LEARNING THE HARD WAY Linda Skerritt

HANDS UP if you think you understand about Primary Open Angle Glaucoma. Until early 2016 I thought I did but then I learned more – the hard way. I knew that, after 1996 when a PBGV imported from France into England was tested and found to have POAG, there followed intense effort and liaison between the Basset Griffon Vendéen Club, Peter Bedford, Professor of Veterinary Ophthalmology, and the Animal Health Trust in researching and attempting to eradicate this eye disease from the breed. Regular eye testing played a large part not only in the UK but in many other countries.

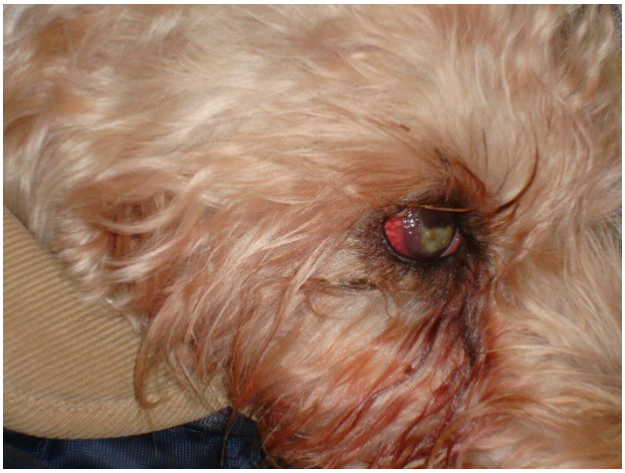
Eighteen years on, late 2014 we were all elated when the Animal Health Trust announced they had finally identified the causal mutation. Validation experiments followed and, amidst great excitement, swab test kits for DNA testing were available to owners for the first time at Crufts, March 2015. I was amongst those who took up this early opportunity to have my PBGVs' DNA checked. One of them was our 10yr old Monkhams Fortune Cookie, a Danish and English Champion and litter sister of Famous Grouse, aka Fabio, who had an outstanding show career in the States. Her test certificate showed her to be a Carrier.

Just 9 short months later I became concerned about Cookie's eyes and, on Christmas Eve, I took her to my vets. The diagnosis was "She has Glaucoma". I declared "SHE CAN'T. She has had a DNA test and the certificate said:

Explanation of terms:
CARRIER: The dog has one copy of the normal gene and one copy of the mutant gene that causes POAG. It will not develop POAG but will pass on the POAG gene to 50% (on average) of its offspring.

Cookie was prescribed Xalatan (Latanoprost) which she needed urgently but Christmas Eve wasn't the best time to get any. Fortunately a good friend living nearby had some for one of her own PBGVs and let me have a bottle so I could try and help her straight away. But I tortured myself over the coming days as, had I suspected that Cookie might be suffering from POAG, I would have taken her to the vets long before.

Early in the new year, Cookie stayed at the vets all day for a check on her eye pressures to see whether the eye drops made any appreciable difference. 9am R – 38, L – 57, Xalatan drops then applied; 11am R – 35, L – 60; 12.30am R – 44, L – 54; 1.30pm R – 29, L – 50. Two days later, I took her to see Professor Peter Bedford, who confirmed chronic bilateral Glaucoma. She was by then blind and he documented that this was pretty much end stage. He undertook to discuss with the AHT.



By tragic coincidence, at the same time Cookie's health deteriorated badly. Her kidney and liver function went down, she had a urine infection, her blood cell count was also down and a mammary tumour started to grow. I got in touch with the AHT asking how I might help their researches when I knew she didn't have long to live. I steeled myself and tried to arrange removal of Cookie's eyes for the AHT but timing was against this as my vets only had a skeleton rota of staff over the weekend. The best I could do was to send further cheek swabs and, following her rapid deterioration, I asked the vet to draw blood before putting her to sleep on January 8 2016.

Four months later the AHT let me know that Cookie's DNA was about to be sequenced again – all 2.4 billion letters of it. It would be analysed over the coming months and they hoped to shed light on the cause of her Glaucoma. Just before Christmas 2017, two years after Cookie's Glaucoma had been diagnosed, I received an interim update and then the AHT let me know their findings:

"We've sequenced Cookie's whole genome and looked for different mutations in genes associated with canine glaucoma and lens luxation. Our analysis for the remainder of the genome hasn't thrown out any other provocative candidate mutations. Basically there is currently no firm evidence that Cookie's glaucoma was the direct result of an alternative mutation which would suggest there is a different form of POAG in her breed which has yet to be determined genetically. Of course, should we identify alternative canine glaucoma mutations we will test Cookie's DNA for them, and if more PBGV Carrier cases come to light then we will re-visit our investigation.
If there is anything further we can report then we'll certainly inform you, especially if it's a significant finding".

During this stressful time, when the AHT asked for DNA samples of PBGVs that were healthy, over 7yr olds, I sent them swabs for our Ch Monkhams Dixie Chick. On July 12 2016 they acknowledged receipt and assured me that the sample would be included in their research programme. The following April I received a test certificate letting me know that Dixie was also a Carrier. However, the Explanation of Terms was far more helpful:

Date: April 6th 2017

Explanation of terms:

CLEAR:	This dog has two copies of the normal gene and will not develop this form of glaucoma, although we cannot exclude the possibility they might develop glaucoma due to other causes, such as trauma or the effects of other, unidentified mutations.
CARRIER:	This dog has one copy of the normal gene and will not develop this form of glaucoma, although we cannot exclude the possibility they might develop glaucoma due to other causes, such as trauma or the effects of other, unidentified mutations. However if bred from, will pass on this mutation to, on average, 50% of all offspring.
AFFECTED:	This dog has two copies of the POAG mutation and will almost certainly develop clinical signs at some stage during their lifetime assuming they live to an appropriate age. They will pass on one copy of the mutation to all offspring.

The new Canine Genetic Testing centre in Cambridge has thankfully now risen from the ashes of the Animal Health Trust and is once more offering a test for POAG. The wording on their website is specific:

Find out if your Petit Basset Griffon Vendeen could develop Primary open angle glaucoma (POAG) caused by ADAMTS17 at CAGT.

They qualify this by explaining that POAG is not painful in its early stages and the slow progression of this disease means that often owners are not aware their dog is affected until they notice eyes have become enlarged (due to the increased pressure) or a vision problem becomes noticeable. POAG is progressive however and the continued rise in intra-ocular pressure will eventually lead to pain and blindness.

And the DNA test certificates now being issued clarify that the test relates to POAG-ADAMTS17. The Explanation of DNA Test Result is more helpful, warning that they cannot exclude the possibility that POAG may develop due to other mutations not detected by this particular test.

DNA Test Result: CLEAR

Explanation of DNA Test Result

"Clear" dogs have two normal copies of DNA. Clear dogs will not develop primary open angle glaucoma as a result of the POAG-ADAMTS17 mutation, although we cannot exclude the possibility they might develop primary open angle glaucoma due to other mutations they might carry that are not detected by this test.

Whereas PBGVs have an inversion mutation in ADAMTS17 intron 12, there are other similar ADAMTS mutations such as:
ADAMTS10 exon 9. Mutation leads to Glaucoma in Norwegian Elkhounds.
ADAMTS10 exon 17. Mutation leads to Glaucoma in Beagles.
ADAMTS17 exon 11. Mutation leads to Glaucoma in the Basset Fauve de Bretagne.
ADAMTS17 exon 2. Mutation leads to Glaucoma in Basset Hounds.

This in itself points to there being similar mutations which might emerge other than the one already detected in the PBGV.

Over the years since Cookie developed POAG, I have heard of a couple of other PBGVs in other countries who had suffered the same fate and I became aware that, in another breed, a similar situation had cropped up in the early 2000s. Research showed there was more than one strain of the identified eye problem (Progressive Retinal Atrophy), so the DNA test was amended and general eye testing continues to this day.

We cannot therefore become complacent. While it is indeed wonderful to have this DNA test I hope that, in some small way, Cookie has played a part in helping owners to understand that they can't assume their PBGV's eyesight is safe once the DNA test has confirmed they are either Clear or a Carrier. Everyone needs to continue to eye test as there are other diseases that might be detected, especially as your loved Petit gets older. Picking up any problem early will help your PBGV by allowing for early treatment and also prevent it becoming an issue for the breed in the future.