The analysis of the risk on PMDS.

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Introduction..

Persistent Müllerian Duct Syndrome (PMDS) was diagnosed in the male Basset Hound Jonker Govert v.d.Ravenstee, born in 1989. A male with PMDS has normal male reproductive organs (and is fertile), but also a uterus. This uterus is not connected to a vagina as in females, but is attached to the prostate gland of the male. In some cases of PMDS this uterus is, through the prostate, connected to the urinary tract. In this way urine may reach the cavity of the uterus, which will become infected, causing serious, lifethreatening, illness. PMDS is an inheritable disease. That is why an investigation was started by the Nederlandse Basset Hound Club (NBHC), in collaboration with the Clinic for Pet Animals of the Veterinary Faculty of the University of Utrecht.

Results of the initial investigation.

The investigation is performed by ultrasonography (like a “scan” in pregnant women). After the diagnosis of 25 cases of PMDS it could be ascertained that

a) the disease was inherited in an autosomal recessive way, with its expression restricted to males.

b) in all 25 cases only the female Beacontree Calender was on both sides of any pedigree. Calender was born in England in 1971 and moved to The Netherlands in 1973, and

c) that (unintended) positive selection of PMDS had occurred in the Dutch breeding population. This had resulted in a high prevalence of PMDS in the 1990 Dutch breeding population, which was above 50% of the genes and about 8 times higher than expected from chance alone.

The inheritance.

Autosomal inheritance means that the gene is present in twofold in the DNA. And recessive means that both genes must be in error to bring the PMDS anomaly into expression. When a male Basset Hound carries only one faulty gene, no uterus will be present, but he can pass along that faulty gene to his children. Such dog is called PMDS-carrier. If a female has only one faulty gene, she is also called carrier. A bitch can also have inherited two faulty genes, but we can not diagnose it because bitches do always have a uterus. Therefore, we call such a bitch double-carrier.

The fraction of PMDS-genes.

If a male inherits a faulty gene from both parents, he will develop a uterus and will be called affected (A). We can express that with the socalled gene fraction. Affected males and double-carrier females have a gene fraction of 1.0. Carriers (C) have only one faulty gene and thus a fraction of 0.5. And hounds with two normal genes are called free (F) and have a fraction of 0.0. The (average) gene fraction of children is formed by the average of the gene fractions of their parents.

The breeding protocol.

After the initial study, all potential stud dogs are investigated by ultrasonography. By now, more than 50 affected dogs were diagnosed and excluded from breeding. Affected dogs get a gene fraction of 1.0 with the code A. His parents will both have at least one faulty gene and receive the code non-F (= not PMDS free, at least carrier,

or even affected or double-carrier). Their gene fraction is modified according to the fact that they can not be PMDS-free. If the male parent has been investigated himself and has no uterus, he must be carrier and is denoted as fraction 0.5 code C. If a potential stud dog proves to have no uterus, he gets the code non-A (not affected) and his gene fraction is modified accordingly. All other dogs get as gene fraction the average of their parents gene fractions.

Gene fraction adjustment, how is the fraction modified?.
Suppose a male dog is born with a gene fraction of 0.4, because his parents have fractions of 0.2 and 0.6 respectively. In that case the probability to have two faulty genes (PMDS-affected=A) is 0.2 * 0.6= 0.12 (is 12%) and the probability to have no faulty genes (PMDS-free=F) is (1-0.2) * (1-0.6)= 0.32 (is 32%). Then the probability to have one faulty gene (PMDS-carrier=C) is 1-0.12-0.32= 0.56 (is 56%).

If this dog is examined for PMDS and no uterus is present, we are sure the dog is not affected. So, the probability to be affected has decreased to 0. But he will be either free or carrier and the ratio between their probabilities will remain the same. Further, the probabilities must add up to 100%. This means that the probability to be free becomes 0.32/(1-0.12)= 0.36 (is 36%) and to be carrier becomes 0.56/(1-0.12)= 0.64 (is 64%). The corresponding modified gene fraction is 0.64/2= 0.32. To indicate that the fraction is adjusted to the fact that no uterus was found, we add the code non-A. A dog with the code non-A will always have a gene fraction that is lower than the average of his parents. By consequently using only non-A dogs for breeding, the average gene fraction in the breeding population will therefore decrease in successive generations.

If this dog has not been examined and one of his sons is diagnosed als PMDS-affected, we are sure that he has at least one faulty gene that was inherited by his son. Thus, the probability to be free has decreased to 0. He will either be carrier or affected. The probabilities are modified accordingly: 0.12/(1-0.32)= 0.18 (is 18%) to be affected and 0.56/(1-0.32)= 0.82 (is 82%) to be carrier. The corresponding modified gene fraction becomes 0.18+0.82/2= 0.59. And the code non-F is added to indicate that the dog is not PMDS-free. When a dog has an affected son, then his adjusted gene fraction is always higher than the average of its parents.

Because an affected dog inherites a faulty gene from both parents, the mother can neither be PMDS-free. Her gene fraction has to be modified in the same way and again the code non-F is added.

If a dog has been examined and no uterus has been found, but he has an affected son, then we are sure that he is not affected and also not free. So, he must be carrier, with a gene fraction of 0.5 and the code C.

Additional entries and the data base.
With the accumulating results of the investigations, it was found that Beacontree Calender got the PMDS gene from her great-great-grandfather Crochmaid Bold Turpin of Blackheath. Bold Turpin was imported from America in 1958 to provide new blood into the diminished English population that had survived World War II. The trail of PMDS could even be followed further back. With all of this knowledge, using specific statistical methods, several ancestors could be identified as missing links

between known carriers. They all got the code non-F with the accordingly adjusted gene fraction.

Meanwhile a data base has been formed with more than 25,000 (mostly breeding -) hounds, going back to the start of the Basset Hound in 1891 with the mating of the female Blood Hound Inocculation and the male French Basset Nicholas.

The data base is contineously updated.

The risk of PMDS.
Using this data base and the system of gene fractions, we can make an estimate of the risk of PMDS in any living Basset Hound. The same can be calculated for any potential mating. For example, we find a fraction of 0.4 in a specific dog or preferred mating, with fractions of 0.2 and 0.6 in the parents. Then, as shown above, the probabilities to be affected are 12%, to be free 32% and to be carrier 56%, respectively.