

## The Pox of the Popular Sire by Carol Beuchat PhD

The most common admonition of the geneticist to the dog breeder is to "avoid the Popular Sire Syndrome". At the same time, the most common advice from breeder to breeder is to breed "the best to best". So the conundrum is obvious and the consequence predictable - the "best" dogs are the most sought after, so they sire the most offspring and become popular sires.

### The Popularity of Popular Sires

Even a century ago Williams Haynes (1915) was writing about the "Effect of the popular sire", noting that in three terrier breeds that he examined - Irish Terriers, Scottish Terriers, and Fox Terriers - about 40% of the puppies were sired by only 20% of the sires. Back then, "popularity" was quite different than now - his "prolific" dogs sired 5-7 litters, which would be completely unremarkable today. And surprisingly, the point of Haynes' paper was that Popular Sires actually benefited the breed by contributing to the preservation of variability in type.

*"Superficially it might appear that if approximately 40% of the puppies each year are sired by but 20% of the stud dogs this would eventually result in the greatest uniformity of type. The selected sires are all to a greater or lesser degree exceptional animals, but they are not selected by any uniform system. Most of them excel in some particular physical point, but they do not excel in the same points or in the same degree, nor even, in some cases, in the same direction. Here the personal equation, the ideals of different breeders, is at work, and the result is that since a few males not themselves of uniform type sire a greater-than-average number of offspring they disturb the race average of the following generation and introduce abnormal amounts of variation. The fact therefore, that artificial selection gives to certain selected, but not uniform, males an undue preponderance of influence must always keep the type of domestic animals in an unstable state. This seems to me an important factor in the great variability always noted among domesticated breeds."*

Haynes thought Popular Sires were a good thing, because he thought they were sufficiently different from each other that they prevented the breed from becoming too "uniform". How then did the popular sire go from contributing to the quality of the gene pool in 1915, to the source of a problem to be avoided by breeders 100 years later? What is this "syndrome" that today's geneticists are so concerned about?

### Breaking Bad: DNA

To understand the problem, you must understand a bit of genetics. You probably know about mutations - bits of DNA that are not replicated perfectly or are perhaps damaged by some environmental toxin. If the mutation is dominant and affects some vital process, it is removed from the gene pool by natural selection when that individual fails to pass its genes on to the next generation successfully. But many mutations have no ill effects because their paired, dominant allele functions normally. These "recessive" mutations are silent in the genome and can be passed to the next generation the same as any other gene, and as long as the offspring has a copy of a normal allele the mutation remains silent. The mutation becomes a problem when an individual inherits two copies so is homozygous at that locus. Without at least one copy of the normal, unmutated allele, the gene does not function properly, and the consequence can range from something relatively trivial (e.g., a different eye colour, or slightly shorter legs) to the catastrophic (e.g, blindness, disruption of a critical biochemical pathway, cancer).

Mutations happen all the time. The ones with immediate ill effects are removed from the gene pool by natural selection, while the recessive, silent ones remain in the genome as the "genetic load". Every dog - in fact, every organism - has its own unique collection of damaged alleles that causes no harm as long as there is also a copy of a normal allele of each that can do the job it is supposed to.

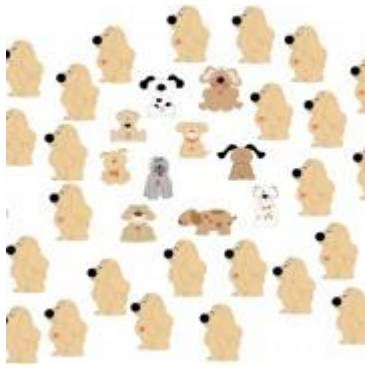
### A Star is Born

Now consider what happens in a population of purebred dogs. Let's pretend that this cute collection of dogs represents your breed, with the phenotypic variations among them representing the nuances of type that would be obvious to a serious breeder.



We've given each dog a (typographic) recessive mutation, a bit of DNA damage that is not expressed so it has no detrimental effect on the dog. If each dog in our population has a litter of puppies this year, the frequencies of these various alleles in the population will stay about the same in the next generation.

But what happens if one of these dogs wins big at an important event and becomes a star? If it's a bitch, she will have a litter of much sought-after



puppies, and it will probably be at least a year before she is bred again. But if our star is male (let's call him "Hank"), he will be bred many times and produce dozens (or more!) puppies in a single year. Hank will pass half of his genes, both good and bad, to each of his offspring, so many copies of his recessive, silent mutations get distributed in his puppies.

As long as Hank's deleterious mutations are paired with a normal allele in his puppies, they are not expressed and cause no ill effects. But if you could view the gene pool of the breed in the new generation, you would see that now it is markedly different. Hank's mutation has in just a single generation gone from being rare to common, and now lurks silently in the genomes of dozens of his offspring. In this generation, no-one is any the wiser. The prized puppies that carry their sire's recessive mutation will appear to be no different than the ones that don't.

### The Next Generation...



But in the next generation we start to see the first hint of trouble. Perhaps there were a few half-sib matings, or father-to-daughter, and some puppies are produced that are homozygous for Hank's mutation. Perhaps the mutation is lethal and these are stillborn pups, or maybe the puppies are born with a disease. But the breeders will be mystified - they have never had this problem in their line, or even in the breed, so maybe it's just bad luck? Nobody can see yet that this is just the tip of the iceberg.

In one more generation, however, the trouble really begins. Carriers produced by the first generation will pass on the mutation to half of their offspring, and half-sib matings or line breedings back to the sire will begin to produce affected puppies. Even while the number of affected puppies is still relatively small, the number of carriers will by now be significant, and remember that our popular sire probably continues to produce more than his fair share of the offspring in each generation. You can see where this is headed. The seeds have been sown.



Every litter produced by this popular sire is one less reproductive opportunity for any of the other potential sires in the breed, so the frequency of genes carried by those unused sires will decline in the population. At the same time, multiple bitches are producing puppies sired by Hank that will be half-sibs to the dozens of other puppies in their generation. The temptation to capture a bit more of that popular sire's star qualities will probably result in a few line breedings that will put carrier with carrier.

### Uh-oh, We've Got A Problem

This is about the time breeders begin to notice that there is a "problem" in the breed. It won't take a pedigree sleuth to trace the growing population of affected dogs back to Hank, our popular sire who will now be blamed for introducing this new disease into the breed. Geneticists will be called in to hunt for the defective bit of Hank's DNA and to develop a reliable test. Then breeders will begin the mission of trying to eliminate Hank's formerly valuable genes from the gene pool, with proportional collateral damage to the genetic legacy of all of the bitches he was bred to. The genetic carnage resulting from attempts to purify the breed of the unfortunate mutation will continue for generations. The ultimate damage to the gene pool can be catastrophic.



This happens over and over again in breed after breed. Of course, the problem isn't poor Hank. Wind back the clock, and if the judge had pointed to a different dog at that fateful show - let's say it was Rosco who got the nod - the trajectory of the breed would have been completely different but the consequences pretty much the same. Rosco will leave his genetic legacy behind in dozens of lovely puppies, half of which will have that one nasty mutation that will emerge a few generations down the road to bite the breed. Breeders will eventually catch on, sound the alarm, and the effort to

identify and eradicate the offending mutation will begin. The gene pool will be purged, and the next time a big winner appears that happens to be male, the cycle will begin anew.

### **The Unfortunate Legacy of the Popular Sire**

The really unfortunate thing about the Popular Sire is that the negative genetic consequences of his popularity don't begin to manifest for generations, by which time the breed already has a really significant problem. The large number of breed-specific disorders known to be caused by a single recessive gene (175 as of this writing; OMIA) is testimony to the prevalence of the problem (indeed, some breeds now suffer from multiple recessive genetic disorders).

Of course, it is not just the recessive mutations that are disseminated widely by popular sires. Any genetic disorder can become quickly widespread, especially in the absence of any means of documenting the appearance of a new disease and if breeders are not willing to be completely transparent about issues they are aware of. Unacceptable aggression in English Springer Spaniels, which used to be one of the most popular family dogs in the US, appears to be genetic and has been traced to one popular sire from a prominent kennel (Reisner & Houpt 2005; Duffy 2008). Twenty-five percent of Bernese Mountain Dogs die at an average age of only 8 years old from histiocytic sarcoma (Dobson), a fatal cancer that apparently originated from a single dog in Switzerland, and the flames were fanned by a prolific great-grandson in the US that spread the malignant genes far and wide in the gene pool (Dobson 2013; Moore 1984; Moore & Rosin 1986). Many Dobermans die at an early age from sudden heart failure caused by dilated cardiomyopathy, which can be traced to seven popular sires in the 1950's, three of which died of heart failure (<http://bit.ly/1anuIN>). A serious - usually lethal - susceptibility of Miniature Schnauzers to infection by *Mycobacteria avium* (referred to as "MAC" for *Mycobacteria avium* complex) is thought to be traceable to a sire popular in the mid-1980s and is found now in dogs all over the world (<http://bit.ly/1gZbGy7>; <http://bit.ly/1ciVxNP>). There are no doubt many other similar examples that have never been documented.

Leroy (2011) has identified popular sires as the single most important contributor to the dissemination of genetic diseases in purebred dogs. Recognizing this, the FCI has issued a recommendation to breeders that no dog should have more offspring (presumably in its lifetime) than equivalent to 5% of the number of puppies registered in the breed during a five-year period, and a number of national kennel clubs have followed suit (e.g., Finland). But without cooperation of breed clubs, or in the absence of some authority that would oversee registrations and be in a position to police such a breeding restriction, it is hard to see how such a recommendation would have any effect at all on current breeding practices. (Which 5-year period? Which population of dogs - the worldwide breed, or just the dogs in your country? Who does the counting - the owner of the sire, the owner of the bitch, the breed club, the kennel club??)

The only people benefiting from the explosion of breed-specific genetic disorders are the molecular geneticists, who have discovered dogs as an ideal research animal because many of the same disorders occur in humans (Ostrander 2012). But as useful and fascinating as dogs might be for their research, I suspect all would prefer to see dogs that are free of genetic disease, for they have so much more to offer in the family home than in the lab.