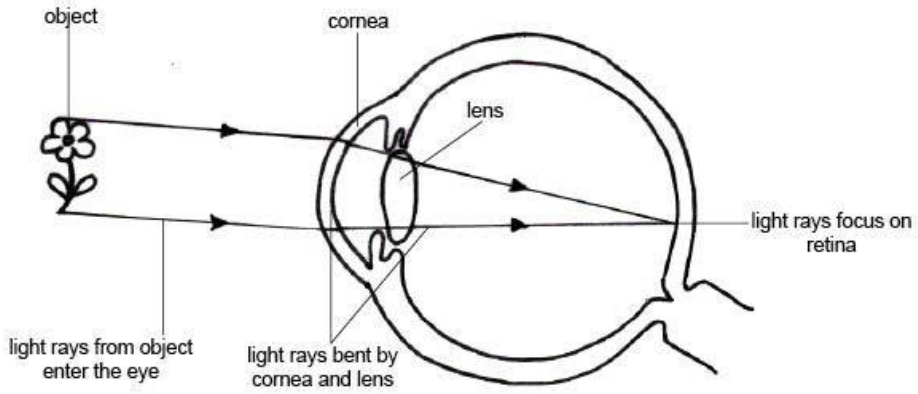
LIFTING THE GENETIC BURDEN
PRIMARY LENS LUXATION in MINIATURE BULL TERRIERS

Primary Lens Luxation (PLL) is a serious health condition affecting the eyes of many Miniature Bull Terriers. It is of great concern as it has a genetic origin and, because the effects (pain, swelling and blindness) only appear after a number of years, afflicted individuals have often already produced offspring by the time they are diagnosed, and so have passed these faulty genes onto the next generation.

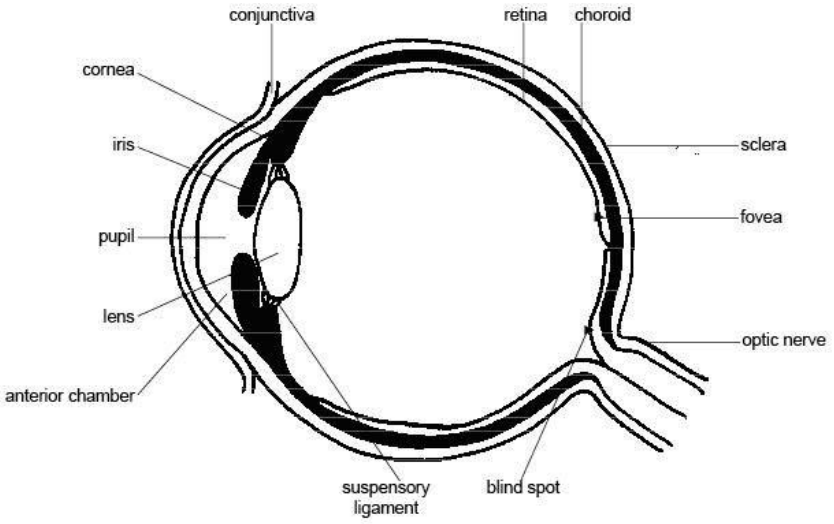
Unfortunately, PLL is rife in the worldwide Miniature Bull Terrier population and this has threatened the existence of the breed in the past in the U.K., and been responsible for failed and delayed attempts to establish the breed in other countries. All of this changed in September 2009, when a team of international scientists led by Dr Cathryn Mellersh identified the mutation causing PLL. This opened the door for the development of a DNA test (which was available by the next month) and at last, there was the opportunity to avoid breeding with PLL-affected dogs before they presented symptoms, and to avoid seemingly normal carriers from producing puppies that would go blind.

The eye is a fairly simple sensory organ which functions in the following way.



Light reflected off the observed object, enters the eye and is focused by the lens on the retina at the back of the eye. This stimulus is sent to the brain via the optic nerve where it is interpreted as a visual image.

The eye has the following basic structure:



Central to the eye is the lens, a transparent, convex structure made of connective tissue, which focuses the light entering the eye on the photo-sensitive retina at the back of the eye. The lens is held in place by suspensory ligaments (also known as zonules) just behind the pupil, which is a hole in the coloured part of the eye known as the iris. In front of the lens, iris and pupil is a front (anterior) chamber or space filled with a watery substance known as the aqueous humour. Behind the lens is a back (posterior) chamber or space filled with a more jelly-like substance known as the vitreous humour. These liquids exert a hydrostatic pressure inside the eye enabling it to maintain its spherical shape.

Lens luxation is the name given to a movement of the lens into an incorrect position in the eye. It is caused by deterioration or damage to the zonules so that they are unable to hold the lens properly or in the correct position. If the lens is still held by some zonules and has moved just a little out of position it is said to be sub-luxated. If the lens is no longer held by any zonules it is fully luxated. Lens luxation is called Primary Lens Luxation if it is the first thing to go wrong with the eye. Primary Lens Luxation can either be caused by degeneration and breakage of the zonules which are supposed to hold it in place, or by an injury to the eye which damages the zonules. Other eye afflictions, for example infection, inflammation, a tumour or glaucoma, can damage the zonules and cause the lens to move out of position. This is known as Secondary Lens Luxation. In the case of predisposed breeds of dog, the Primary Lens Luxation is an inherited condition whereby the gene that codes the protein that the zonules are made of is faulty, so the zonules are not strong enough and degenerate and break, causing luxation.

Many breeds of dog are affected by PLL e.g. Jack Russell and Parson Russell Terriers, Fox Terriers, Scottish Terriers, Welsh Terriers, Sealyham Terriers, Skye Terriers, Manchester Terriers, Tibetan Terriers, Cardigan Welsh Corgis, Lancashire Heelers, Border Collies, Australian Cattle Dogs, Brittany Spaniels and of course, Miniature Bull Terriers. PLL in these breeds is believed to be caused by a gene mutation but not all in the same part of the DNA. Carriers of the gene may suffer from the condition or they may not, but they all can pass the condition on to their offspring. As the gene causes the zonules to weaken or break, they can no longer hold the lens in the correct position so the lens shifts position. It may move forward into the anterior chamber, in which case, if treatment is sought quickly it can be surgically removed. This procedure, if done in time, can save some sight in the eye for the animal. The lens may move backward into the posterior chamber, in which case, it is very difficult to surgically remove it. If the displacement is not too severe and it is still near to the iris, medical eye drops can be used to maintain a small enough pupil to trap the lens close to the iris. If the lens moves too far into the back of the eye there is risk of it damaging the retina. Both anterior and posterior luxation can cause glaucoma which is increased pressure in the eye. Glaucoma is an extremely serious condition which, if left untreated for even as little as six hours, can result in permanent damage to the retina of the eye and the complete loss of sight. Interestingly, if glaucoma can be avoided, dogs that have had both lenses removed can still see well enough to live normal lives. The cornea is able to focus light sufficiently for the brain to compensate and interpret; such that, in some cases the animal appears to suffer no loss of sight at all.

The symptoms of PLL are pain (seen by rubbing or pawing at the eye which can also cause redness and swelling), tearing or watering of the eye and loss of sight. Sometimes, the eye can appear asymmetrical or cloudy. Any change in eye appearance should be followed up immediately with a veterinarian. PLL should be considered a medical emergency as treatment in the first 24 to 48 hours can prevent the damage that can cause permanent blindness. Unfortunately if a dog of a predisposed breed develops PLL in one eye, it is almost certain that the other eye will also become affected soon afterwards.

Inherited PLL tends to appear only at the ages of 4 to 7 years. This was a big problem in the past, as in most cases, these animals would have already been bred and produced offspring. It was with great relief and jubilation that the Miniature Bull terrier enthusiasts welcomed the news that after many years of research, the gene mutation causing this problem had been identified. The Animal Health Trust and Orthopedic Foundation for Animals rapidly designed a genetic test for it to identify carriers before they produce any

offspring. A cheek swab sample is taken and analysed for the presence of the gene mutation and the possible results of the DNA test are:

PLL CLEAR - this dog has two copies of the normal gene and will not develop Primary Lens Luxation as a result of the mutation being tested for;

PLL CARRIER - this dog has one copy of the mutation and one normal copy of DNA, is unlikely to develop Primary Lens Luxation but may pass the mutation onto their offspring;

PLL AFFECTED - this dog has two copies of the mutation and is at risk of developing Primary Lens Luxation. This dog will definitely pass the mutation on to all of its offspring.

At present, these two international institutions are conducting the DNA test for PLL – the Animal Health Trust (AHT) in Suffolk, U.K. (Bryan.mclaughlin@aht.org.uk) and the Orthopedic Foundation for Animals (OFA) in Missouri, .S.A (ofa@offa.org). The test procedure is simple. A test kit can be requested via email from anywhere in the world. The test kit is posted out and once received, a qualified vet has to oversee a simple cheek swab procedure and verify the identity of the dog. The samples are mailed back to the test facility and the results are emailed two weeks later. Puppies can be tested as soon as they are weaned i.e. around three weeks and so the results can be known before they are old enough to leave their mother. A printed certificate with a unique test result number is posted out afterwards. So far, of all the Miniature Bull Terriers tested by these two facilities, nearly 65% of the population worldwide are carrying at least one copy of the abnormal gene!

The existence of the DNA test has enabled scientists to prepare guidelines for breeders of Miniature Bull Terriers. It is recommended that PLL-affected dogs are not used in breeding programmes at all. Even though a PLL-affected dog when bred with a PLL-clear dog can produce a litter of PLL-carriers, these carriers seem to be at a higher risk for PLL with a number of such dogs actually developing PLL too. Although it should not be allowed to breed two PLL-carriers because of the one in four probability of a PLL-affected dog, PLL-carriers from this type of mating are also at a higher risk of developing PLL themselves. The only acceptable matings are those between a PLL-carrier and a PLL-clear or two PLL-clears. Of course this has raised the concern of reducing an already small gene pool as only 35% of the world's Miniature Bull Terriers are clear of PLL but a healthy, small gene pool is more important than a large, unhealthy gene pool.

Primary Lens Luxation has been known for more than a hundred years but it is interesting that the gene mutation is not present in Standard Bull Terriers. As a desperate measure to combat PLL in the past, interbreeding of Standard Bull Terriers to Miniature Bull Terriers was approved by The Kennel Club under strict rules. One of these rules was that all the offspring must be registered as Miniature Bull Terriers in order to protect the Standard Bull Terrier gene pool. Unfortunately interbreeding did little to reduce the occurrence of PLL. All that it ensured was that in the first generation no afflicted dogs would be produced. As soon as this generation reproduced though, the odds on an afflicted puppy were present again. The discovery of the gene mutation causing this awful malady and the subsequent DNA test to detect it, is a turning point in the history of the Miniature Bull Terrier breed. At last we can responsibly manage and eliminate the mutation over time and protect our breed from this age-old genetic burden.

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