A 'Histio' History and The BMD 'Cancer Test'

Steve Green (BMD Health Co-Ordinator) January 2018

(N.B. This is an expanded, modified version of the original article which was published in the December 2017 BMDC of GB magazine. It introduces elements not included in this context in the original article but written about elsewhere in the December 2017 magazine, e.g. see Section 6.9. The author thanks the presenters both from the University of Rennes, Benoit Hedan, and from Antagene, Dr Anne Thomas, for their permission to use the slides from their presentations. Another point to make is that some the graphics in the article will definitely benefit from colour and this was not possible when published in the magazine, so this full colour web version has several advantages over the original).

I have heard much confused talk about this disease, and particularly the test for it, so the original purpose of this article was to clarify a few things. However, whilst at first intended to be only a quick explanation of the test and the potentially exciting updates about it from the recent (September 2017) International BMD Seminar in France, the rationale and purpose of the test is very intertwined with the deceptive features and history of this complicated disease. This means the test cannot be discussed without a decent appreciation of the background and characteristics of the disease to give proper context and hopefully understanding. So, this article turned into a much fuller account of this disease and it's relationship with our breed, more of an all inclusive layman's guide to 'Histio' perhaps with an eye on potential future developments not just with the test itself but the legalities of dog breeding in the UK. There is certainly a case to be made to bring together the full story about such a significant disease for our breed and make it available in one place, so maybe you should even bookmark this page in your browser.

I make no apologies for this as 'Histio' is *proven* by surveys in numerous countries over many years to be the single biggest serious health issue for our breed and it is time we gave it more attention in the UK. **In any rational and logical assessment 'Histio' is a bigger actual health problem across our breed than hips, elbows and DM put together. Whilst any individual cases are all tragic, overall for the breed 'Histio' causes more pain and suffering for dogs, more deaths of dogs and anguish for owners than these three other issues put together and it is time we in the UK got our heads around the potential for addressing it.** This situation will not improve on it's own, without the intervention of breeders and all the rationale and information needed is included here so please do not dismiss this as another example of *'Steve banging on about health again'*. **'Histio' is by far our breed's biggest health problem but it is a problem we CAN do something about and this article's revised main aim became to make the case that the time has come for action**.

Whilst not for one minute advocating any complacency about everything else, it is perhaps the case that we have taken our eye off the ball a little bit with 'Histio' in recent years**.** This disease is complex and complicated to even recognise, let alone address, and because of this many people just accept it and still refer to people being 'unlucky' when it strikes. Alternatively, due to the general lack of accurate diagnosis some choose to ignore and forget it and deny it's existence. We have to move on from this viewpoint or we will never progress.

If you don't have time to read it all this article just go to the headings you are interested in although some sections do refer back to others so maybe reading it in stages might be a better option in order to be properly informed about where we are today. **I hope everyone at least reads the last sections 9 and 10, the Summary and Conclusion and, if they have any problems with this overall concept, then section 6 may address those problems.**

If you cannot be bothered to read any of it then please accept this summary

The BMD 'cancer test' makes real sense and is badly needed by our breed, so please use it to improve your own lines and the breed as a whole.

1] What are we talking about?
Firstly, just to be clear the disease we are talking about here has been referred to by the veterinary scientific community in a number of ways over the years, Malignant Histiocytosis (MH), Histiocytic Sarcoma (HS) and Systemic Histiosarcoma (SH) being just a few of them. As you will have already noticed, for the purposes of this article I shall stick mainly to the commonly used reference of 'Histio' as I think that will be easiest for everyone, and less typing for me!!

I have written about the disease regularly in club publications and on this web site for well over a decade now but, to summarise briefly for the purposes of this article, it is a serious aggressive cancer condition, always fatal and usually within just a few weeks after symptoms are first noticed. It is also found in humans but much, much more rarely and specific other breeds are noted as having different versions of it but generally it is rare in the general canine population but far and away a more serious manifestation when presenting in Bernese than in any other breed.

According to the Antagene website, referenced below, 'Histio' *" ... is a major cause of death in the Bernese Mountain Dog. It is a cancer of the histiocytes, cells responsible for immune function, which are present in the lymph nodes and a number of organs. No treatment is effective to date, and the disease is fatal."* This is a succinct summary of what is an awful disease for our breed which, for most experienced people, is still the most serious health problem we have in the breed as it is massively far more widespread than DM for example and much more difficult to address. DM can be practically eliminated as a clinical problem in a single generation but **'Histio' will take a sustained and consistent push across the breed for several generations to make major progress but this is not a reason to ignore what we could be doing. In fact, it is a reason to make a start as soon as we can and as hard as we can.**

Whilst not for one minute advocating any complacency about everything else, it is perhaps the case that we have taken our eye off the ball a little bit with 'Histio' in recent years and spent much time debating conditions such as DM which in turn pushed out hips and probably more particularly elbows as subjects for discussion in the near past. 'Histio' is complex and complicated to even recognise, let alone address, and because of this many people just accept it and still refer to people being 'unlucky' when it strikes. Alternatively, due to the lack of accurate diagnosis some choose to ignore and forget it and deny it's existence or it's effect on our beloved breed. **We *have* to move on from this viewpoint or we will never progress.**

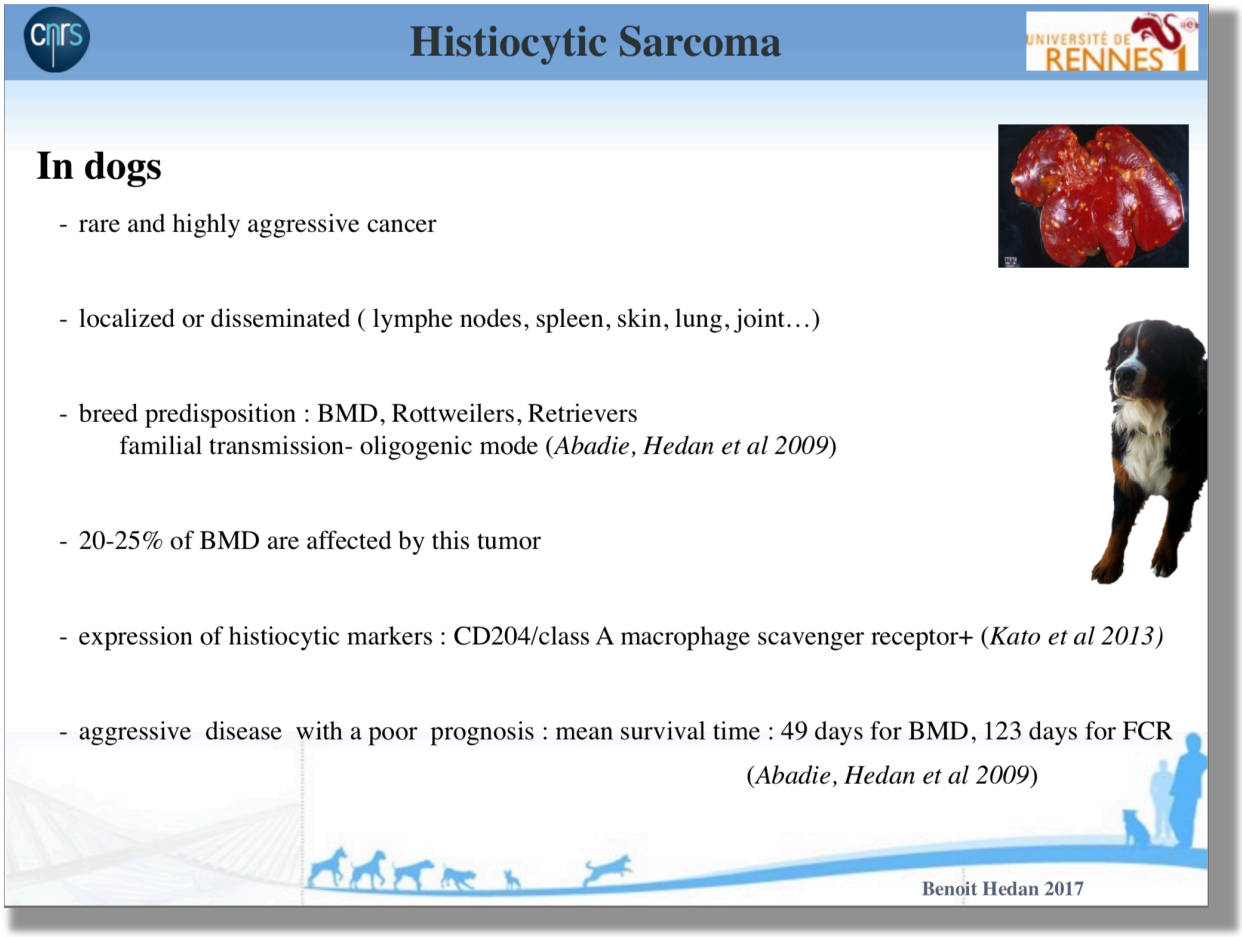

Figure 1

What are the Symptoms? As already mentioned, one of the biggest problems with 'Histio' is that it can present with a variety of symptoms making it hard to be sure what you're dealing with, especially at first. Unlike other forms of the disease experienced in other breeds, the disseminated form that affects Bernese can be particularly difficult to diagnose because it manifests itself in many different areas of the body. This means the symptoms of 'Histio' are many fold depending on which part of the immune system, function or organ any particular case affects the most, see *figure 2*, it aggressively attacks just about any part of the dog's body.

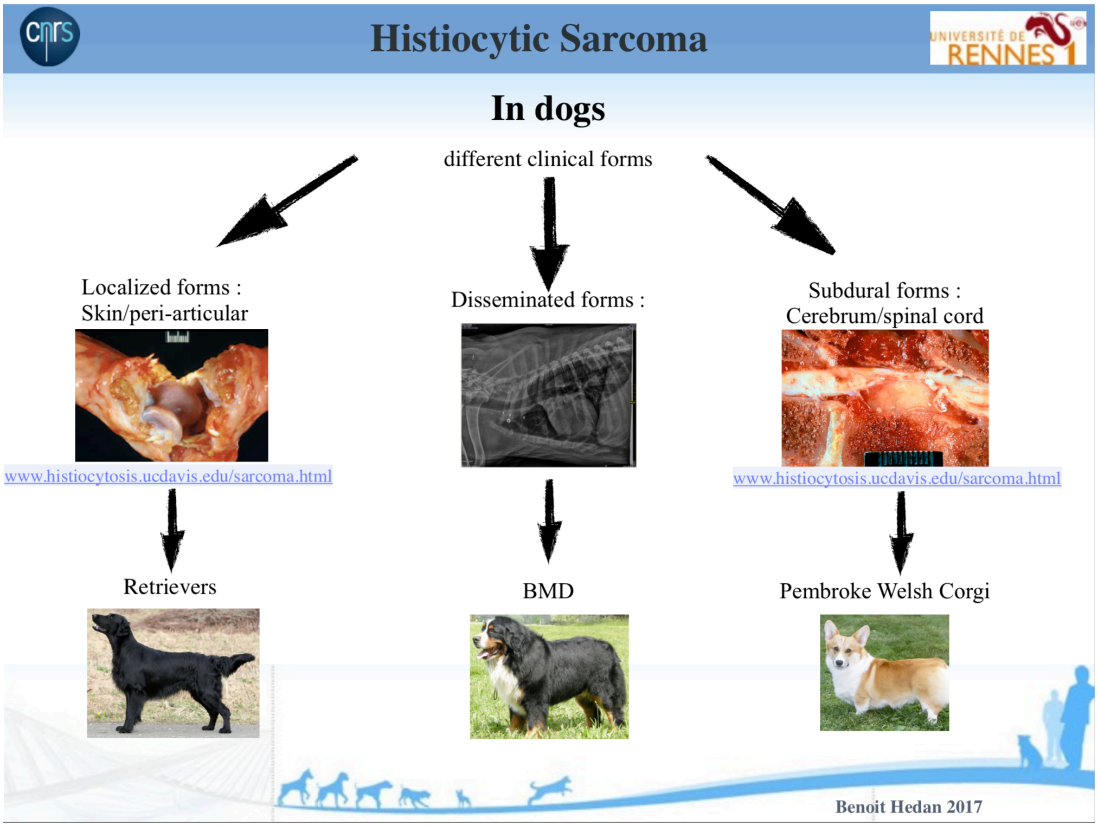

Figure 2

This means it is often just considered to be cancer of the area the tumours are discovered in, probably most typically but by no means exclusively, the lungs but it can cause tumours to appear in any organs. Another common, but again not exclusive, symptom is a severe anaemia producing extremely pale gums. In common with many other serious diseases there is always lethargy, loss of appetite, low energy and general, increasingly serious, malaise.

'Histio' can be fatal in just a few days from first noticing symptoms in your beloved pet. If you are definitely dealing with this disease then the prognosis for your Bernese family member is, to put it bluntly, extremely poor. The average life span after diagnosis is very short and although sometimes there may be a briefly encouraging response to steroid based treatment, this is usually short lived and sadly only slightly delays the inevitable.

Most typically, but not exclusively, 'Histio' affects what should be considered as middle-aged dogs with the average age of onset being around 6½ – 7 years but older and, even more tragically, younger dogs can, and do, develop it. If we choose to carry on doing nothing then it is only logical to expect things to get worse with younger onset age. '

Most non specialist vets do not have a good knowledge, if any, of the disease nor it's presentation. Typically by the time the tumours are discovered by scan, X ray or surgical investigation the dog is too ill to make further treatment or investigation of them a viable option so they are frequently, and completely understandably, not subjected to proper histology or diagnosis. In the returns to our UK Bernese Death Survey many dogs are described as having tumours on their brain, lungs, kidneys liver etc without the word 'histio' being used by the vet. These tumours are frequently not subject to biopsy or further investigation so are just recorded as 'cancer' but it is certain that at least a significant proportion of these will be 'histio' cases so it is equally certain that 'Histio' has a larger impact on our breed than the figures actually say. Despite the best part of two decades of effort there is currently no remotely effective treatment, nothing beyond sometimes temporary effects on the symptoms, and certainly no cure for affected dogs. The only slight mercy of sorts, if that is the right word for it, is that the suffering does not normally go beyond weeks with, according to French research, the average time to death being around 7 weeks from first symptoms being noticed.

It is perhaps important to mention the point that this is not the only form of cancer to affect Bernese but even though it is *certainly* under diagnosed it is still the single most commonly recorded disease AND has been for years. It is devastating in it's impact on the dog and heart breaking for the owners and their family to watch their beloved Bernese suffering from this cruel, aggressive and fast acting disease.

It is a well accepted fact, across the canine world as a whole, that, as represented in *figure 3*, generally speaking, the larger the dog the less the expected life span but Bernese do not fit into the general pattern with average death ages below those that would be expected with their size. The general dog population shows that relating to their size Bernese should live to an average of around 9 – 9.5 years but the, (I think French), research shown in *figure 3* has them a little under 7 years. Our own UK Death Survey so far has the average at around 7.5 years. Whichever figure you want to use it is nowhere near high enough, Bernese are not a giant breed and should not have a giant breed's shorter life span. 'Histio' is the single biggest identified killer of Bernese so is a major factor in the reason Bernese do not, on average, live as long as they should and without a doubt has a major impact on our breed's reputation for lack of longevity.

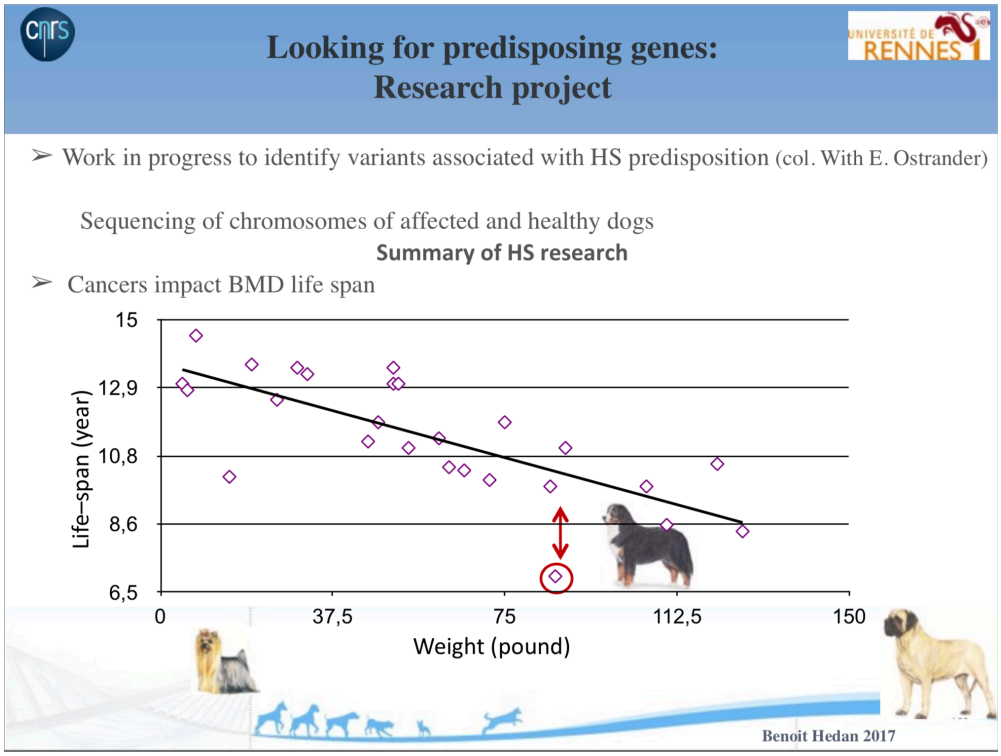

Figure 3

In September (2017) I attended the latest International Health Seminar and Berner International Working Group meeting, in France, where amongst other interesting presentations were the latest, potentially extremely exciting, updates about the 'cancer test' that our breed so desperately needs. However, before I get to the latest news I feel I need to bring everyone up to date with the situation and how we arrived where we are today because it is necessary to understand the history and the problems to fully appreciate the potential of the developments AND what part everyone has to play in fighting back against this curse on our breed.

2] Some Background

To paint the full picture and give comprehension to the need for this test I should outline some of the historical BMD breed background to this disease and some understanding to the hopeless situation that formed the platform to the development of the test. People coming into the situation relatively recently might not understand how much the breed needs to engage with this test if they do not understand the depth of the problem.

As long ago as the 1980s in some countries there were concerns about the prevalence of cancer in our breed. In the UK the very earliest times when we began to believe/realise our breed was generally susceptible to various forms of *'cancer'* in the UK, probably around 30 years ago, it was generally accepted by many that this vulnerability appeared to have something of an hereditary influence, that is to say certain lines appeared to have just a little bit more susceptibility than others, but it was a very indistinct link and impossible to quantify to any significant level so no one took it too seriously because we couldn't do anything about it anyway. It was definitely not an identifiable recessive gene type autosomal mode of inheritance which we could have addressed with population genetics analysis, but something much vaguer than that.

The amount of '*cancer*' encountered was realised to have a widespread detrimental effect on the breed and our low average age at death was much talked about and '*cancer*' was widely quoted and accepted as the biggest factor in this. The problem was that we were not looking at one kind of cancer. Whilst other breeds would have specific problems to deal with, ours seemed to be a general susceptibility to various forms of the disease in all areas of the body. At the time cancer treatment in humans was moving on in the public eye and we were being encouraged to think of cancer as not a single disease, 'the big C' was a common term up until the late eighties, but a generic term covering hundreds of technically different diseases each requiring different very specific, and increasingly effective, approaches. In short, the general thinking was that you needed to identify a specific disease in order to properly tackle it and because we couldn't it was impossible to engage with the problem in any meaningful way. So, basically, we just learnt to live with it and accept the bad things as part of the Bernese package.

As explained below, looking back with that most effective of teachers, hindsight, I now feel many of these various cancers were being initiated by the, yet to be identified, Malignant Histiocytosis. The real (unknown) enemy was 'Histio' and many of the other cancers we were identifying were actually secondary cases. I also feel this is where the reputation of Bernese as 'giving up easily' and 'not putting up much of a fight' against disease came from. It seemed that Bernese dies very quickly from, admittedly serious, diseases where other breeds lasted much longer after diagnosis and responded better to treatment. We were treating the secondary problems and not even realising the real underlying issue was different to the apparent one we were seeing. I am the first to admit this is a personal theory which can never be proved, or disproved, but looking back now it just makes so much sense to me. At the time in the UK we just considered we were prone to a variety of cancers and that was, sadly, simply the way it was. Due to the non specific threat we were at something of a loss as to what to do so we just got into the mindset that if you wanted to stay in our fantastic breed then you had to accept things as they were because there was nothing we could do about things. Unfortunately, this attitude became so engrained that today, we have to make a really big effort to move on from it all these years later now that there is something we can do about things!

In some other countries, most notably the USA and France, the existence of Histio and it's threat to, and impact on, the breed was understood much quicker and, more importantly, acknowledged and accepted by the owners and breeders. In these countries the battle against 'Histio' was engaged much earlier. Although others have since joined in, these two countries are still the main front line for the breed against this insidious problem and, in my opinion, our breed has much to thank them for.

Working through the Breed Council and in conjunction with Dr Jane Dobson at Cambridge Veterinary school I launched a tumour sample survey to try and home in on our problem for the breed in the nineties together with a fund to underwrite costs but this was never well supported by the breed and had to be discontinued after a few years. A little after this the Northern Carters notably funded a separate cancer investigating scheme with Dr Matthew Breen at the AHT, Dr Breen later left to continue this work in America and is still connected with the breed research in the USA. Overall though, in the UK, we never established a particular type of cancer to investigate and failed to achieve any real focus to the disease in the Bernese population in the UK. We mostly just carried on accepting that the breed was affected by cancer and on average Bernese didn't live as long as they should. As I have already said, it was, and for many still appears to be, the way the situation was viewed.

In a few other countries this attitude was not the case and research was continued and supported by samples and information. The first papers I can find describing the first few *identified* cases of Histiocytic Sarcoma in Bernese are from the mid eighties but this was not widespread knowledge across the world. By the mid nineties there was much more recognition of this disease in our breed and papers describing a '*familial*' type inheritance were beginning to appear from researchers such as Dr Padgett in the USA supported by the BMDC of America. Dr Padgett presented his research to the breed at the second BMD International Seminar in Switzerland in 2002. In the UK we were still mostly referring to 'cancer' in a very vague, generic and accepting way.

Definite Hereditary Influence

In the early 'noughties' supported by their large French Bernese population the AFBS (French Swiss Breeds club) began to address the situation and approached Dr Catherine Andre at the University of Rennes to investigate. This was the first stages of what became, and still is, a massive project to investigate pedigrees of affected Bernese and this proved that there were hereditary connections to this disease. Thousands of dogs were looked at and I remember a presentation (in Italy in 2006 I think) with a massive family tree explained with (I think) about 900 mostly French Bernese shown on it and a trail of connections to the 'Histio' cases could be tracked down the generations whilst other areas of this mass of Bernese lines were virtually clear. The Hereditary aspect has therefore been accepted for well over a decade and has been reported numerous times by myself over the years in handbook and magazine articles.

I am not making this hereditary aspect up for my own purposes and it is not a recent discovery. The very first published scientific studies going back to the 1980s already referred to, suspected an hereditary element from the very early days and familial links to the very few dogs looked at in the early studies were commented on. As time progressed the acceptance of this became stronger and by the

time we reached this century, no one with any proper knowledge of the disease was doubting this. There is a summary of some of these papers on our club web site if anyone wants to review them, (click here).

There simply are ***no links*** to any published papers that say that Histio is ***not*** hereditary because ***no one looking at the issue scientifically has concluded this.*** **Every research project that in any way covers the genetics of 'histio' concludes that it has an hereditary aspect to it.** There are clarification questions about this link to establish the detail of it but the fact that the disease has an hereditary link is not being questioned. There may be other factors at work as well as the hereditary one and you will see references to Histio being polyfactoral, i.e. having other influences when it occurs as this is the only way to explain the inconsistencies in it's occurrence but the more is discovered about the genetics of the disease and if further genes are involved then the more these inconsistencies will be understood.

The whole basis of the investigation for the fight against histio for the last 12 - 15 years or so has been the basic principle that it has a definite hereditary influence. There would have been no point spending the massive amounts of time and finance in several research programmes around the world, chiefly in France and the USA, if there was not a genetic element to exploit in trying to defeat it. If this were not the case research would have had to totally focus on treatment.

Despite this long standing knowledge, in a breed feature in one of our weekly canine newspapers in the summer (2017), several breeders completed an "ask the breeder" type feature during which they were inevitably asked about health issues with the breed. All of them mentioned cancer, which is (sort of – from an honesty point of view) a *good thing*, but from memory, and apologies if this is wrong, all of them said words to the effect of there being no pattern or inheritance to it and whether your dog developed it or not was completely down to luck, which in my opinion is a very *bad thing* to say. I was a little disappointed to read this but not surprised as I have heard it from many UK sources for years despite it flying in the face of all the evidence from research and studies. Many people in the breed in this country just don't seem to be able to accept that *'our main cancer'* has an hereditary aspect to it. It seems some will believe that some people have a lot of bad luck so, in effect, people appear to be accepting that bad luck can run in lines but not cancer. Some cancers do not have any known hereditary factor and their occurrence is effectively 'random', and we certainly get our share of those, but 'Histio', our single biggest problem in Bernese, does have an hereditary connection.

I am sorry to labour this 'hereditary factor' point but it acceptance of it is crucial to the rationale of the test and how breeders and owners view and engage with it, so I do so as a response to the fact that there seems to be a reluctance to accept that the hereditary aspect exists in some quarters.

Establishing beyond doubt that there is at least some kind of hereditary factor at work means logically that, with the right guidance, the disease can be reduced, generation on generation, by the correct breeding choices. The trick is to make the right breeding choices and there are many problematic issues here. 'Histio' generally does not reveal itself until after the age when most dogs have already first been used at stud or for maternal duties so a means of identifying the 'vulnerable to Histio' Bernese would be invaluable, if not essential, to the breed.

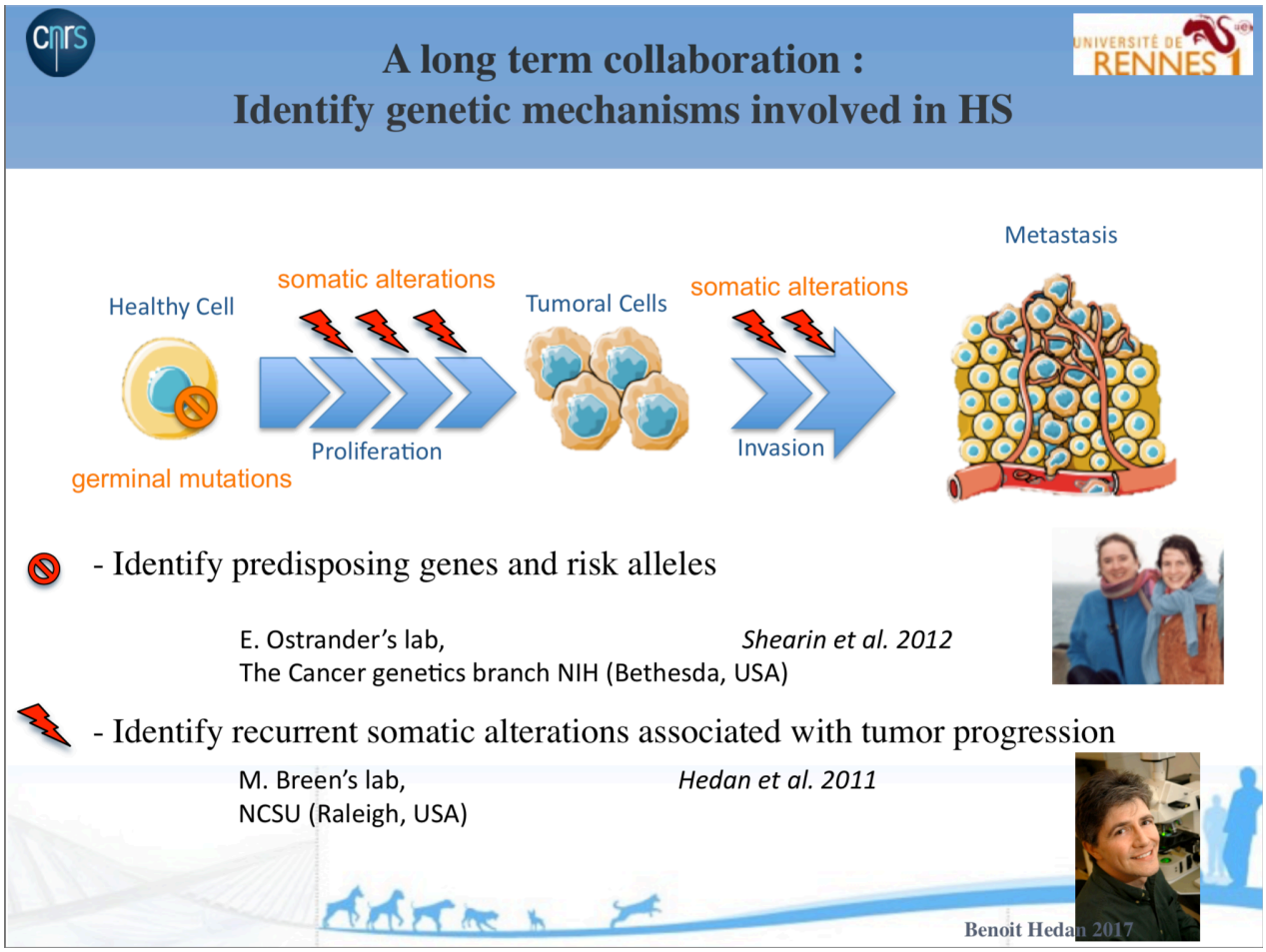

Figure 4

Anyway back to the history, we were moving into the modern era of widespread DNA analysis and this was an obvious route for the research to take. If patterns in the DNA of affected dogs could be found that weren't present in healthy dogs then in the future these could perhaps be searched for by genetic screening of young dogs prior to breeding. The research required lots of samples from healthy and affected dogs of course and the French club really got behind the project and supplied plenty of both and continue to do so. There is a constant queue to provide blood tests throughout the day at their main club show which Antagene always attend.

Looking for DNA patterns sounds like an easy principle but proved extremely difficult in practice. The old analogies about looking for a needle in a haystack are no longer adequate for the astronomical numbers involved in genome projects. We are more like looking for a needle in a haystack in a world jam packed full of haystacks. The team at Rennes, who do liaise closely with counterparts in America, presented their progress to successive international BIWG meetings and were supported by various funding donations from breed clubs around the world. They were able to expand including the addition of Dr Benoit Hedan who, some will remember, presented the update at the British International Health seminar in 2011 and has addressed the international Bernese meetings several times since then.

However, with the aid of increasing computer power and after the best part of a decade, specific areas of the Bernese genome were found to have fairly consistent differences when comparing between healthy and 'Histio' affected dogs. From this landmark position it was possible to take the next step to develop a test to check these markers as a screening process. After much hard work a meaningful test was evolved and after a period of validation work, which is a continuing constant process, it was launched a few years ago by the French company Antagene working in collaboration with the team at the University of Rennes. We should not underestimate the pioneering scientific achievement here. In 2016 at the KC Breed Health Co-Ordinator's seminar, KC geneticist, Dr Tom Lewis' presentation on canine genetics mentioned that this Bernese Mountain Dog test was the absolute first and only one of it's type in the world and he used this to make the point that these types of tests are incredibly difficult to produce. Just think for a moment what that means, despite all the health problems in all the breeds in all the world no one else anywhere in the world, has managed to produce a test of this nature. This is not the usual, *becoming-very-common* type of genetic test looking at simple recessive gene inheritance, this is ground breaking 'world first' type science. In my opinion the breed owes a massive debt of gratitude to the team at Rennes for their persistence in this project for the benefit of the Bernese Mountain Dog.

3] What is 'the test'?

The test has been around for several years and is often referred to as the 'Bernese Cancer Test' although it is much more specific than that. It is well established in France and becoming more widely accepted in other countries as it's validity and efficacy become more proven and accepted.

In it's basic principle the test is very simple. Working from a blood sample, except in very young puppies where a saliva swab is sufficient, the test currently looks at markers in 9 areas of the dog's DNA. These markers have been found to have significant numbers of differences in dogs developing 'Histio' compared to those who stay healthy into old age, usually at least the age of 10 is used as a reference for 'healthy' dogs. Therefore the findings in these areas can be used to give an indication of the likely 'Histio' status of the dog. The more the indications in these areas are in line with those found in the definitely diagnosed 'Histio' affected dogs the more likely the grading is to be an 'C' and conversely the more they are similar to the those found in the healthy dogs the more likely the dog will be a 'A' grade. The given meaning of the awarded grades is defined as follows

Index	Explanation
A	The individuals tested have four times the chance of NOT developing Histiocytic Sarcoma.
B	Neutral index
C	The individuals tested have four times the risk of developing Histiocytic Sarcoma. The risk of the markers associated with the disease being transmitted to offspring is greatly increased.

Source - Antagene web site 2017

As part of the drive to improve the test more areas of the Bernese DNA are being researched as potentially of relevance and the involvement of more areas would obviously increase the efficacy of the test. Of course it could be that some healthy dogs used as reference comparison could just be 'Histio' dogs who haven't manifested the disease yet so to caution against this a healthy dog, as used for reference in the analysis is usually defined as a dog over ten years who has exhibited no symptoms as it is fairly reasonable to expect that 'Histio' would have struck before this age.

'C' Graded Dogs - The providers and developers of the test are keen to stress that it is not a reason to discard the 'C' graded dogs from any breeding programme and of course many of these will live normal healthy lives. The grading is not a absolutely accurate guide at this stage but from the emerging figures discussed in section 4, you can see that overall, 'C dogs' are a less represented in dogs that live to good ages and more represented in Bernese that die younger than we'd like and the converse applies to 'A dogs'. All Bernese can have a contribution to make to widen the gene pool with the importance of genetic diversity being increasingly well understood. 'C' graded dogs can still contribute other positive aspects to the breed so the current advice is to *make sure* that 'C' graded dogs are not mated with other 'C ' graded dogs.

4] Validation of the Test

The test is criticised in some quarters for it's lack of a definitive and clear result and is negatively compared to other simpler tests which check for a single recessive gene and give a *'Clear, Carrier or Affected'* type result. Everyone understands this concept of autosomal inheritance and can easily accept the results and their implications. The diseases involved in these tests have a simple mode of inheritance whereas Histio does not. Histio is genetically polyfactoral and has genetic and probably also environmental influences to make it happen. This makes it simply impossible to give an absolute *'Clear, Carrier or Affected'* result but **does not mean it does not have a genetic mode of inheritance** playing a part every time it occurs. This is a crucial point, and means it is worth saying that just because it is not as straightforward or as definite an influence as other diseases does not mean that a genetic inheritance factor is not at work with this condition. Any environmental or other factors that may exist and be needed for it to occur would not have any effect without a dog having the genetic predisposition to 'Histio' in the first place.

So, having got to this point and introduced the test, the way to validate it was with experience and seeing how it fared 'in the field' as it were. Looking to see if healthy dogs are mostly graded 'A' and affected dogs are mostly graded 'C' and check if dogs tended to pass on their own gradings to their progeny, because if they didn't there was no point to any of this. Here are a sample of figures from the latest update presented in France in September 2017 by Benoit Hedan.

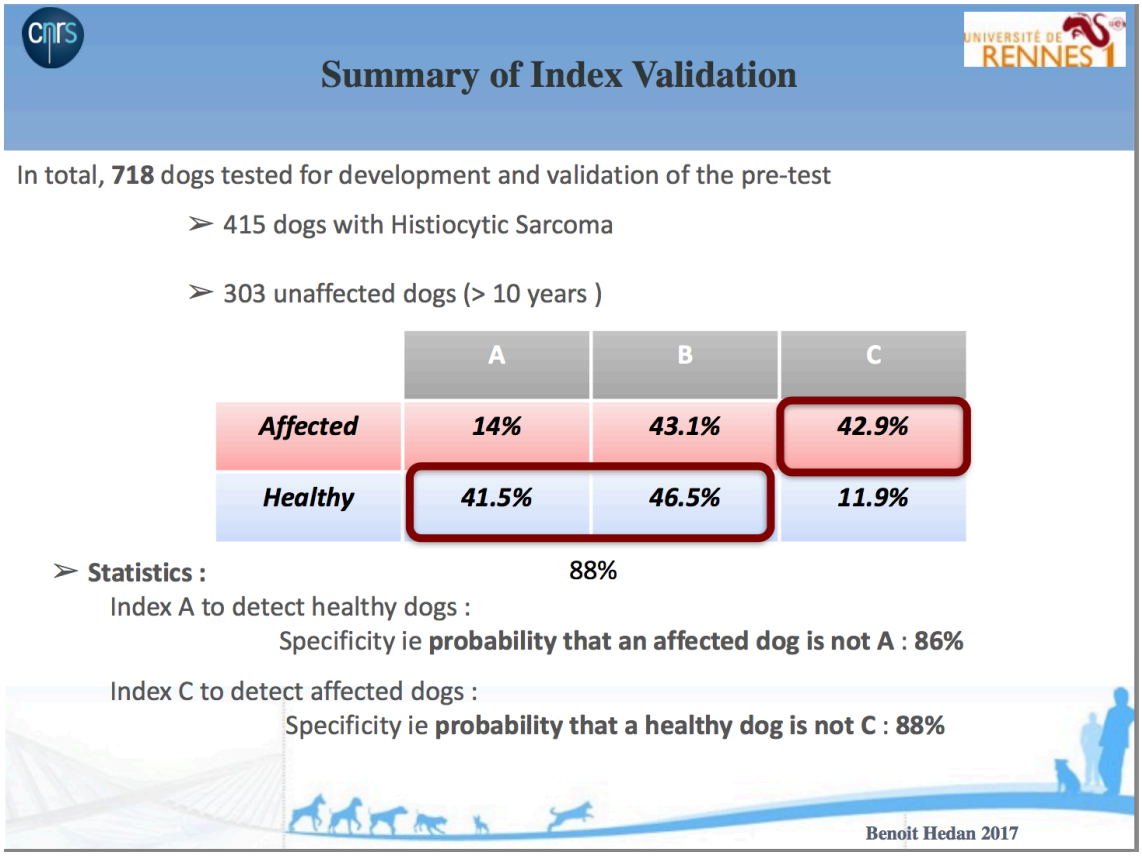

Figure 5

As you can see in *figure 5* from a sample of 718 Bernese from European and American populations 88% of the 303 healthy dogs, that is dogs unaffected and at least 10 years old, were either 'A' or 'B' category dogs. Conversely of the 415 dogs developing Histio only 14% were 'A' graded.

In the next slide, *figure 6,* showing 1,846 dogs tested by Anatgene since 2012 the overall distribution of grades was 23.8% of 'A', 44.5% of 'B' and 31.7% of 'C' but the interesting part of this is that if looking only at dogs of 10 and over the percentage of 'C' dogs drops to 15.6% whereas (obviously) the other two categories increase especially the 'A' category which doubles to almost 47%.

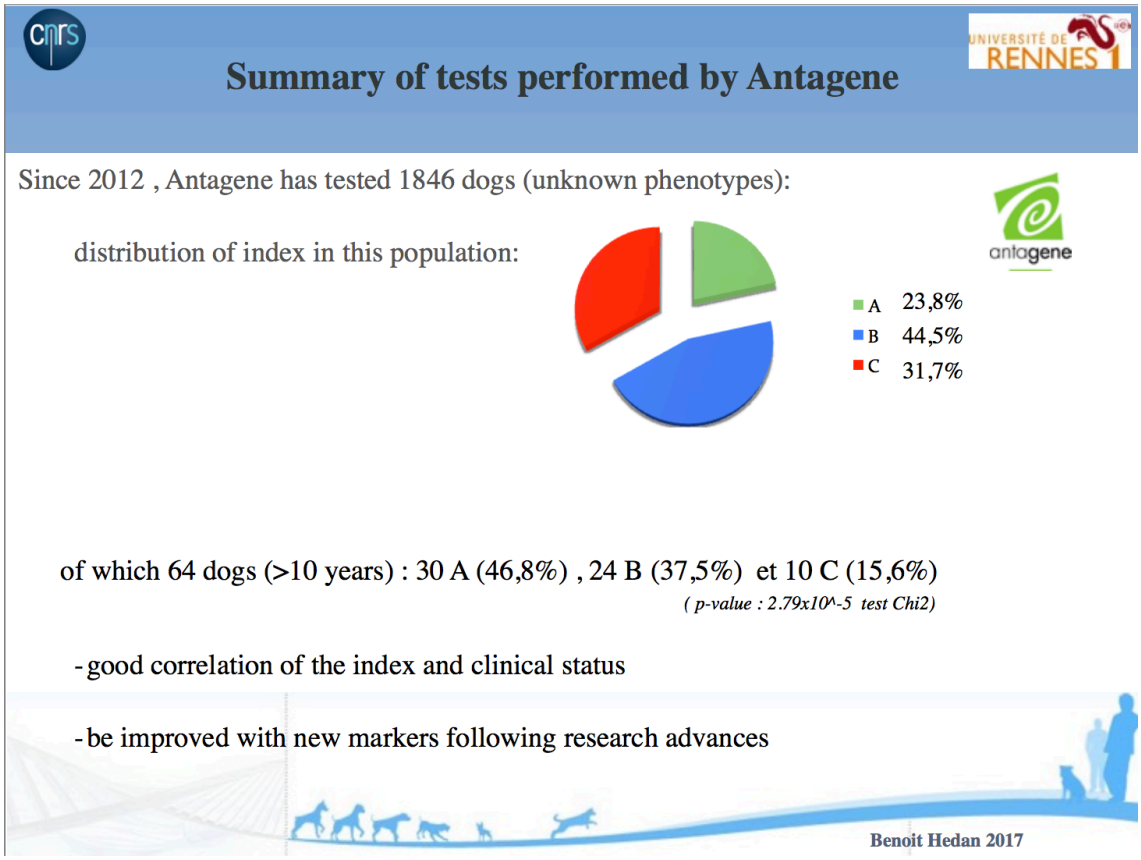

Figure 6

Figure 7 shows the same 1846 dogs but looked at another way. Here ages at death were looked at and specifically those had had died by the age of seven. From these 49.1% were graded 'C', 35,8% 'B' grade and just 15.1% were graded 'A'.

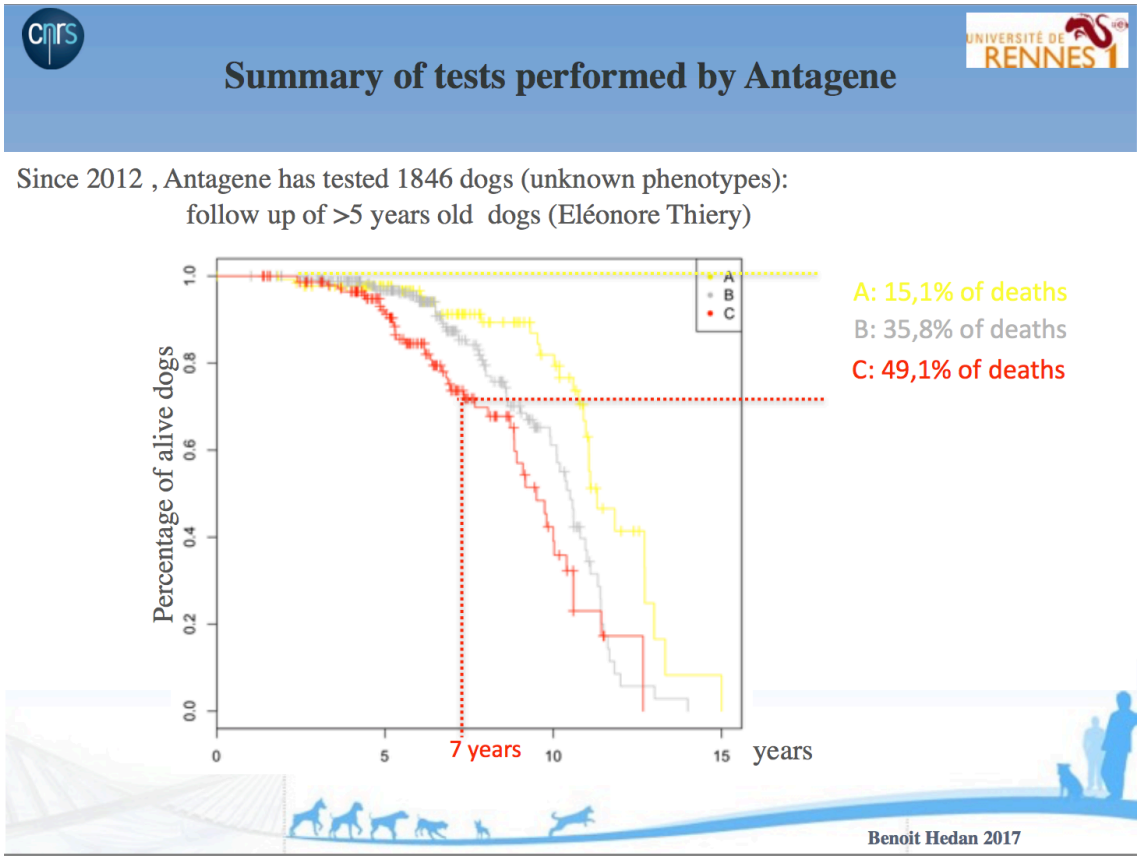

Figure 7

So, basically almost half of the dogs that had died by the age of 7 were 'C' grade dogs whereas only 15% of the deaths were of 'A' grades.

There were lots of figures of this nature given in the French presentations as well as more analysis but all, basically, demonstrating that more dogs with Histio and that die younger are from the 'C' category and more dogs that live longer and do not die of Histio are graded 'A' and vice versa.

In a separate presentation from Dr Anne Thomas of Antagene, (more of this presentation later in 7.3), *figure 8* was shown. This shows that in 112 puppies from 18 litters, all with tested parents, there was a good degree of heritability to the grades.

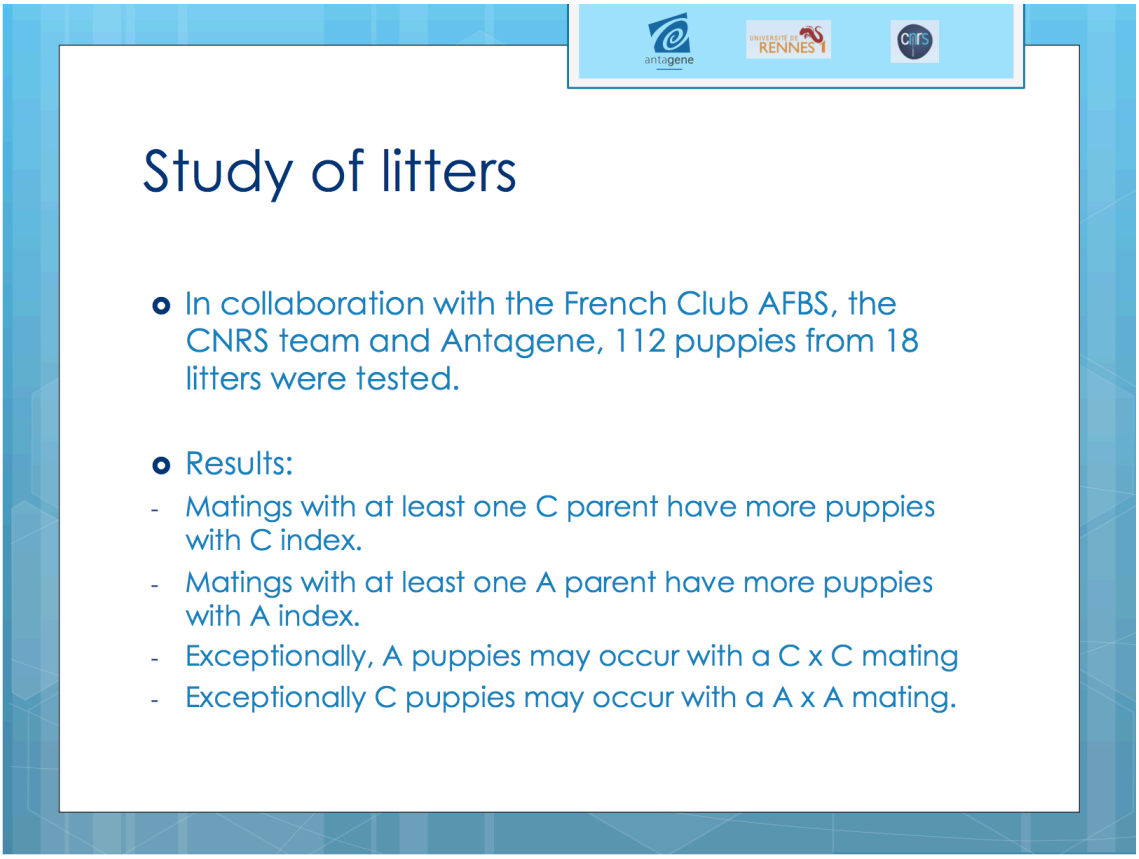

Figure 8

However, as you can see from *figure 9*, this inheritance is not of a totally fixed predictability mode and there is a good degree of variation to matters. However, the *overall* trend is that you will 'get out' predominantly, but not necessarily exclusively, what you 'put in'

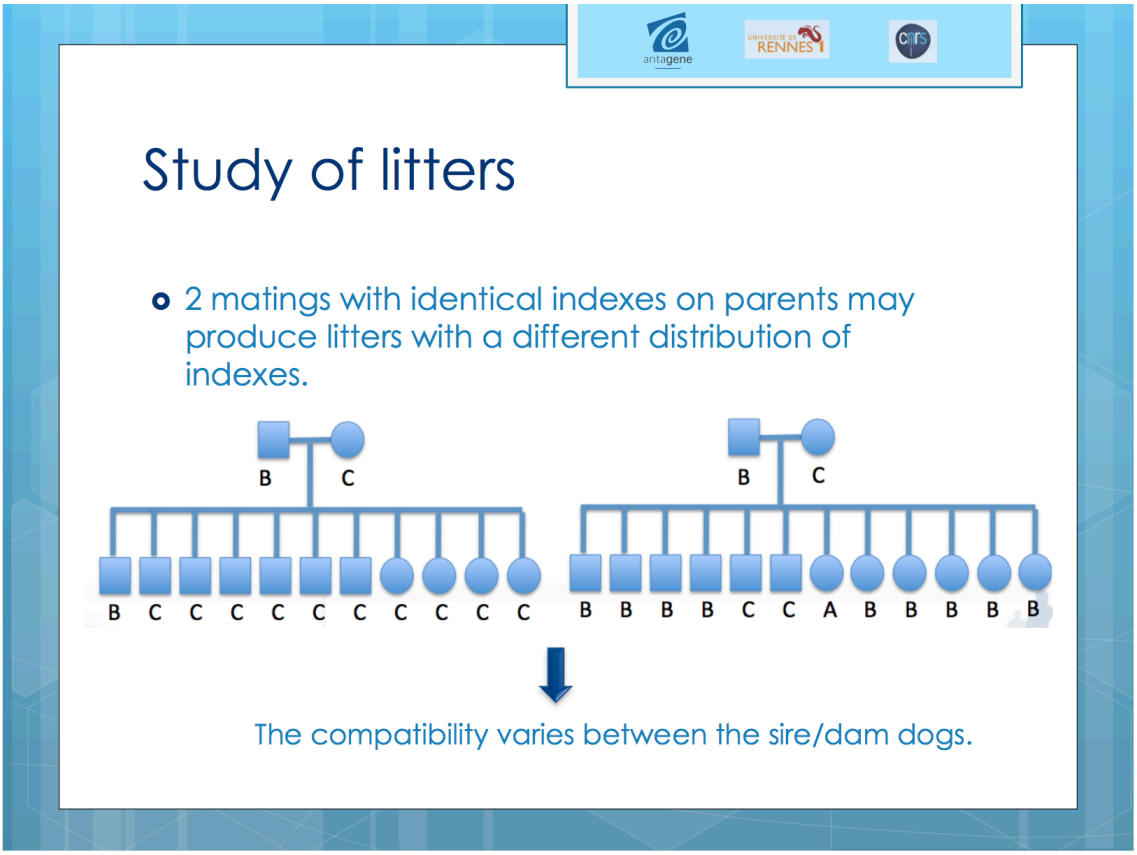

Figure 9

So, hopefully you can see that whilst any individual dog's outlook cannot be reliably predicted *at this time*, it seems to be an increasingly established fact that 'A' graded dogs have a better chance of living longer and being healthy and avoiding Histio but most importantly of all generally passing these characteristics on to any progeny. After statistical analysis the test result certificate refers to 'A' grade as having a 4 times higher chance than neutral B dogs of not developing Histio and NOT passing it on to any offspring. 'C' grades on the other hand have a 4 times higher chance than neutral B dogs of developing Histio and the same increased chance of passing this grade on to their offspring. These figures may change slightly as time goes on with continuous assessment and re-evaluation of the test but the trends have been clearly identified with *statistically significant* numbers of dogs to validate the test in it's current form.

5] Not a precise tool

The developers and the providers of the test are well aware of it's current limitations and lack of preciseness. They do not claim it is an overnight panacea for all our breed's cancer woes. They are fully cognisant of the fact that as the test is now there will be anomalies and exceptions such as plenty of long living, healthy 'C' dogs and conversely some 'A' dogs succumbing early to Histio.

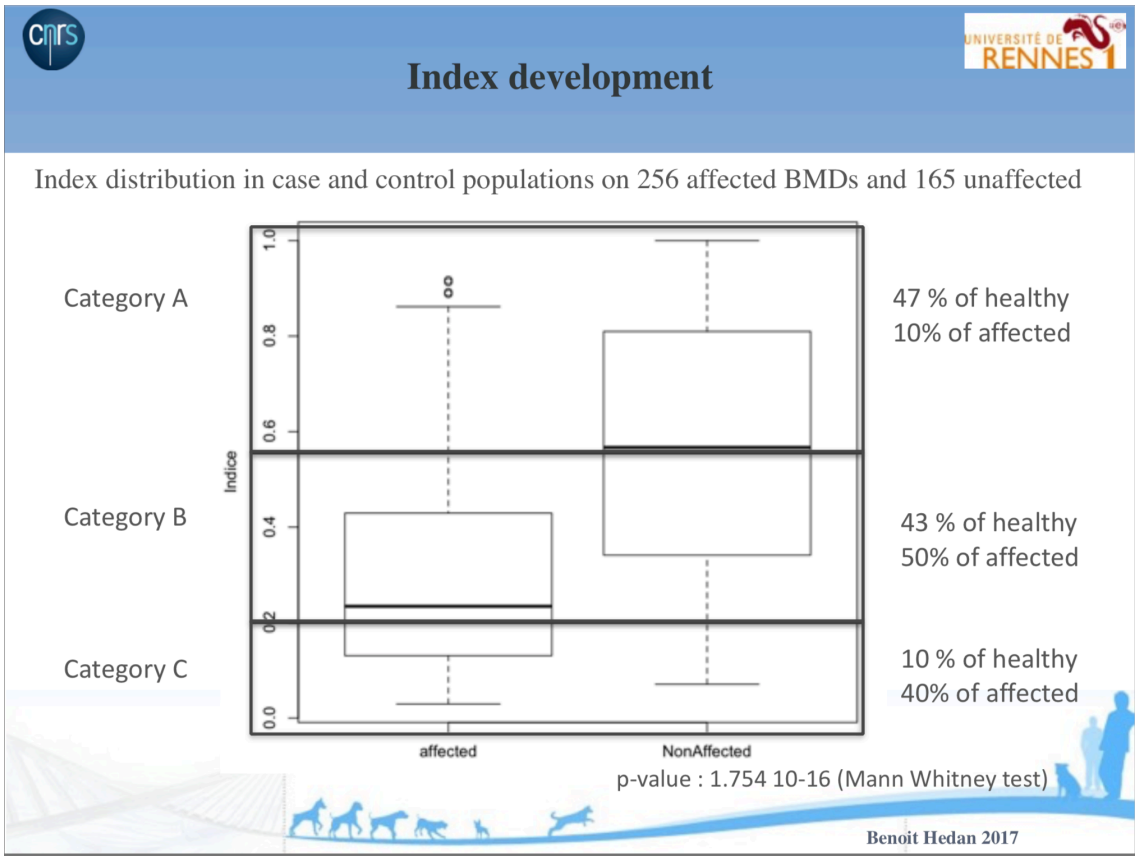

Figure 10

However, the existence of such dogs does NOT mean the test is worthless as some people claim and Antagene's reference to it as a selection tool to reduce 'Histio' in Bernese Mountain Dogs is a legitimate description that stands up to logical assessment.

'Overall', 'on average', 'by and large', 'generally speaking' - use which ever phrase you prefer, the evidence clearly shows that using the test and taking heed of the results will make a difference to the individual breeder's stock and, perhaps more importantly for the rest of us therefore, the overall state of the breed. If used for a few generations you can quickly improve the outlook for your puppies. It may well be considered a blunt tool but overall it is still a positive tool for the breed.

6] Complaints about the test - reasons given not to do it

Over the last few years I have heard, both first hand and indirectly, several reasons why people are not engaging with the test. I comment on some of these below.

6.1] It's too expensive – How can people even say this for their breeding dogs when considering the price of puppies and stud fees? There are occasional sales held by Anatgene when the price is dropped but generally the test itself currently normally costs 115 Euros, which, since the Brexit vote, is not much different to the same amount in pounds, say £105. You have to pay your vet to take the blood sample and send it off which will vary. Over the years I have heard of some vets charging ridiculous amounts for breed research samples but others do this very cheaply, or even free, for regular customers as it is for health testing. If you are sending a few together the postage cost will work out less per sample and your vet may do a 'package' deal for you for the sampling. We sent 6 tests recently and the postage to France was around £8 recorded delivery, (this may go up after Brexit of course). However, as a ball park figure for consideration let's say around £150 for a complete single test.

If you are testing a stud dog this cost is only a fraction of the price of a single stud and set against several fees it becomes insignificant. As for testing a brood bitch and setting it against the income from several litters of puppies then, again, it becomes insignificant if you are breeding for the right reasons. It is less than 10% of a standard puppy price or stud fee and a lot less in some cases, so if the bitch has 10 puppies *in her lifetime* it is less than 1% of the income from that bitch. It is significantly cheaper than submitting hips and elbows to the BVA/KC scheme and all serious breeders do that and just accept the cost, so why should this be declared too expensive?

Also, as you can read a little of elsewhere in this magazine, undertaking health tests could be part of your protection against potential court costs if your dog develops problems. Most knowledgeable people feel this will become a more frequent occurrence in the future and, if it does, £150 for a test will pale into insignificance against the legal costs and fees breeders could be made liable for.

So, personally I think the financial cost argument is a very feeble one for responsible breeders and, now the test is established, just sounds like making excuses.

6.2] It doesn't mean anything, it's not definitive, it's only a guide, it's not accurate/when it gets more accurate I might think about it – hopefully this has been dealt with above in all the preceding explanation of the test. If you want to reduce the chances of Histio in your puppies then why would you not want to do whatever you could to improve matters in this most significant area for our breed?

To draw a parallel in principle, the hip and elbow scoring schemes are also not definitive in, effectively, the same manner but virtually 'everyone' does them and all responsible people would say that people should. You do not *absolutely* guarantee good hips and elbows in any specific one of your puppies by using hip and elbow scores as part of your breeding considerations but you increase the odds and over a period of time with each generation the beneficial effect for BOTH individual lines AND the breed as a whole, of heeding the tests is cumulative and the advice becomes more and more reliable. Every responsible breeder submits to Hip and Elbow scoring but then some of these breeders say the cancer test is not definitive enough. So, if you are in this camp then the logical question from this is do you only hip and elbow score because you feel you *have to* for the KC or Assured Breeder Scheme? If you were not compelled to do them, would you regard hips and elbows as unnecessary?

By responding to hip and elbow scores over several decades the breed, and others, have undeniably improved the health outlook for the breed massively. Not only have hip and elbow *scores* improved but, anecdotally admittedly, there does not seem to be anything like the number of problematic hip and elbow cases around that there used to be and no dogs are reporting death due to hip and elbow problems in the current Death Survey. When problem hip or elbow cases do occur you can usually dip back into the pedigree and find an area or a mating or a dog that is most likely responsible so, mostly, problems do not come completely out of the blue. So, no definite individual puppy guarantees but use of these schemes has improved the breed and some people have lines that are extremely strong in these areas due to applying criteria consistently over several generations.

To say you are refusing to consider the test because it is not accurate enough is to totally misunderstand the whole point and feasibility of the test. Firstly what do you mean by accurate? If you mean you are waiting for a decisive, autosomal, recessive gene type, clear cut result you will have a long wait as it will never be that, the nature of inheritance excludes that possibility. If you understand that then you understand it will never be the same as such a test so what else can you mean?

It is not about individual accuracy but more about overall improvement, just like the hip and elbow scoring. Proper use of the scheme means you will generally improve the health of your line over a period of generations. What if we never had anything better? What if the test was the only thing we ever had to improve the breed and reduce/ remove the curse of early deaths and histio and there was no chance of it ever getting any better? In short it was to be the only thing ever possible to fight 'histio' with. Would it still be worth using? Would the positive effect it can have on our breed not be worth utilising? Or would we just say 'overall positive effect maybe but it's not good enough so we'll just carry on as we are'.

Why should the 'Histio' cancer test be viewed any differently to hips and elbows which 'almost everyone' does test? To me if you say you are not using the test because it is not accurate enough then the logical application of that statement is that you are not interested in improving hips and elbows either but presumably score them because the KC say you have to. Is the principle not exactly the same? So, I can only repeat why would anyone acting responsibly for the breed not want to do whatever they could to improve matters in this *most significant* area for our breed?

6.3] I had, or know of, a 'C' dog who was healthy into old age (or 'A' dog who died young) so the test is useless – this is the same argument as above really and if you have read the article so far, hopefully you will understand that this is not a reason to ridicule the test as these dogs are to be expected. The test is currently about the overall numbers game and not necessarily individual dogs and as usage of the test begins to bear influence on the breed it is only logical to expect these the percentages of these dogs to become more reduced.

6.4] There's no point in knowing because you can't do anything about it / I don't want to know about my dogs – well in one way you cannot argue with defeatism, it's a point of view that by definition cannot be broken and it is true that you cannot genetically help dogs that have already been born. However, clearly this is a wrong premise as the test is about looking forward because as a breeder you CAN do something about the future and play your part in beginning to move the breed to a better place by improving ***the next generation of your own*** dogs. If you know the status of your own dogs you can look to improving or maintaining this status in the next, and future generations. If you find out your dog is a 'C dog' it is not a guarantee that he or she will develop Histio or will die at young age, if you are not intending to breed with your dog then there is no real need to score him or her at all. Of course some breeders may elect to test all potential breeding dogs in a litter in order to aid their choice of the most suitable for their breeding programme.

6.5] If you're going to get cancer you are going to get it anyway– at the moment this is probably true where no one has tried to take any positive action but in future litters you can still reduce the odds in your favour for the future of your own stock. Of course, as was said near the beginning of this article, there are other cancers and some of these do not have any known hereditary link and these *can* be considered plain bad luck as far as we know at this time. However the fact remains that 'Histio' is our biggest cancer and you can do something to reduce the chance that '*... you are going to get it ...*" in any dogs bred from your lines.

6.6] It's just depressing to talk about it – this certainly can be true and no one will be in this breed for too long without experiencing some heartbreak and this may often be due to 'Histio'. However, surely it is more depressing to accept things are bad and simply just be depressed about them rather than embrace a chance to do what can be done to improve future matters for the breed. The test is definitely not about the inevitability of 'Histio' being disheartening, this would be the case if there wasn't a test. On the contrary it is the beginnings of the breed, at last, being able to take some positive action. It is a chance for the breed, through it's individual breeders, to begin to fight back, it is a cause for some optimism and as the first real tool we have been given, a reason to be at least a little bit cheerful. Surely the most depressing thing is to do nothing and keep perpetuating a bad situation when there is a chance to do something to improve it.

6.7] It's too complicated – here I would perhaps have *a little* empathy as I think the Antagene web site could be a little bit more user friendly but it is possible to work it out and the help is really good if you email them. I have now met several of the people who staff this project at Antagene and most of them have really good English. Hopefully, the step by step guide below, section 8, will be of some help to anyone trying to use the test or if I can help please feel free to contact me.

6.8] Bernese don't have a cancer problem, people like Steve make too much of it – sorry, but the facts do not bear this out. We may be a bit lacking in hard statistics in this country, a fact the Death Survey is seeking to begin to improve, but the early signs from the Death Survey and anecdotal feelings expressed by breeders and owners for decades all point to a cancer problem. You could say that the dogs in other countries where the extent of 'Histio' is more documented than here, are a different gene pool but like it or not all the dogs came from the same gene pool and the world is shrinking and there is much international breeding nowadays. This makes it extremely illogical to make a case that several countries could have such a widespread problem that was not present across the whole breed. Initiatives such as the Death Survey only seek to establish the true position so responses can be considered and assessed. "*People like Steve*"' in any country do not enjoy highlighting issues and only seek to improve the breed, this cannot happen until there is widespread understanding of our real issues and what we can do about them.

6.9] My lines are healthy and long living, I don't need to concern myself with Histio – it is perfectly true that at times over the years we have identified some kennel lines that exhibit good longevity. So if you have good long living lines then well done, but surely you want to keep them? If you introduce a 'Histio' dog into your lines you do not get a slight drop in your average life span in your dogs in the way that if all your dogs lived to 10 years previously they will now only live to 9.5 years. It simply doesn't work like that. You will still get some dogs with good longevity the same as before because they will be unaffected but some of your dogs will now develop 'Histio' and will die at younger ages. Some of the families that buy your puppies will lose them at 4, 5 or 6 years. This will be the case in subsequent generations as well and at some point you will need to utilise the test over a period of time to begin to address it. If you have established a reliably longer living line then I would say think very carefully nowadays before risking this precious asset by using an untested or a C graded dog on an untested dog of your own.

6.10] I don't need to take reasonable steps to not breed unhealthy dogs – OK this point hasn't been raised in this way but it is a line used here to introduce the current background tectonic plate movements that may be happening and applicable in the near

future to the breeding of dogs. I quote from my other article in the December 2017 BMDC of GB magazine, which confusingly starts with a quote;

"The headline of ***Our Dogs*** canine newspaper of October 27th "**Government to prosecute breeding dogs with 'genetic defects'** was covering the way the legal basis of breeding and outlining how the government are considering changing the way the Animal Welfare Act (2006) is applied. It was reported that a government spokesperson had stated that "… *anyone knowingly breeding animals with genetic defects could be considered to be committing an offence under the 2006 act*"

The point made later was that breeding dogs with genetic defects could be deemed to be *'unnecessary cruelty*' under the act and therefore a prosecutable offence. It is entirely possible that even if the consultations over this act decide that this is not covered by the act then those driving this process could amend the 2006 Act to definitely say this if this is the way they want it to go.

There has been a big review of the Animal Welfare Act taking place over the last few years. Two main drivers for this are the amount of puppies being smuggled into the country and unhealthy puppies being bred by 'legitimate UK breeders'. Some of the movers for the reforms to the Act consider that many breeders of pedigree dogs are irresponsible and don't take enough care when it comes to the health of the puppies they are breeding. When you set this against the massive explosion in the number of DNA tests available for various canine diseases that are now available then the possible requirements of this act or the areas any legal cases resulting from this might look into, are quite clear. Scaremongering? Maybe, but the wording used in the *Our Dogs* article and quotes from government spokesperson leave little room for ambiguity.

The way the forthcoming legislation finally appears and is applied could have massive effects on dog breeding. There are other factors to taker into account but just stop to consider how " ….. *knowingly breeding animals with genetic defects* ….." could be legally applied. As a breeder you sell a dog that dies of 'Histio" at say 4 years old. The owner seeks legal advice because they find out there is a test that if applied to the parents would have reduced the chances of her puppy developing this disease. After taking advice from a 'no win no fee' legal adviser the dog's owners decide to prosecute the breeder for distress and anguish caused to their family as she expected the dog to live a lot longer. They sue to breeder for not taking reasonable steps to reduce the chance of this happening to their puppy. The breeder in her defence in court says she did not need to use the test when choosing a mate for her dog because her lines are healthy and the test isn't accurate or effective enough. The judge says her lines clearly aren't healthy as she has produced a dog that has died of an hereditary influenced disease, so point dismissed. The exact accuracy of the test is irrelevant because it has some accuracy and represents the only evidence the breeder could have given to prove she did take reasonable steps to produce healthy dogs. The judge says that this is the biggest cause of death in this breed and this breeder did not take the only quantifiable mechanism available to reduce the chances of her puppies going on to develop the disease. The owner's case can only be deemed proven and breeder has to pay several thousands of pounds out in costs and damages. If the breeder had used the test and acted upon the results then whatever happened to the puppy the breeder could have made a defence that due care was taken.

In potentially applying this scenario to this case, a court may consider that it been possible to use the 'Histio' test for several years so any changes in the legislation could be applied to dogs bred since it was available but who die after the introduction of the reformed Act, not just those bred in the future. Even if you use it and apply it according to recommendations and things do go wrong because the test is 'not accurate' then any breeder can mount a defence that they did what they could and what could reasonably be expected of them. Ignoring the test could be seen as absolutely not taking reasonable steps to not produce a 'Histio' affected puppy and completely negate a breeder's defence to any legal case brought. Apart from the ethical 'health of the dogs' perspective my personal opinion is that breeders ignore any health testing for their breed at their peril in the world we appear to be moving into.

7] Important POTENTIAL Developments for the future

The more astute readers may have noticed in the foregoing several references and sentiments such as "….. *currently*….." and " …. *at this time…. "* and this is because several potentially exciting developments for the 'Histio' test arena were announced as part of the update presentations given in France although it cannot be stressed enough that two of these are a long way off yet but included here as causes for a bit of optimism. The other can be progressed as soon as funding can be found.

There was news of **……**

7.1] A blood test for the presence of 'Histio' tumours? – it is very early days and presenter Benoit was very keen to stress this is nowhere near fruition but the basics have been developed to make such a test theoretically possible. This could confirm the definite presence of Histio much, much earlier compared to what happens now. Typically now a dog presents at the vet's as 'off colour' and, depending on the exact symptoms, the vet might try anti inflammatory medication, antibiotics then steroids and then maybe refer on to a specialist after a couple of weeks. In this time the disease will most likely have progressed a massive amount without even being diagnosed and the chances are the dog will be too far deteriorated for further tests to ever reveal the true illness. At some point the malaise will perhaps be written off as lung cancer or non specific cancer when in actual fact it is Histio at work. The only current definite diagnosis is to visually examine tumour biopsies under a microscope. As Histio tumours are frequently extremely inaccessible and difficult to find until post mortem, which rarely happens, such a test would be quite a break through. If there was a simple blood test available to try immediately that revealed that there were Histiocytic tumours present somewhere in the dog a] the dog would be *correctly* diagnosed as suffering from histio, b] there would actually be a diagnosis rather than dragging on as an often unsolved mystery, c] owners would not be spending lots of money on unnecessary tests and speculative treatment and d] the true extent of the disease across the breed would be much more apparent and measurable. However, without an effective treatment better and earlier diagnosis is only of limited real value.

7.2] Beginnings of a Treatment? – there was also news of maybe the origins of a potential treatment for Histio. Again, it could not be stressed enough that this was very experimental at the moment but 'Histio' tumours grown artificially in the lab had been adversely affected by this treatment. There are numerous big and lengthy steps to move this to a viable treatment and we are talking years away from this stage but at least it is a bit of hope for the breed in an area where there has been absolutely no hope previously.

Obviously an early diagnosis test is no use without some kind of treatment and treatment is not so good if only administered in the later stages. However, if these two pieces of news are looked at together then the world of Bernese with them both present and fully working would be a dream land compared to what we have now so we can only keep our fingers crossed and wish the University of Rennes well. Their announcement was very low key within the presentation but when talking afterwards the amazing potential of these two facets was really well appreciated and then confirmed in conversations over the week-end with the Antagene and University of Rennes researchers and we could give them the 'wow moment' of realisation they deserved.

7.3] Histio Test Web site? - There was even more potential good news like the others still over the horizon, but at least giving us some promise of better things to come. This was referred to as HSIMS in a presentation by Dr Anne Thomas from Antagene and I will try to explain this as best as I can. (I definitely have the potential practical application right even if I am not quite getting the technical details correct).

You will recall from earlier in this article that the current test checks the markers in nine different sites. Each of these markers can be in three different states so the number of potential variations in just these 9 areas of DNA is 3^9 (3 to the power of nine) which is a little under 20,000. So each dog can have almost 20,000 possible options just in the areas of DNA currently looked at for Histio indicative changes. These areas are looked at for each test and basically the number of differences to the DNA of the healthy dogs is counted and from the number of variations the index figure of 'A', 'B' or 'C' is calculated. That is to say if a dog has only a few variations it will be graded as an 'A' and if it has a lot of variations it will, unfortunately, be graded as a 'C'. In between the extremes will be the 'B' neutral dogs whose variations come within the numbers considered as average under statistical analysis.

So, a dog can be graded a C due to a lot of changes observed and for example a second potential mate could also be graded as a 'C' but, although having many changes they could still be a largely different set of changes present. This *could* mean, in theory at least, that those two dogs, although both graded 'C' might not be completely disastrous to put together as none of their variations were being doubled up on. It could also be the case that putting a certain two C grades together could be absolutely disastrous and produce a predominance of C dogs with a poor prognosis for longer life. At the other end of the scale exceptionally two 'A' graded dogs could have very few changes observed but these could be completely the same variations present so all the changes would be doubling up if those dogs were put together. This could mean that those two *particular* 'A' dogs would not necessarily be as good a combination for Histio as previously thought. Remember we are only talking about the changes observed in the 9 areas of DNA found to be genetically significant in 'Histio' and whilst such scenarios may occur they will still be in the minority.

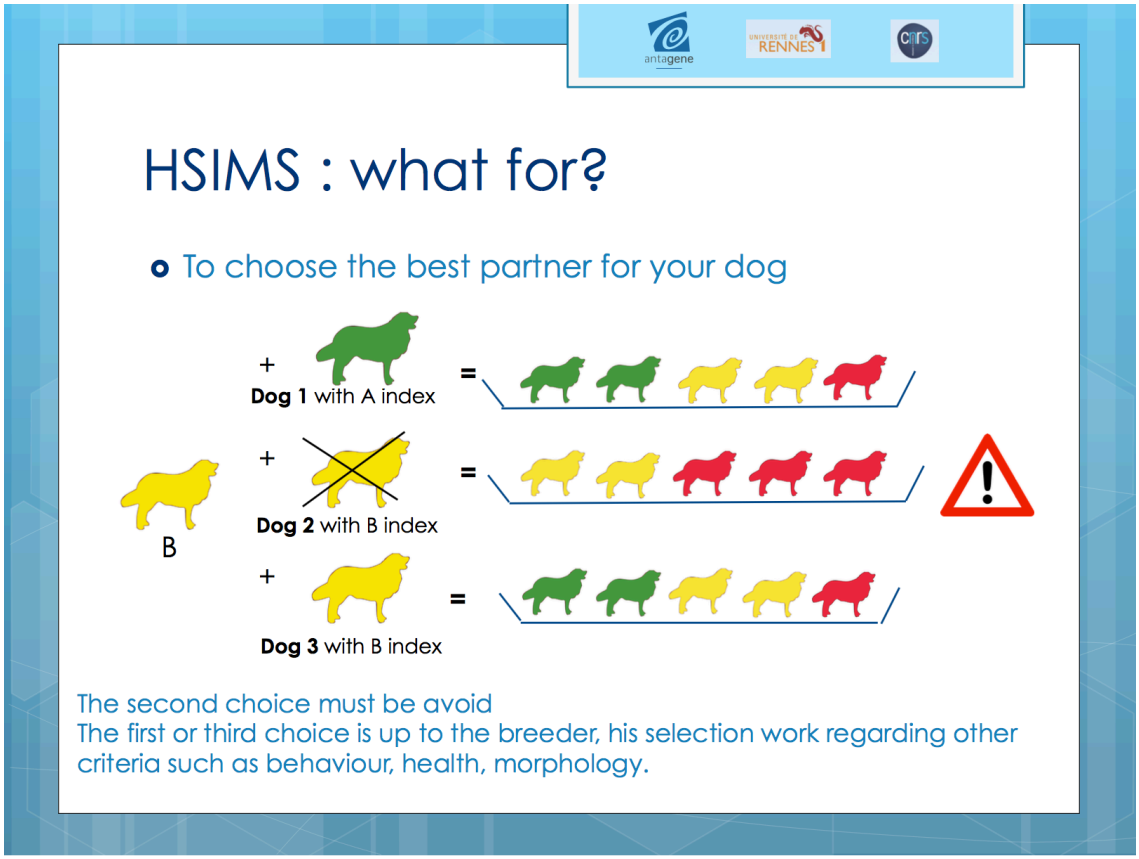

Figure 11

Figure 11 demonstrates this principle showing that two potential matings of a 'B' graded dog to an 'A' grade, a 'B' grade or a second 'B' grade. Under the current system you would expect the 'A' combination to be the best but you can see that it may be the case that a specific 'B' graded dog could be just as good as choosing the 'A' grade option producing the same breakdown of 'A' 'B' and 'C' puppies. However, a different 'B' dog could be much worse, even disastrous, producing 60% 'C' grades. Under the current system there is no way of predicting these outlooks, well an extremely lengthy examination of each proposed pairing could be undertaken but at this would be extremely time consuming and totally impractical, but if HSIMS were introduced it would give these much more specific and accurate predictions in an instant on a web site freely available to all.

Do not misunderstand this, at the current time as far as anyone can say 'A' dogs will produce a much better chance of healthy long lived dogs than 'C' dogs but if it was possible to assess an individual mating, a more accurate potential result for any *exact* combination could be estimated. This could only be done if it were possible to compare in detail all (near) 20,000 possibilities on an individual dog against the same 20,000 possibilities on another individual dog. This is one reason why Antagene do not recommend that the breed discards all C graded dogs from the breeding programme but just uses them carefully.

Figure 12 demonstrates that with due care it is possible to utilise 'C' dogs within a breeding programme as long as they are used in good combinations. HSIMS would make it possible to be more sure of these safer pairings.

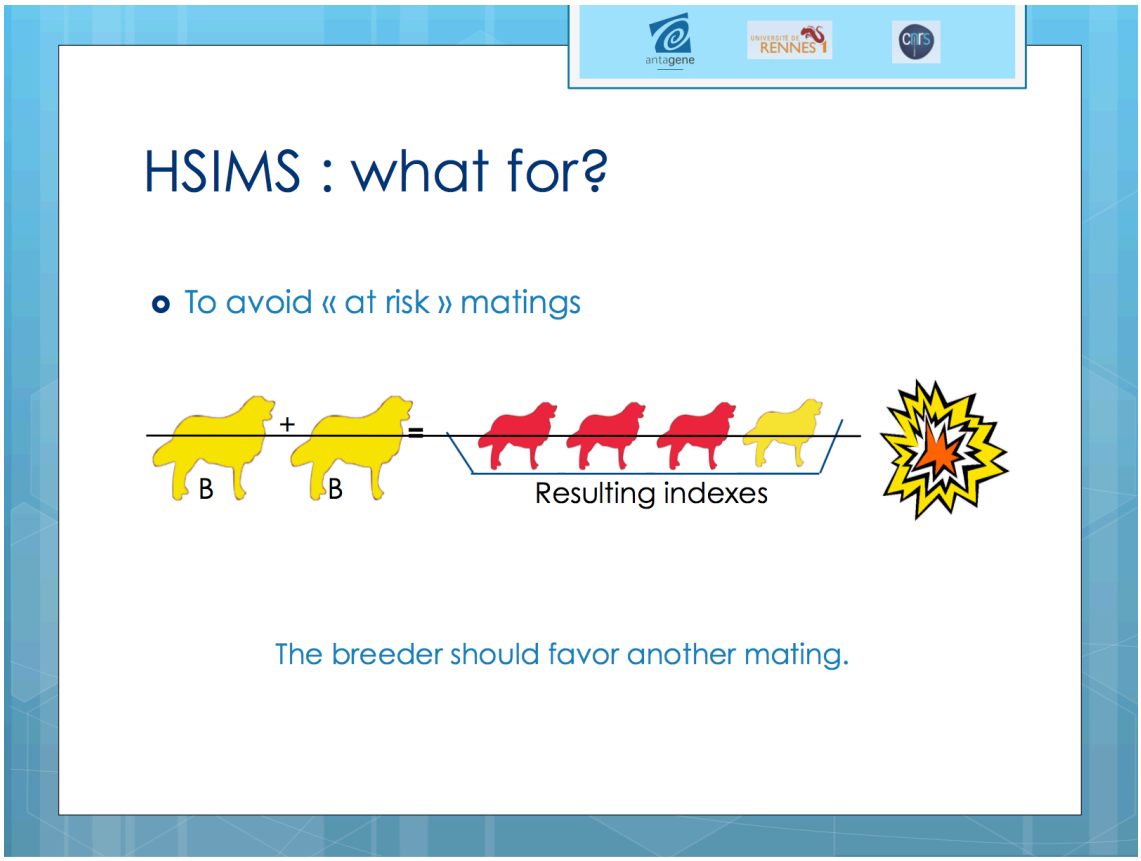

Figure 12

Antagene announced that they want to set this facility up for Bernese owners and they want it to be free to use. They want to design a web site interface for the database of test results in which you could put your proposed dog and bitch combination and you would get an exact probability prediction of what those two specific dogs would combine together like and what mix of 'A' 'B' and 'C' you could *expect* vastly more accurately than the current test. Obviously this could only work for dogs and bitches who were tested but just think of the possibilities. Every single potential mating could have an exact individual 'Histio' rating. This would not be the same as an EBV type system based on antecedents and the effects of the cumulative contributions of relatives, this would be a direct prediction unique to two specific dogs combining together, drawing the data it uses to give the result directly, and only, from the test results of those two dogs.

Antagene's Anne Thomas' whole presentation was on this project , the full name of which is Histiocytic Sarcoma Index Mate Selection. Some of the many possibilities were demonstrated with these hopefully self explanatory slides amongst them.

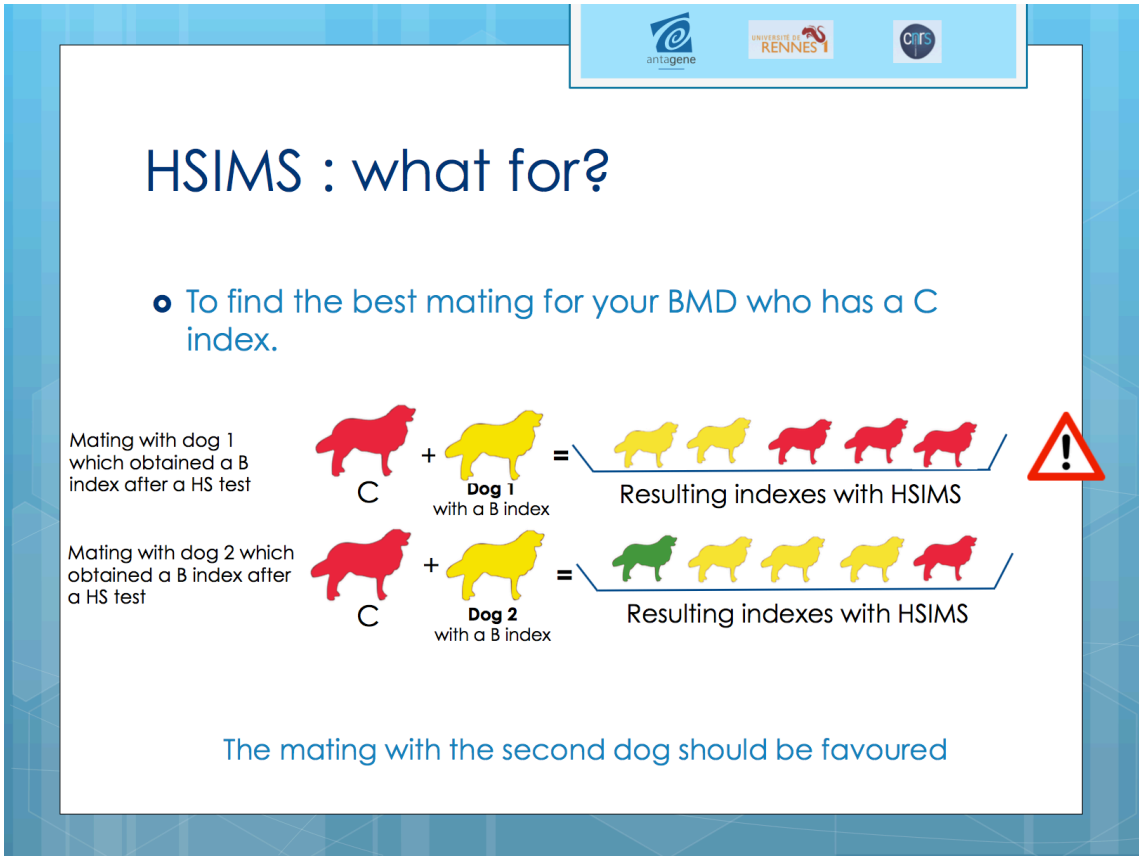

Figure 13

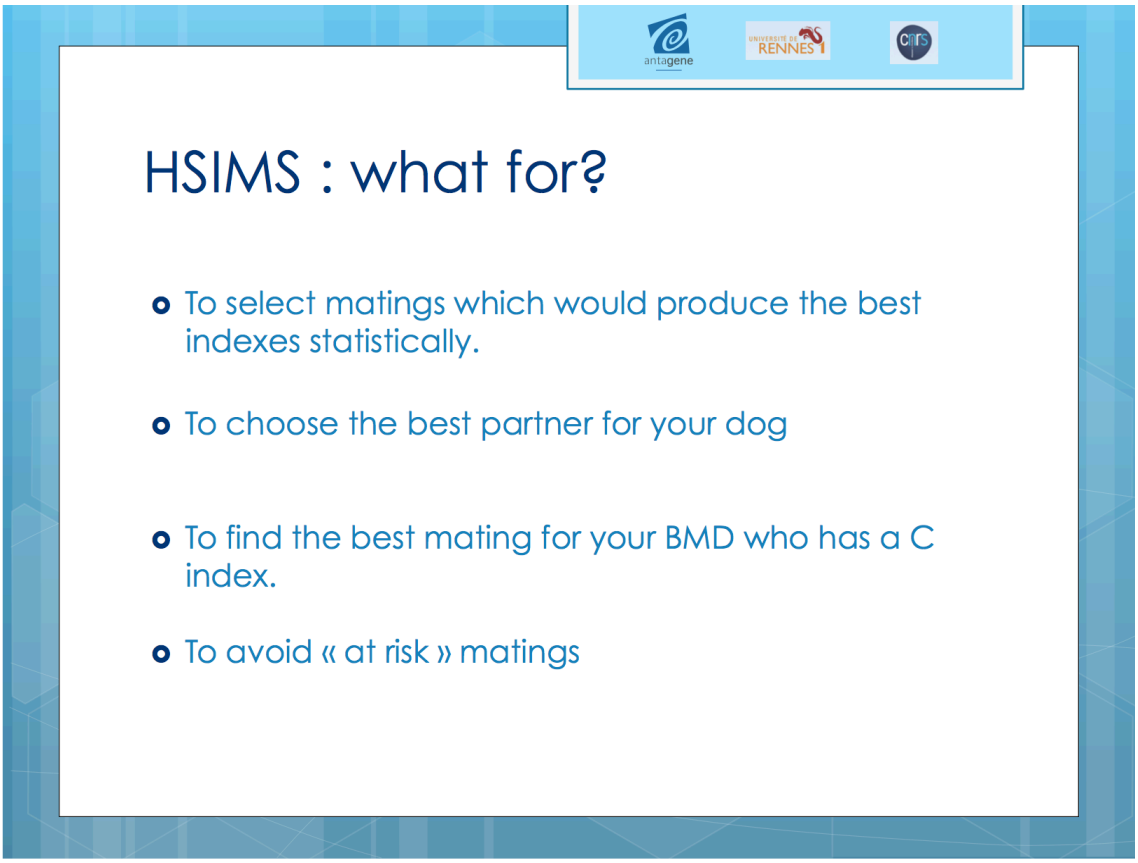

Figure 14

Anatagene said they needed funding of €11,200 (euros) to develop the database and interactive web site to go with it and outlined a few principles that would apply. Several countries said they would go back and consider ways of raising this money and there was a generally optimistic view afterwards that this would not be a big problem for the breed across the world to raise this money in view of the incredible, potential value for the breed of this initiative. The French club held a collection, literally moving around the show with a bucket and inviting contributions, throughout their week-end events following the presentations and collected almost €850. Any contributions or ideas for fund raising can be forwarded to myself.

A pdf of the whole presentation on HSIMS, with these slides and the rest, will be available on the GB club web site.

8] How to use the (current) test – the practicalities

As previously stated this can be a slightly confusing process when first undertaken, it is actually quite logical and the purpose of each step is clear, it is just the explanation and instructions maybe lose a little bit in translation.

To utilise the test you firstly need to access the following link on the internet
http://www.antagene.com/en/commander/histiocytic-sarcoma-test

(This link is amongst those at the foot of the 'Histio' page within the health section on the club web site so it can be accessed from there). This page contains lots of information about the test, what it means and how to use it but I outline the basic procedure here to assist.

Having read the page you need to be at the section towards the bottom headed "**What is the procedure for requesting the test for Histiocytic Sarcoma ?"** which holds the key links to the whole process.

Firstly, you need to click on the grey "Memorandum of Agreement" link and when the page opens print off two copies, one is to keep for yourself and the other needs completing and signing and must be sent with the first sample you send. After this you would not need to submit it for future samples.

Secondly, you need to arrange payment for your sample, so you need to print off or refer to the page you access from the "payment" link. You can either pay direct by direct bank transfer, in which case you need to print off the receipt page or acknowledging email and include it in your sample package, or you can pay by card by adding your details to the payment sheet and including that sheet.

Thirdly, you need to click on the "sample certificate " link and print and partially complete a certificate for each sample you are submitting leaving the section for your vet to complete.

You are also asked to submit a copy of a pedigree for this dog if possible.

There is also a link to a research form for you to complete for your dog but your sample can be sent without this and it can be completed at a later date and then updated if there is any change in your dog's condition. This is a valuable part of the research aspect for the breed of this test so please remember to contribute it if you do not do so at the time of the sample.

You then need to take to the vet's the dog (!) and the….

- completed Memorandum of Agreement form,
- receipt of payment,
- partially complete sample certificate to your vet along with the dog.
- A pedigree and the research form if possible can be included.

The vet can then check the microchip of dog matches the one you have given on the certificate and take the blood sample, it is usually the case there is no need for shaving with our breed. There is no spinning or other treatment of the blood required by the vet, it just needs placing in an EDTA tube to preserve it which is very standard procedure. The vet needs to complete his/her section of the form confirming the dog's identity via the microchip and date of the blood taking, complete the packaging and post it to Anatagene. If submitting more than one dog the vet needs to mark each EDTA tube with a number or letter to tie it to a single sample certificate.

The whole lot should be packaged up and posted BY THE VET to the address given in France as part of the validation process. (If you were allowed the take it away afterwards to post it yourself the vet could not guarantee to Antagene that the sample has not been swapped and the validation process is compromised). This is not a bad thing but a good thing for the credibility of the test and all well designed tests have validation and credibility as an essential feature. (We recently sent 6 samples to Antagene and the receipt showed the vet paid only £8 for recorded delivery so this step is not a prohibitive cost).

There is also the option to contribute a sample just for research without paying an Antagene fee. This means you receive no feedback but your dog's Histio status is recorded as part of breed research.

9] Summary

In compiling this article I have tried to include everything I feel is relevant about the disease and the test so that anyone just coming to it can be properly informed and hopefully understand how important it is for them to engage with it, especially if *breeding* Bernese Mountain Dogs. I feel the breed club in France and the French BMD owners should be thanked by us all because their efforts over the last 15 years have really enabled massive strides for the Bernese Mountain Dog against this curse on our breed. Not only have they provided funding and samples at a high level of support they have introduced other ways to encourage support for the testing. These measures include the fact that it is impossible for a Bernese to be a Champion in France unless he or she is 'Histio' tested and the results published via the club. That really is the Kennel Club supporting the breed club! Only twenty six miles away across the channel but can you imagine that happening here anytime soon, although to be fair to the Kennel Club the structure of the system under the FCI governance in many ways makes such things easier to facilitate. With such support the scientists and Antagene have now moved things on to where there is the chance for the breed to begin to turn the tide against this cruel unforgiving disease.

In essence, no one is claiming this test is yet the finished article, no one is claiming it will eliminate all our 'Histio' woes in a generation, no one is claiming it is anything it isn't and the creators and providers of the test are all very honest about it's current limitations and real meaning and are working to improve the test and the way it can be used.

'Histio' is the single biggest serious health issue for our breed and this test is currently our only weapon to fight back with. The test in it's current form is of value for the breed if people engage with it and there are potential future improvements that will boost it's benefit to our breed much, much further. All of these potential improvements would be able to use existing test data, so waiting for possible future developments is no reason not to test now.

So, in summary the, what seems to me totally ***obvious***, logic chain goes something like this.

FACT - Cancer is, by a massive distance, the biggest killer of Bernese Mountain Dogs and has been for decades accounting for over two thirds of Bernese in the UK on current figures.
FACT – Despite certainly being under diagnosed the most prevalent and serious cancer recorded as affecting our breed, is 'Histio'.
FACT – There is no treatment or cure
FACT - The only way we can decrease it's impact on our breed is to prevent it occurring in the first place
FACT – 'Histio' has a PROVEN genetic aspect.
FACT – The good news about a genetic aspect means that with correct guidance the incidence of the disease can be reduced with good breeding practices
FACT – There is a test that can give an estimation of the *likelihood* of any individual dog passing on, or developing, 'Histio'.
FACT – If every breeder used the test AND acted appropriately on it not only would they have a *better chance* of not producing affected dogs for their own lines and puppy buyers but the overall state of the breed could only improve.
FACT – The nature of 'Histio' means that the test *cannot* give *definitive* results for individual dog's or combinations of dogs but it is proven to give *meaningful* results. In time these results ***will*** become better and better but as a breed it is all we have at the moment to improve our situation.

IMPORTANT POINTS OF NOTE – It is *absolutely not* the intention here to say to breeders that 'Histio' testing should always be *the* single most important factor in breeding considerations and should simply override everything else.
Neither is it the intention to say only use 'A' grades in breeding, this is just not practicable or feasible for several big common sense reasons and would not be in the best overall interests of the breed. The use and application of the test is just to say that consideration should be given to Histio alongside everything else and for the time being try to avoid mating 'C' to 'C' or, logically extending that principle, also avoid 'C' to untested.
Lastly no-one is saying simply do not use any 'C' rated dogs and Antagene and the University of Rennes researchers are the first to say this, but as a responsible breeder just try to be careful when you do, especially if there are more 'C' rated dogs closely related to that dog. The current 'Histio' test is completely about not using 'C' with 'C' and definitely NOT about not using 'C' at all. 'C dogs' are far too large a proportion of the gene pool to discard completely.

IF YOU ARE A BREEDER – this is absolutely about *your* dogs and *your* breeding. It is about following up your puppy sales and looking for repeated occurrences of early deaths and 'vague cancer diagnoses' or unknown but terminal conditions in your lines, even if 'Histio' is not specifically mentioned. It is about being honest to yourself and your lines and your future puppy owners.

It is not necessarily about telling me or the club or the KC or the world generally about any issues you may have in your dogs but at least opening up to them for ***yourself*** and then being prepared to begin to address them. This is not an easy step from the mind set some appear to have now of just ignoring the issue. For me, we have an elephant in the room scenario and until a few more people are willing to admit to themselves that the breed has a problem and accept that their dogs are actually a part of the breed and therefore could well be a part of the problem we cannot make any real widespread progress. This is a vital principle for the owners and most importantly breeders to absorb. All our dogs today are a part of the problem which is bad news but the good news is this means we and all our dogs are a part of the solution by using and sensibly applying the test.

IF YOU ARE A PUPPY PURCHASER – Whether first time Bernese buyer or seasoned owner, you too have a part to play in this, by asking the breeder about 'cancer' testing when you are looking at any potential puppy. You will be encouraging breeders to take it seriously and helping to establish the 'Histio' test in the modern psyche of the breed, it will make it harder for people to ignore it. Older dogs may not be scored but as outlined in this article there is no good reason why any parents of puppies should not be 'Histio' tested now in order to avoid 'C to C' matings. It is true this will not give you any cast iron guarantees about the long term health outcome of your puppy but even the most sceptical people surely cannot just ignore the growing evidence from the test validation outlined in this article and will have to admit it will improve your chances.

10] Conclusion

We have this horrible problem in our breed and Histio will not go away unless we tackle it but we now have the means to begin to *do something* about it.

It is perhaps just worth mentioning that it is possible to become too embedded in the depressing news when discussing Histio and it's effect on the breed but I would remind every reader that many Bernese, whatever their 'Histio' grading might be, will have healthy and reasonably long lives. We should not allow the gloomy aspects to depress us but neither should we let that stop us from investigating with a view to improving matters. We have to enjoy all the good positive aspects of the breed we love and stay pragmatic about the not so good news but make decisions to address things that can be addressed.

So, please, please, please consider use of the test in your breeding stock and abide by the results whenever possible, at least don't double up on 'C dogs'. It may currently be difficult to find 'A' scored dogs, especially when taking other breeding considerations into account as well, but if people can start to use the test properly then this should slowly get easier in time as the percentage of 'A' dogs is bound to increase. It is not the only thing to consider in breeding choices but it should be high up in the priorities for anyone who truly cares about the breed and especially those using lines which have had a number of early or middle aged deaths in them. The more people use the test and act upon it the better the test will become and the easier it should become to find 'A' tested dogs in the future. The HSIMS development will be a great step forward *when* it comes but that will only build on the testing that as already been done so the future promise of this is not a reason to delay beginning to fight back now.

We have been given this tool to begin to improve our breed now and, whilst it may currently be something of a blunt tool, it is still a valuable tool so, as owners and especially as today's breeders with responsibility for improving the breed for the future, it is up to us to use it.

It appears to be a part of the fabric of our love for the breed in the UK to just accept all cancers as a price we, and of course more importantly, the dogs, have to pay. The time has come to move on from this culture of acceptance and begin to proactively do something about it. It can only be up to YOU as a breeder to do *your* bit for your own dogs and the right thing for the breed.