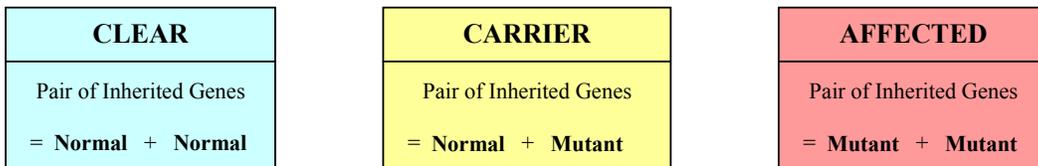# AN EXPLANATION OF HOW SOME GENETIC DISEASES
(SUCH AS GPRA & FUCOSIDOSIS)
ARE INHERITED IN THE ENGLISH SPRINGER SPANIEL

- All of the genes inherited by dogs are contained within 39 different sets of chromosomes.   There are thought to be between 20,000 – 30,000 different genes.
- Any chromosome between number 1 and 38 is called an *autosome*.   The 39th chromosome determines the sex of the dog.
- The genes responsible for diseases such as **GPRA** and **Fucosidosis** are inherited as what is known as an ***Autosomal Recessive Trait***.
- Chromosomes (and therefore genes) are inherited in pairs, with one copy of each chromosome being inherited from each parent, making up the total of 39 pairs.
- With all diseases that are inherited as simple autosomal recessive traits, every dog can be classified **genetically** in one of three ways (using GPRA as an example, but the same applies to other diseases which are inherited in a similar way, such as Fucosidosis):

> ❑ **CLEAR** This means that the dog has TWO NORMAL COPIES of the gene for GPRA.   A CLEAR dog will not, therefore, suffer from the disease, neither can it pass on the faulty (mutant) gene to its offspring. **It is both <u>clinically</u> and <u>genetically</u> CLEAR.**

> ❑ **CARRIER** This means that the dog has ONE NORMAL COPY and ONE FAULTY (MUTANT) COPY of the gene for GPRA. A CARRIER will not itself suffer from GPRA, but will pass on the mutant gene to approximately half of its offspring. **It is <u>clinically</u> clear, but is <u>genetically</u> a CARRIER.**

> ❑ **AFFECTED** This means that the dog has TWO FAULTY (MUTANT) COPIES of the gene for GPRA. These dogs will be <u>**genetically**</u> **AFFECTED** (even though they may show no *clinical* signs of GPRA) and **they will <u>always</u> pass on the mutant gene to their offspring.**

The three types of genetic status described above are illustrated in the following diagrams:

CLEAR	CARRIER	AFFECTED
Pair of Inherited Genes	Pair of Inherited Genes	Pair of Inherited Genes
= **Normal + Normal**	= **Normal + Mutant**	= **Mutant + Mutant**

- When two dogs are mated, the puppies inherit one copy of each gene from each parent, resulting in a number of possible combinations depending on the genetic status of each parent.
- The following diagrams illustrate the possible results from each different combination of matings.
- The results show what will happen *'statistically'*, or *'on average'* with each combination of mating.   For example, if two carriers are mated together, *statistically* a quarter of the litter will be genetically CLEAR, half of the litter will be genetically CARRIERS and the remaining quarter will be AFFECTED.

- **Any one individual mating can vary enormously from the statistical averages – this is where the element of 'chance' comes into it, rather like the tossing of a coin. For example, a litter of 8 puppies should, *statistically*, be made up of 50% dogs and 50% bitches. Yet we all know that in any one litter, this can vary greatly, and it is perfectly possible to have a litter containing 8 dogs and no bitches, or vice versa. On average, though, over the course of thousands of litters, the numbers would even out in line with the statistical probabilities, and the same is true of genetically inherited diseases.**

- The following diagrams, therefore**, show what CAN and WILL happen** *statistically***, and they illustrate the 'risks' involved with each type of mating.**

- **The *matching* pairs of coloured arrows show each possible combination of genes that can be inherited by each puppy from its parents for each different type of mating, and the genetic results.**

1. The first diagram illustrates what happens **when two genetically CLEAR parents are mated together:**
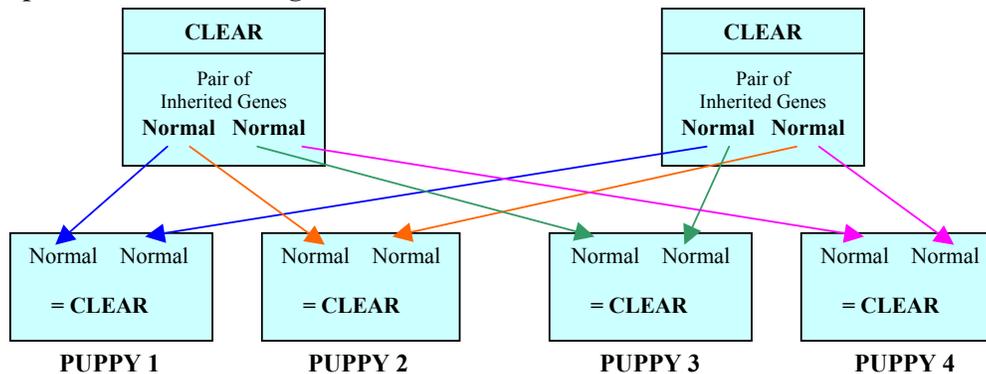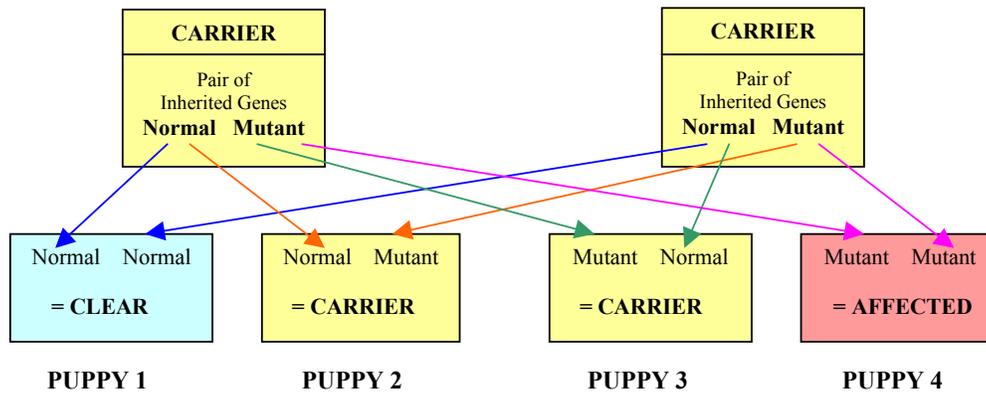

The above example shows that, whatever combination of genes each puppy inherits, because both parents are CLEAR, only normal copies of each gene are available for inheritance. Therefore every puppy will automatically inherit TWO NORMAL COPIES, making it genetically CLEAR.

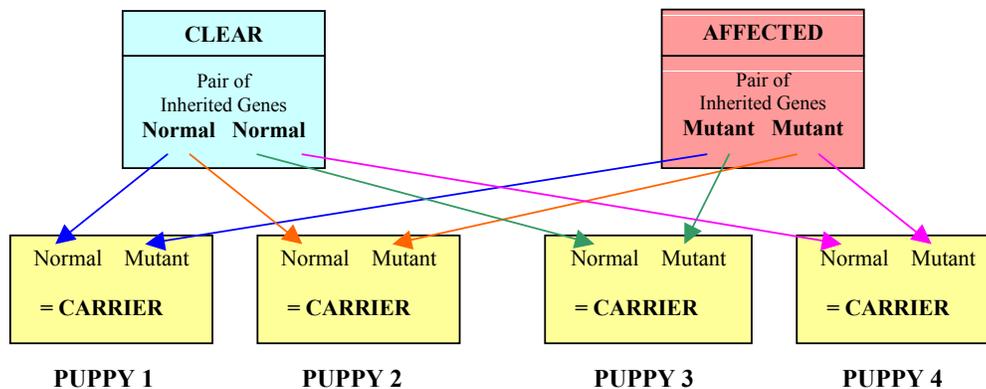2. The second diagram illustrates what happens **when a CLEAR is mated to a CARRIER:**
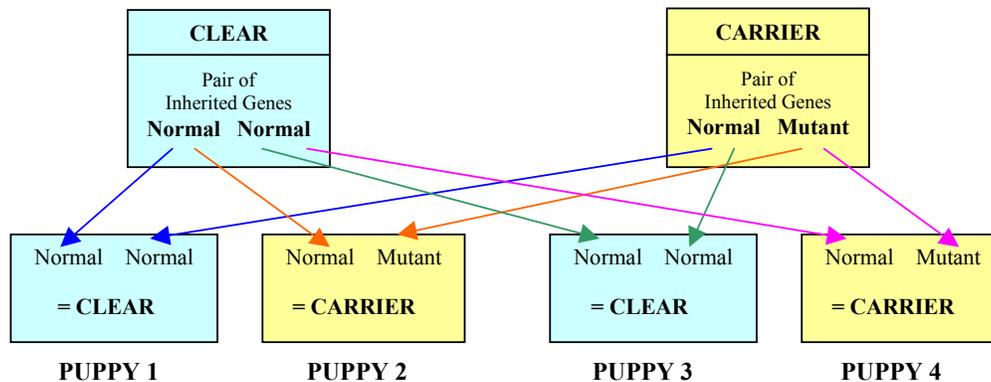
This example shows that when a CLEAR is mated to a CARRIER, statistically half of the litter will be CLEAR (having inherited TWO normal copies of the gene), and half the litter will be CARRIERS (having inherited ONE normal copy and ONE mutant copy).

3. The third diagram illustrates what happens **when a CARRIER is mated to another CARRIER:**

CARRIER	CARRIER
Pair of Inherited Genes **Normal Mutant**	Pair of Inherited Genes **Normal Mutant**

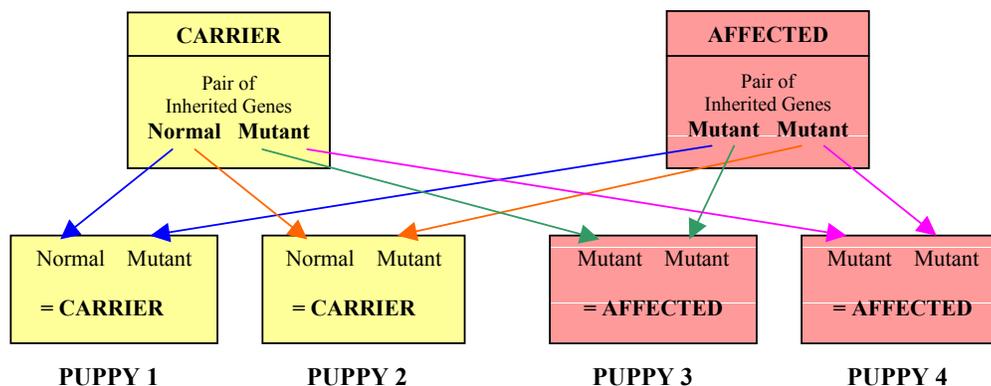| Normal Normal = CLEAR	Normal Mutant = CARRIER	Mutant Normal = CARRIER	Mutant Mutant = AFFECTED
PUPPY 1	**PUPPY 2**	**PUPPY 3**	**PUPPY 4**

This example shows that when TWO CARRIERS are mated together, statistically half of the litter will be CARRIERS (having inherited ONE normal copy of the gene and ONE mutant copy), a quarter will be CLEAR (having inherited TWO normal copies), and a quarter will be AFFECTED (having inherited TWO mutant copies).

4. The fourth diagram illustrates what happens **when a CLEAR is mated to an AFFECTED:**

CLEAR	AFFECTED
Pair of Inherited Genes **Normal Normal**	Pair of Inherited Genes **Mutant Mutant**

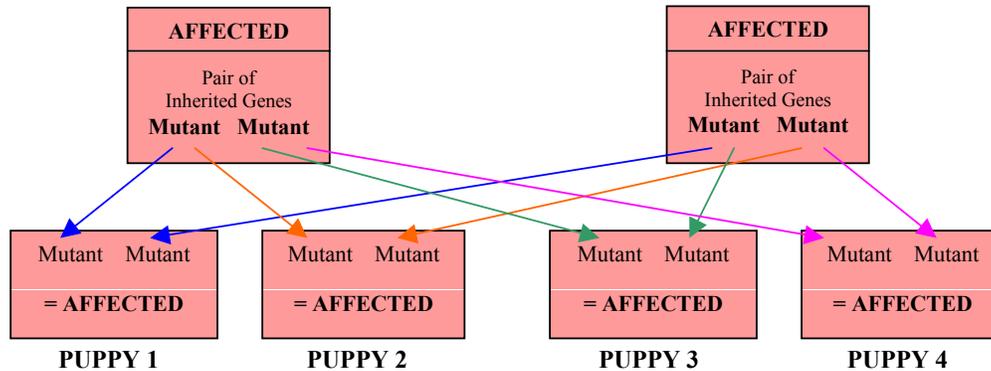| Normal Mutant = CARRIER	Normal Mutant = CARRIER	Normal Mutant = CARRIER	Normal Mutant = CARRIER
PUPPY 1	**PUPPY 2**	**PUPPY 3**	**PUPPY 4**

This example shows that when a CLEAR is mated to an AFFECTED, **all** the puppies will be CARRIERS, having inherited ONE normal copy of the gene from the CLEAR parent and ONE mutant copy from the AFFECTED parent. Note that ALL the offspring of an AFFECTED parent will automatically be at least CARRIERS even if mated to a CLEAR.

5. The fifth diagram illustrates what happens **when a CARRIER is mated to an AFFECTED:**

CARRIER	AFFECTED
Pair of Inherited Genes **Normal Mutant**	Pair of Inherited Genes **Mutant Mutant**

Normal Mutant = CARRIER	Normal Mutant = CARRIER	Mutant Mutant = AFFECTED	Mutant Mutant = AFFECTED
PUPPY 1	**PUPPY 2**	**PUPPY 3**	**PUPPY 4**

This fifth example shows that when a CARRIER is mated to an AFFECTED, statistically half the litter will be CARRIERS (having inherited ONE normal copy of the gene from the CARRIER parent and ONE mutant copy from the AFFECTED parent). The other half of the litter will be AFFECTED (having inherited TWO mutant copies, one from each parent).

6. Finally, the sixth diagram illustrates what happens **when two AFFECTED dogs are mated together:**

AFFECTED	AFFECTED
Pair of Inherited Genes **Mutant Mutant**	Pair of Inherited Genes **Mutant Mutant**

Mutant Mutant	Mutant Mutant	Mutant Mutant	Mutant Mutant
= AFFECTED	**= AFFECTED**	**= AFFECTED**	**= AFFECTED**
PUPPY 1	**PUPPY 2**	**PUPPY 3**	**PUPPY 4**

This example shows that when two AFFECTED dogs are mated together, all the puppies will inherit TWO mutant copies of the gene and they will therefore ALL be genetically AFFECTED.

WHAT DOES ALL THIS TELL US??

➢ **Fundamentally, this tells us that AFFECTED dogs CAN be produced from THREE possible matings:**
   a) **CARRIER TO CARRIER**
   b) **AFFECTED TO CARRIER**
   c) **AFFECTED TO AFFECTED**

➢ **It also tells us that AFFECTED dogs can NEVER be produced PROVIDED at least ONE parent is genetically CLEAR.**

   To break this down even further:

➢ When two genetically CLEAR dogs are mated together, **all** the resulting offspring will be genetically CLEAR. When two genetically AFFECTED dogs are mated together, **all** the resulting offspring will be genetically AFFECTED.
➢ When mating a genetic CLEAR to a genetic CARRIER, **no** AFFECTED dogs will be produced, but, *statistically,* **half** the litter will be CARRIERS.
➢ When two CARRIERS are mated together, *statistically,* **half** the litter will be CARRIERS and a **quarter** of the litter will be AFFECTED.
➢ The offspring of AFFECTED dogs will **all** automatically be CARRIERS at the very least, even when mated to a CLEAR dog.
➢ The parents of AFFECTED dogs will **both** automatically be CARRIERS or AFFECTED.

❖ *A Code of Ethical Guidelines* in respect of Fucosidosis has been agreed by all the UK ESS Breed Clubs in an effort to give guidance to breeders on how best to eliminate the risks of breeding affected dogs, whilst still breeding for quality, type and temperament. It is intended to agree a similar code with regard to GPRA following the availability of a DNA test for this disease.

❖ **Further information is available from the HEALTH CO-ORDINATORS:**
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   Louise Scott: Tel: 020 8427 3396   Email: louise@goldcliffe1.freeserve.co.uk