their regulations.

The announcement at our 2010 National Specialty that the LPN1 gene had been found and a test would soon be available was greeted with excitement. However the announcement was colored with some underlying confusion and gave rise to many questions regarding genetics and future LCA policy.

This is the first time that many Leonberger owners and breeders have been required to make serious decisions based on a clear understanding of modern genetics and a complex disease process. Breeders and club leaders have been asked to climb a very steep learning curve in order to make good decisions. It is our hope that this paper will help make the ascent and future decision making a little easier.¹

**LPN1 is a Breed-specific Inherited Disease**

Peripheral polyneuropathy is an umbrella term that refers to a group of disorders that involve more than one nerve outside the central nervous system. Any combination of peripheral nerves can be affected. “Poly” means many and "neuropathy" means that some part of the nervous system isn’t functioning properly. Something causes damage to nerve cells that interferes with sensation and/or movement. Muscles that don’t receive the proper nerve signals become weakened and prevent a dog from functioning normally.

Polyneuropathies come in many different forms and have a wide variety of causes. Some polyneuropathies are inherited and others are acquired later in life. Some polyneuropathies are caused by toxins. By the same token, metabolic diseases such as diabetes and hypothyroidism can cause polyneuropathy by damaging peripheral nerves. Other conditions that cause inflammation of the muscles, joints and kidneys also can lead to polyneuropathy. There is even an infectious organism that can cause the problem. So different causal factors can look like the same disease. Did the dog inherit this or was there a poison or another disease process involved? Differential diagnosis by an experienced veterinarian is important to assure that the correct type of polyneuropathy is being clinically addressed.

¹ Please note that the work and words of the researchers at the University of California San Diego, the University of Minnesota and the University of Bern have been used rather freely and without specific detailed attribution throughout this document. The authors made this choice to simplify your reading and hopefully allow you to focus on the content. The sources are cited at the end of the document and specific quotations and citations are available from the authors at the request of any Board Member.
A Leonberger may suffer from any one or more of these forms of polyneuropathy. However, when we speak of LPN or Leonberger Polyneuropathy (LPN) we are referring to a specific inherited disease, which comes in at least two genetically distinct forms that affect the longest nerves of the body. Research findings indicate that there may likely be a group of several genetically distinct, but clinically similar diseases.

Until 2010 there was no way to clearly prove that a Leonberger had an inherited form of the disease. DNA testing can now clearly show whether or not a dog is suffering from the LPN1 form. Furthermore, preemptive testing can demonstrate if a dog has the LPN1 genetic mutation even if there are no visible clinical signs.

The LPN1 test currently available identifies the mutation responsible for approximately one third of the cases of inherited polyneuropathy in Leonbergers. The other two thirds of cases are apparently caused by different genetic mutations. Our researchers compare this to Charcot-Marie-Tooth (CMT) disorders in people, where it has been observed that many different mutations can present with an extremely similar neurological disease. It is clear that the LPN1 test is the vital first step in addressing a serious disorder in our breed that can ruin a Leonberger family’s quality of life.

A Leonberger with LPN suffers from slowly worsening exercise intolerance. The dog may have noisy breathing, a raspy bark, or difficulty breathing due to involvement of the larynx and laryngeal folds. Gait abnormalities, such as an exaggerated hitched step especially in the hind limbs. There is often wasting of the hind limbs muscles. Eventually the disease may progress to the point where the dog can no longer support its own weight or breathe well enough to maintain the oxygen levels necessary for life.

Biopsies of tissue from affected dogs show degradation of the nerve fibers and loss of myelin, the insulating material that normally helps speed messages along nerves. Muscle biopsies show atrophy resulting from nerve loss. It is important to note that older dogs can also display some or all of these signs and suffer from disease, although typically when dogs are affected at an older age, the disease is less severe.

“Early onset” in this disease means that clinical signs are clearly noticeable before the dog reaches the age of four years. The manifestations of the disease severely impact a dog’s quality of life and are often fatal. Later onset and/or less severe clinical signs may be so mild that families adapt to the dog’s limitations and the dog is never properly diagnosed.
This Is Not A New Disease

This disease didn’t just pop in off the street. Clinical descriptions believed now to have been cases of one form or another of LPN have been reported on and off in Europe since the 1970s. The amount of international importing and exporting of stock over the past four decades suggests that LPN could quite possibly be identified in every country that has Leonbergers.

Now that we have a DNA test for LPN1, we know that Leonbergers in America born at least as early as 1990 had the disease. Ann Rogers’ first Leonberger, Kiersche v.d. Heckenrose, was born in 1990. In retrospect, she had mild clinical signs, that Ann didn’t immediately recognize. When research began in the mid 90s, Ann began submitting blood and biopsy samples for study. Over a period of years, data was collected and analyzed on two of Kirsch’s offspring born in 1993 and one of her grand-offspring born in 1998. A number of her great grand-offspring born in 2001 were also tested as well as a great grand offspring born in 2002 who had a tie back last month. All of these dogs have at least one copy of the LPN1 mutation present in their genome. Three of the dogs had two copies of the faulty allele, one from each parent. One of these died before the age of three. All of the dogs that were tested showed some clinical signs during their lifetimes. The ones with one copy of the faulty form of the gene showed milder clinical signs.

Kiersche obviously had at least one parent carrying at the least one copy of LPN1. By 2009, there were 82 Leos identified by biopsy as being affected. Not many owners and breeders have put procedures in place so that this can be done when they are in the midst of grieving. So the 82 dogs identified with LPN prior to 2009

* It is interesting to note, that since the DNA test for LPN1 has been made available, at least three Saint Bernards at the University of Minnesota Veterinary School have been found to carry the LPN1 the genetic mutation.
represents only a minority of the dogs that probably died of LPN in the past decade or so. Sending a post-mortem sample to a research laboratory is one of the hardest things that a dog owner is called upon to do. Indeed, it is a heroic act. We are working to simplify the process.

### How Does a Leonberger Get LPN?

All Leonbergers have the LPN1 gene. This gene provides coded instructions for causing a string of amino acids to combine into proteins necessary for the proper function of long nerve cells regulating the complex system controlling a Leonberger’s sensation and movement. The longest nerves in the body, such as those innervating the hindquarters and the larynx, appear to be the most susceptible to damage.

In the mutated version of LPN1, the genetic code is corrupted preventing the dog’s body from making proteins essential to certain nerve cells. This causes the nerves to function improperly resulting in weakness in the muscles that are innervated by these nerves. Biopsies of nerves from affected dogs show degradation of the nerve fibers and loss of myelin, the insulating material that normally helps speed messages along nerves. Biopsies of muscle show atrophy resulting from nerve loss. LPN is progressive, debilitating, and if the larynx is involved it can be fatal.

The LPN1 mutation is in fact a ten DNA base pair deletion. Our researchers have designated the letter D to label the mutant (10 base pair deficient) form of the LPN1 gene and the letter N for the normal (or wild type) form. Each dog receives one copy of this gene from its father and one copy from its mother. The combination of a dog’s N and D copies is the genotype for this trait. The three possible genotypes are N/N, D/N, and D/D.

All D/D dogs develop a severe form of polyneuropathy, which usually manifests before the age of three years. Dogs with the N/N genotype will not develop LPN1. It’s important to remember, however, that they may become affected by other forms of polyneuropathy.

Leonbergers with one copy of the mutant version of the LPN1 gene (D/N) rarely show the severe clinical signs that LPN1 homozygote dogs with two copies of the gene exhibit. This suggests that the mode of inheritance could be dose-dependent, meaning the more copies of the mutated gene the worse the clinical signs. However, it does not exclude the possibility that a D/N dog might also have another form of polyneuropathy. According to fundamental genetic principles, Leonbergers found to be D/N will transmit the mutant form of the gene to approximately 50% of their offspring. The balance of their offspring will receive a normal copy of the gene.
Dr. Kari Ekenstedt, DVM, PhD from the University of Minnesota has kindly provided us with an illustration that demonstrates what has happened to the LPN1 gene in its mutant form.

A quick reminder of the basics may help clarify what is happening in the illustration. DNA comprises the complete instruction manual for how to make and maintain a Leonberger.

- Leonbergers have 78 chromosomes, made up of 39 pairs. There are 76 paired chromosomes (called autosomes) numbered 1-38 according to size from the largest to the smallest and two sex chromosomes: X and Y.

- The chromosomes consist of two very long thin strands of DNA chains twisted into the shape of a double helix and are located in the nucleus (the ‘control center’) of the cells.
• Certain segments of the long strands of DNA that make up chromosomes are genes.

• Since the chromosomes come in pairs, genes also come in pairs.

• In each of the over 19,000 canine genes there is genetic information which guides growth, development and health and is in the form of a chemical code, called the genetic code.

• The genetic code in the DNA, is virtually identical across all living organisms and is like a recipe book for the body to make proteins.

• The DNA code is made up of very long chains of four chemical ‘letters’: Adenine (A), Guanine (G), Thymine (T) and Cytosine (C) stored in the cell nucleus. It is permanent storage that is often compared to the reference room of a library where materials are stored and cannot be removed from the room. Information must be copied in order to “leave” the library.

• In the DNA code, each ‘word’ is a combination of three of these four chemical ‘letters’ A, G, C and T. Each three-letter word (a triplet also known as a codon) is the recipe that must be followed if a cell is to produce a particular amino acid that will be used to form proteins.

• When a protein is required by the body the appropriate code is transcribed as RNA (with all the “T”s transcribed as “U”s) and carried outside of the cell nucleus where it is translated into strings of amino acids that form proteins.

• The sequence of three-letter words in the gene enables the cells to assemble the amino acids in the correct order to make up a protein. Each three-letter word corresponds to a specific amino acid. There is some duplicity in the code, and also some flexibility (for example, the third base in a codon is often called the “wobble base” as it may be a different letter, but still code for the same amino acid).

• Different genes are active in different cell types, tissues and organs, producing the necessary specific proteins; some genes are ‘switched off’ and others are ‘switched on.’

• Changes to the genetic code can mean that a particular protein is improperly made, produced in the wrong amounts or omitted.
In summary, a gene is defined by its functionality. It is a sequence of DNA (permanent storage) with a three letter code that is transcribed into RNA, a temporarily stored message, that says start (e.g. AUG), a sequence of triplets coding for amino acids, and a stop code (e.g. UAG) It is capable of being transcribed and translated from DNA to protein language.

Just for an example, a highly simplified gene (with spaces inserted between the triplets or codons) might look like this:

**AUG UUU UUU UCA UCG UUU UAG**

This piece of code gets translated into a protein made up of strings of amino acids. AUG codes for the amino acid, methionine, UUU for phenylalanine, etc. However, if letters are inserted or deleted the code is corrupted and may become unreadable.

Let’s use three letter English words for an example:

**THE FUN LEO RAN AND SAT**

If you remove the initial T the code the letters reassemble into triplets that can’t be understood. The code makes no sense.

**HEF UNL EOR ANA NDS AT***
To function correctly, each cell depends on thousands of proteins to do their jobs in the right places at the right times. When a mutation alters a protein that plays a critical role in the body, it can cause a medical condition. This is what has happened with a mutant copy of the LPN1 gene. When a Leonberger has inherited a mutant copy of the LPN1 gene, the proteins that are required for proper neuromuscular function are corrupted.

**How Many Leonbergers Have LPN1?**

The short answer to this question is we don’t know for sure. But, as anyone who has ever lived with an LPN affected dog can confidently say, whatever the number, it’s too many! Before the end of 1999, most information was anecdotal and largely unconfirmed. It has only been a decade since the disease was clearly identified and named and less than a year since we have had testing data to work with. Without complete, accurate, and open databases covering all dogs, the best we can do is estimate the actual incidence.

The best data we have available at the present moment comes from the University of Minnesota’s records (which include data from the University of Bern). As of May 2011, we have test results on 603 American dogs and 1250 dogs outside of the United States (including Canada).

<table>
<thead>
<tr>
<th>Population with Results</th>
<th>DD - two copies of the mutation, one from each parent</th>
<th>DN – one copy of the mutation</th>
<th>NN – two normal alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>25 dogs or 4.1%</td>
<td>105 dogs or 17.4%</td>
<td>473 dogs or 78.5%</td>
</tr>
<tr>
<td>N = 603</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Other Countries</td>
<td>17 dogs or 2.3%</td>
<td>180 or 14.4%</td>
<td>1053 or 84.2%</td>
</tr>
<tr>
<td>N = 1250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N = 1853</td>
<td>42 or 2.3 %</td>
<td>285 or 15.4%</td>
<td>1526 or 82.3%</td>
</tr>
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</table>

So we know we have at least 17.4% of the tested US dogs carrying one copy of the mutant LPN1 gene and another 4.1% carrying two copies of the mutant gene. This is far more dogs than have been reported to the public databases. The public databases are the best and most accessible source of data for the largest number of people interested in the understanding how LPN is affecting the Leonberger.

In the United States as of June 2011, we have 21.6% abnormal LPN1 tests (Leos with one or two copies of the abnormal LPN1 allele) and therefore the incidence of the LPN1 mutation in the tested US population is 21.6%. Using statistical analysis, the incidence in the total US Leonberger population is estimated to be lower. Our best estimate now is that is in the neighborhood of 15%. In an ideal world we
would have test results on all dogs in the population or test results on a large enough randomized sample to generate a truly accurate incidence figure.

Currently, our data can only be suggestive. To add a little perspective and food for thought, consider the following comparative data: In May 2011, the OFA reported that 13.5% of reporting Leonbergers have abnormal dysplastic hips; 4.1% abnormal elbows; and 19.4% have thyroid disease.

Even though we do not have a complete sample of dogs, these data still indicate that we have an alarming genetic flaw in our closed gene pool. We are not isolated. This is a worldwide Leonberger community problem. The steps we take to arrest the incidence of the disease in the US will have broad ramifications and may impact our future ability to import and, now that we are AKC, export our stock.

**Recommended Breeding Practices**

Immediately eliminating all D/N dogs from breeding would have negative consequences for the genetic diversity of the breed. Important lines within the breed should be maintained. Our researchers suggest that we could set both a mid-term and a long-term goal of reduction and then elimination, respectively, of the LPN1 allele from the breeding population.

In Summary, good D/N dogs should and will be bred to retain their great qualities. The philosophy of geneticists like Dr. Jerold Bell, the University of Berne and the University of Minnesota researchers plus the International Leonberger Union is **“breed excellent D/Ns and replace with a clear.”** In this way each breeder will preserve what they have been striving for and improve their breeding programs tremendously by keeping the clear offspring that are phenotypically better than their parents.

No one is recommending selecting dogs for breeding based solely on their both being N/N for the LPN1 gene. Such a drastic strategy, although more quickly eliminating the possibility of producing D/D genotypes and LPN1 affected dogs, also has the undesired effects of constricting an already small breeding pool, and losing many of the outstanding traits expected of Leonbergers.

The best approach is to continue to use of some of the many excellent D/N dogs by mating them to N/N dogs. This will produce litters of only D/N or N/N puppies, and none with the severe, early-onset form of LPN1, giving a choice of dogs to use for future breeding. By mating desirable D/N dogs to N/N dogs, the frequency of the D form of the LPN1 gene can be progressively decreased.
According to professor Tosso Leeb, chief researcher at the University of Bern, allowing the breeding of D/N dogs until 2015 may represent a sensible measure to be considered by breed clubs.

**Mandatory vs. Optional Testing**

There have been lively discussions and debates on the Leonberger Internet discussion groups, primarily Harveys Leos, LCAMembers, LCABreeders and LHF lists regarding the efficacy of a mandatory testing requirement for receipt of a CHIC number. Many issues have been raised and debated. The questions regarding science were gathered and submitted to the University of Minnesota researchers for response. See: [http://www.vdl.umn.edu/ourservices/canineneuromuscular/leonberger/lpn1faq/home.html#spread](http://www.vdl.umn.edu/ourservices/canineneuromuscular/leonberger/lpn1faq/home.html#spread). The science was clarified and the researchers remain open to answering any other questions that arise within their area of concern and expertise.

The question now focuses on making the best possible policy decision for breeders and for the breed as a whole.

**Surveys and Formal Recommendations**

This spring, all LCA breeders and stud owners were invited to participate in a survey to assess their opinions regarding mandatory vs. optional testing. Two-thirds of the respondents were breeders with half of those owning stud dogs also. The other one-third were stud owners.

Approximately 70% of the total number of people who identify themselves as LCA breeders responded. The survey results indicate that a clear majority of breeders believe that the LPN1 test should be a mandatory requirement for obtaining a CHIC number. When asked if the test should be optional or required, 69.4% stated they believed the test should be required. When asked to rate the two testing options, 70.8% indicated that mandatory testing was a Good or Excellent idea, with most indicating the Excellent choice. 18.2% rated the mandatory option as Poor or Terrible.

The **LCA Board of Directors** initially voted to make the LPN1 test a requirement for receiving a CHIC number. The Members Practices makes having a CHIC number a requirement for breeding.

The **LHF and the LCA HEC** have unanimously recommended mandatory testing. Their joint resolution supporting mandatory testing has been forwarded to the Board.

The 100-member International **HarveysLeos** support group for owners of dogs with
LPN initiated the investigation of LPN disease in Leonbergers. This group is largely responsible for introducing this Leonberger disease to the research community first in the United States and then in Switzerland. Their members represent not only LCA breeders but also a large number of breeders from Canada and Europe. As a group they wholeheartedly support and are firmly invested in seeing all national Leonberger clubs and especially the groundbreaking LCA require LPN1 testing for their member breeders.

The six-member LCA Breeding Committee has recommended that LPN1 testing be optional.

Authors’ Review

The authors of this paper closely followed the discussions on all of the lists and the public record of the LCA Board of Directors. We have further reviewed the positions of both the Breeding Committee that recommended optional testing/reporting and the positions of those who favor mandatory testing for acquisition of a CHIC number.

Those who favor optional testing and CHIC reporting appear by all measures to reflect the view of the majority of the members of the Breeding Committee and four frequent contributors to Internet discussion groups.

Those who favor mandatory testing for acquisition of a CHIC number by all measures appear to reflect the majority of LCA breeders and the membership at large. Points of view both for and against mandatory testing reflect perspectives that 1) have a direct and immediate impact on LCA breeders and 2) the wider focus that takes into account the possible national and international repercussions of LCA AKC Parent Club policy for the breed as a whole.

The Case for Optional Testing

The Breeding Committee opinion and a composite of points made on Internet discussions.

1. Making LPN1 an optional CHIC test will allow public posting of test results to existing CHIC profiles.

The Fine Print: In adopting the Member Practices the LCA placed a strong emphasis on encouraging breeders to make informed breeding decisions on health based upon public listing of health information on CHIC. Making LPN1 testing an optional test through CHIC is consistent with existing club practices, and will allow LPN1 testing information to be posted on each tested dog’s CHIC profile (Assuming the results are sent in). According to the BC’s survey, over 90% of Breeders are already testing their breeding Leonbergers without a mandate. However, most test results have not yet been entered in CHIC. Simply sending existing test results to OFA would immediately create a large database of useful information. As a sign of support for the breeding community, and in order to promote a comprehensive database, the BC would suggest that the LCA consider paying to enter
all LPN1 test results for a period of a year ($15 per test).

2. It is not necessary to make LPN1 a mandatory test because it is already strongly supported by the breeding community.

The Fine Print: As noted above, the BC’s survey shows that over 90% of Breeders are already voluntarily testing without a mandate. The survey also shows that just over 2/3 of breeders and stud owners support making LPN1 a mandatory CHIC test, which shows they are willing to continue testing. Given this strong support, the BC feels an optional system is about as likely to result in a comprehensive, accurate, and public database as mandatory testing, but with the advantage of fewer complicating factors.

3. Requiring LPN1 testing for a CHIC number injects needless complication.

The Fine Print: Mandatory testing will require grandfathering of Leos that already have CHIC numbers, but CHIC profiles do not indicate the date a CHIC number was assigned. This could make it difficult to figure out exactly which dogs are grandfathered, and which are not. On the other hand, an optional testing program eliminates the need for grandfathering. Since the lack of a test result on the CHIC profile will be conspicuous, optional testing actually encourages registration of LPN1 test results for Leos that already have a CHIC number with the OFA, while grandfathering would discourage it. Unlike other of our CHIC tests, the University of Minnesota does not automatically send test results to CHIC. Instead, the owner needs mail it to the OFA with a processing fee of $15.00, adding additional time and inconvenience when trying to obtain a CHIC number. Would the LCA really wish to discipline a member whose dog has an LPN1 test result, but which only lacks a CHIC number due to the delays inherent in this system? Breeders who have tested Leonberger puppies before they have registered names will have to retest in order to submit results to the OFA database if a permanent ID was not verified at the time of testing. Required CHIC testing may discourage testing of litters. Optional testing also eliminates the need to fashion any sort of rule regarding frozen semen from dogs from the pre-CHIC era.

4. Although testing of each Leo in a breeding pair is preferred, it is not absolutely necessary to prevent the birth of LPN1 affected puppies.

The Fine Print: Whether mandatory or optional, the vast majority of breedings will involve Leonbergers of known genotype by testing. However, as long as one Leonberger per breeding pair is known to be clear by testing, LPN1 affected puppies cannot be produced. Also, although not as reliable as actual test results, given what we know about pedigree accuracy, and carrier rate in the Leonberger population, the odds of producing an LPN1 affected puppy from breeding of a clear (N/N) Leo and a Leo of unknown genotype status, are less than 1 in 4,000. [4.4% pedigree error rate x 15% carrier rate of tested dog x 15% carrier rate of untested dog x 25% inheritance chance for puppy = .025%*] These odds decrease significantly with each generation of screened breedings.

5. With information and education LPN1 will be a disease of the past soon:

The Fine Print: The majority of Leonbergers in the current breeding population already have a known, clear (N/N) genotype. A puppy born from two clear parents will be LPN1 clear as well. The incidence of this particular form of LPN is already quite low. Leonbergers have about a 4-to-6 year breeding window. Combined with a strong educational effort the BC believes that the LPN1 gene mutation can be removed from the breeding population over that same period of time if the BC’s recommendation is implemented.

The BC’s recommendation to the Board did not address three additional reasons for optional testing raised in the group Internet discussions. They have to do with issues of 1) breeders feeling their integrity has been questioned; 2) an unclear “clear by parentage” policy; and 3) a concern that breeders will leave the LCA if mandatory testing for LPN1 is imposed.
The Case for Mandatory Testing

A composite of points from the LCA-HEC, LHF, HarveysLeos, and Internet discussions on the LCAMembers and LeoLists.

1. **A Mandatory requirement implies more gravitas and seriousness than one that is optional.**

   **The Fine Print:** It sends a simple short, powerful signal to the general public and breeders uninformed about the disease that LPN1 is not to be assessed casually or treated lightly. LPN in any form is a very real health threat to an individual dog and the breed as a whole. Mandatory reporting of LPN1 tests to CHIC provides LPN1 equal weight and status as other hereditary diseases (e.g. HD, Elbows, Thyroid).

   When a breeder or puppy buyer sees that either a DNA or clinical test is mandatory, it is a short hand message that proclaims, “this disease is important and these people care enough to go the extra mile to prevent it.”

2. **No LCA breeder wants to breed unhealthy pups. The LCA membership knows this. Puppy buyers and long-time owners have consistently placed great trust in their chosen breeder. The majority of breeders see mandatory LPN1 testing and CHIC reporting as a positive step forward to protect breed health.**

   **The Fine Print:** Most major LCA breeders have been “raised” in a 27-year old club culture that places a high value on health. In the early days breeders formulated, supported, and voted for mandatory health tests and breeding procedures that were much more stringent than those that have been adjusted to accommodate our AKC affiliation.

   At this time, most of the major Leonberger breeders in the US are members of the LCA and, as such, set a standard for those who breed outside of the parent club. They have never shied away from measures to protect and preserve breed health. This was affirmed in April with the BC survey, when a clear majority of breeders indicated that they preferred mandatory LPN1 testing over optional testing.

   LCA breeders have a tradition of assisting other breeders and working in the interest of the breed as a whole. Future breeders will be helped by having a repository of data available to them. This will also, of course, be available to the research community. Mandatory testing and CHIC reporting will assure having data from as many current dogs as possible to add to the DNA data already gathered. Over a decade of semen and blood kept in the CHIC repository for future breeders documents the history of this disease. When the time comes, future researchers will be able to use it to for the search for effective treatments.

3. **LCA Breeders have proven themselves to be long-term breeders who are very supportive of the club and the club’s values.**

   **The Fine Print:** It is highly unlikely that any well-known major breeder who has built their reputation and established their Leonberger relationships within the club would leave in protest over the Board re-affirming its stand supporting mandatory testing. The majority of breeders validated this assessment when they voted in favor of mandatory testing. Many have been breeding within the LCA for more than 10 years and some as long as 30. They are highly unlikely to leave the club, the benefits of advertising in the LeoLetter and the easy open access to other breeders along with networking opportunities at a variety of educational and social events is a strong incentive to belong.

   It is interesting to note in contrast that the AKC estimates a turnover rate of AKC breeders of 5-6 years. We should be aware that new breeders will need good mentoring to assure success and longevity with the breed.
4. LPN is a disease that affects the worldwide Leonberger community. Mandatory LPN1 testing 1) maintains the LCA’s reputation as a leading nation in with regard to breed health; 2) supports the recommendation of the ILU that encourages making LPN1 testing a requirement for breeding; and 3) assures an open, honest, vibrant international trade relationship with the European nations that are requiring mandatory testing.

The Fine Print: Despite initial denials of its existence by some prominent members of the ILU who believed that LPN was a “American fashion disease,” the worldwide severity of the problem became clear when HarveyLeos was initiated in 2003 by Ann Rogers. The US set the example for the other Union nations to follow by taking the lead in inviting and funding the research community to study LPN in Leonbergers. Breeders and owners from Europe and Canada reported dogs whose biopsy results indicated a diagnosis of LPN. Following the leadership of the US, the University of Bern joined the gene search and subsequently the ILU reversed its position and now encourages mandatory testing.

5. Implementing a policy of mandatory LPN1 testing will send a strong signal to the scientific community that we are grateful for their help, serious about implementing their findings, and supportive of further efforts on behalf of the Leonberger.

The Fine Print: Clearly more scientific information is needed to determine incidence, patterns of distribution and the possible common links between different LPN forms and the possibility of finding another genetic mutation on CFA7. The more test data that is provided the better science that will result. Additional research findings are needed not only to help breeders make breeding decisions but also to aid veterinarians in differential diagnosis. None of the researchers can say for certain yet how the disease is triggered by the faulty biological instructions provided by LPN1 gene and which biological pathways are disrupted. Potential cures and ways to alleviate clinical signs or prevent their formation are important topics for further study.

6. LPN1 Policy is the “easy” kind! With the large number of cases recorded during the past decade, there is no evidence to suggest that LPN1 is linked to a phenotypical breed-defining trait.

The Fine Print: We are not in a place like those breeders who had to make a decision to accept possibly fatal stone forming disease as “part of what it means to be a Dalmatian.” The mutated gene is fixed in the breed. Dalmatians with the normal allele always have a spotting pattern that is less than ideal. Our situation is much simpler by comparison. We can set a medium and then a long-term goal to minimize and eventually eradicate the existence of the LPN1 mutation in the gene pool and not worry about whether or not Leo masks, or some other defining feature, will disappear with the mutant gene. Type D/N dogs will and should be bred to retain their great qualities with the caveat that they follow the recommendations of experts like Dr. Jerold Bell to “breed and replace with a clear.”

7. The LCA is known for taking a leading edge role in supporting health and the scientific research community. Mandatory LPN1 testing and CHIC reporting demonstrates our full support for a worthy AKC program and helps to maintain our “alpha dog” reputation in the AKC.

The Fine Print: Two decades of strong support established the LCA/LHF as a leading contributor to the AKCs’ Canine Health Foundation before we were even formally affiliated. The American Leonberger community has raised to date close to $200,000 to support health research. The LHF
has put the American Leonberger Community in the top 5% of donors to the AKC’s Canine Health Foundation. This achievement coupled with our unusually large parent club membership numbers catapulted the LCA into the elite ranks of AKC parent clubs.

8. The probability of producing an LPN1 affected puppy from breeding of a clear Leo and a Leo of unknown genotype status cannot be accurately determined with currently available data and must not be underestimated.

The Fine Print: Probabilities of breeding outcomes where N/D parents are concerned are based on population statistics, specifically the Hardy-Weinberg Principle (HWP). The HWP assumes a large population and random mating. Purebred dog breeding by definition violates the basic tenets of the law since breedings are not random and active selection is present. The Leonberger’s small population, especially in the United States, further complicates statistical analysis. In addition, the population is almost never in equilibrium since breeders often bring in stock or frozen semen from outside the country.

The formula used in the BC’s assessment is flawed by these statistical limitations and because it is missing a significant factor—that of accidental matings. Although we may have a good idea of the amount of pedigree fraud in the US, we have no way to estimate fraudulent pedigree incidence of imported stock or semen. We do know, however, that there have been serious complaints about such fraud especially in the Eastern block countries. We do not know the incidence of accidental bleedings. Our personal knowledge, as 25-year members of the LCA leadership and breeder networks, suggests that it is certainly far higher than the AKC’s estimate of fraudulent pedigrees. Neither author has knowledge of more than one fraudulent pedigree issue (and that one was resolved with no LCA pedigree issued) coming up during the 23 years that the LCA was maintaining the registry. However, both authors can attest to reports of accidental bleedings on the order of 2-3 per year over the past 20 years and some of these were unknown until after the pups were born. Finally, when the scientists reviewed this paper for accuracy they noted that “. . .we have had to deal with incorrect parentage. The correct sire was only confirmed with an expanded panel requested by the owner of the dog that was affected.”

9. If the past is prologue, any survey of the progress of minimizing diseases in purebred dogs clearly demonstrates that education and information are not sufficient to make LPN1 a disease of the past any time soon. Mandatory testing protocols are not perfect but they are effective especially in light of the fact that in the purebred dog world there are no overt rewards for health, but many for beauty and working prowess.

Fine print: Education and information are necessary but insufficient inducements to persuade breeders to consider health as an element of type equal to the phenotypical elements that are judged in the show ring. That is the fundamental reason that mandatory testing for hips, elbows, thyroid, etc. have continually been put in place. Since those disorders involve multiple complex interactions of genes unlike LPN1 we are a long way from reducing their impact on our dogs.

10. Administrative and cost burdens can be addressed by the club or in conjunction with LHF.

Fine Print: There have been a couple of complaints about the cost of the test – which is actually less than the required thyroid test. Further, the thyroid test, unlike the LPN1 test, needs to be repeated every couple of years. In 2010 there were only two members having more than three litters in a year. Most had only one or two. For almost all breeders the cost of a one-time test of breeding stock is minimal. Breeders will have a one-time fee for the one or two bitches they are now using, assuming they have not already gotten their test results and that is it until they add a new bitch to their kennel. Stud owners would be responsible for testing their males and very few stud owners have more than one or two
males. We have not heard any stud owners objecting to the mandatory test. The fee of $15-$30 for getting the results on CHIC is also very inexpensive advertising for their kennels.

It is our understanding that possibilities for easing the burden of CHIC reporting and providing financial assistance to alleviate any burden are currently under Board consideration.

11. A policy and procedure in line with the OFA’s requirements for a “clear by parentage” option can be formulated.

The Fine Print: This can be considered another form of meeting the mandatory requirement. However, the OFA requirements appear to make it more expensive and cumbersome than just testing breeding stock directly.

12. Parent Club Status suggests a Parental Role: Mandatory testing with reporting to CHIC will serve as a firm guideline to assure new breeders that their puppies do not have to suffer from this disease.

The Fine Print: With AKC affiliation there will be an increasing number of new breeders as well as unaffiliated breeders. As the breed’s "parent club" in the US, we are at least nominally responsible for all AKC Leonbergers. Thus supplying information, education and having an infrastructure in place that encourages “best practices" for all Leonberger breeders is the LCA’s responsibility. AKC estimates their breeder turnover rate at 5-6 years. This is quite short compared to our experience with LCA breeders in America. Many of the major European kennels have been active since the end of the World War II and the opening of the Iron Curtain.

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References

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LCA Breeding Committee Recommendations
Leonberger Health Foundation and LCA Health Education Committee LPN 1Joint Resolution

The Basics of Genetics by Betsey Dexter Dyer Wheaton College Recorded Books LLC 2010
The Genetic Connection: A Guide to Health Problems in Purebred Dogs by Lowell Ackerman, DVM, PHD Dipl. ACVD
DNA Science by David A. Micklos and Greg A Freyer, Cold Springs Harbor Pres