New Evidence for PSS Heredity

by Silvan Urfer

In early June 2009, the Journal of Veterinary Internal Medicine published a short communication by the Utrecht research group that has been researching portosystemic shunts in Irish Wolfhounds and other breeds for well over twenty years now. Their article, although based on a rather small number of dogs, offers compelling evidence against the previously accepted theory that PSS is a simple autosomal recessive trait with complete penetrance in our breed. Given the findings presented in the study, the former theory, which was published in 2002, must now be considered outdated.

Study Design

The study was based on three full siblings, one male and two females, all affected with PSS. There were three other males in the litter, none of which had a shunt. All three shunts had been surgically corrected, and all three of the pups had survived the surgery and lived to breeding age. The affected male was bred to both his sisters (one natural mating and one artificial insemination), and the pups from the two resulting litters were checked for the presence of PSS by ammonia testing and ultrasound. The diagnoses were then confirmed during surgery and/or necropsy.

Expected Outcome

Under the premise that PSS is a simple autosomal recessive condition with complete penetrance, one would have expected all puppies from these two litters to be affected with PSS, as illustrated in figure 1 below. Squares represent males, circles represent females; solid black shapes represent dogs affected with PSS, grey shapes represent clinically healthy carriers. It is not known for certain whether the three clinically healthy males in the genogram are carriers, as none of them were bred. Statistically, two of them can be expected to be carriers.

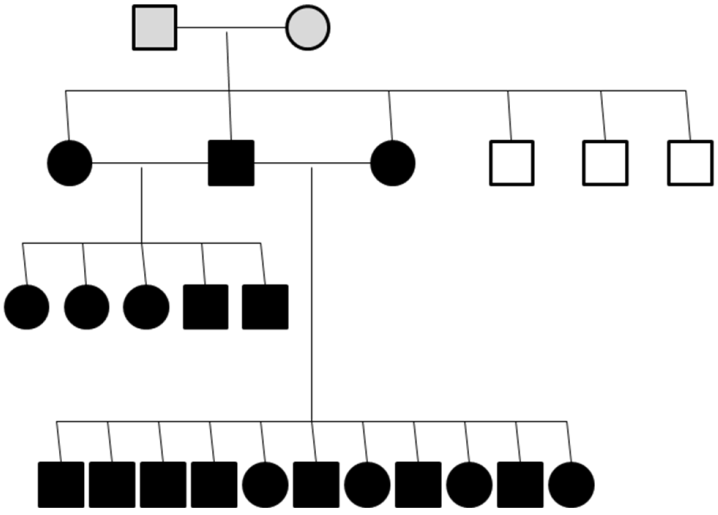

Fig. 1: *Expected outcome of test matings (lines 3 and 4) in a simple autosomal recessive condition with complete penetrance*

Actual Outcome

One of the litters consisted of five pups, all of which were affected with PSS. The other litter consisted of eleven pups, five of which were affected with PSS, and six of which were clinically normal. The latter are represented in figure 2 below by the white shapes.

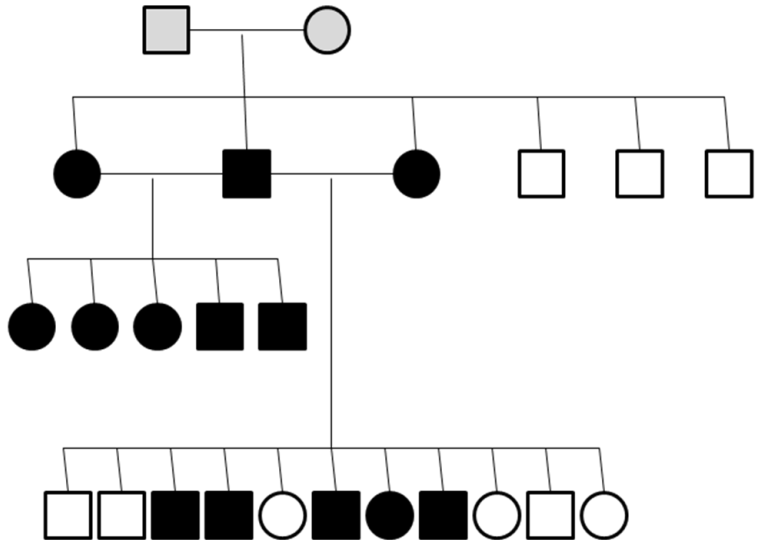

Fig. 2: *Actual outcome of the two test matings (lines 3 and 4) performed by the Utrecht Research Group*

The above occurrence pattern of PSS in the progeny of affected dogs cannot be explained by a simple recessive mode of inheritance with complete penetrance. Even though the sample is rather small, consisting of 16 puppies only, the evidence it offers is compelling in this regard. The conclusion that PSS is a highly heritable condition in Irish Wolfhounds is equally compelling based on the results. This leaves us with the questions of what one can conclude from these data and whether breeding recommendations should be changed.

Discussion

The authors of the study conclude that their results are compatible with a simple autosomal recessive mode of inheritance with reduced penetrance and estimate this penetrance to be around 50%. Due to the limited number of cases in the study, they concede that their estimation has a large margin of error, however.

Reduced penetrance can be caused by either genetic or environmental factors. In the case of PSS, where the phenotype is fully expressed shortly after birth, an environmental influence must be considered improbable, and therefore, the reduction in penetrance is likely caused by genetic factors. In this context, it is remarkable that all the unaffected puppies were born in one litter, which is unlikely (P=0.06) under the assumption that both litters had an equal risk for PSS. The authors therefore believe that this risk varied between the two litters and consider this further evidence in favour of the presence of a genetic modifier.

Although it is not possible to clearly identify the genetic base of the disease based on the two test matings, the authors conclude that the simplest mode of inheritance that could explain the observed disease pattern in these test matings is a simple recessive with an additional modificator gene (digenic, triallelic mode of inheritance).

This would imply that there is a PSS locus with a dominant (P) and a recessive (p) allele, as well as a modifier locus where the modifier is either present (1) or absent (0). Only dogs with genotype pp/10 and genotype pp/11 would have shunt – the modifier would therefore likely be dominant and allow the recessive shunt allele to be expressed when present in homozygous form.

Shunt Genotype	**Modifier Genotype**	**Affected?**	**Shunt Carrier?**
PP	00	no	no
PP	10	no	no
PP	11	no	no
Pp	00	no	yes
Pp	10	no	yes
Pp	11	no	yes
pp	00	no	yes
pp	10	yes	yes
pp	11	yes	yes

Table 1: *Possible digenic, triallelic PSS inheritance in Irish Wolfhounds and its effects on phenotype*

Conclusions

As mentioned before, the hypothesis that PSS in Irish Wolfhounds is a simple recessive condition with complete penetrance has been clearly refuted by the above results. The results also provide clear evidence that the disease is highly heritable in the breed and are compatible with epidemiologic considerations showing that the disease is transmitted by clinically healthy carriers rather than affected animals in the Irish Wolfhound population, as the practice of operating shunt cases and then using them for regular breeding is uncommon and widely ostracised among breeders.

Based on the results of the study, it is still clear that:

- PSS is an inherited disease in Irish Wolfhounds
- PSS is transmitted through the use of healthy carriers in regular breeding
- In the absence of a genetic test, PSS can only be combated through the exclusion of these healthy carriers from the breeding population.

At the moment, it thus seems still prudent not to use dogs who have produced PSS for further breeding, as they must still be considered carriers. The assumption of a simple recessive with one modificator also leads to the conclusion that the clinically healthy full siblings of dogs with PSS still have a two thirds risk of being carriers of the disease and should therefore not be used in breeding either.

Hopefully, the Utrecht research group will be able to produce further evidence in PSS research in our breed, which will be of use in future breeding programs to eliminate the devastating condition that is PSS.

Reference

FG. van Steenbeek et al. (2009): Evidence of Inheritance of Intrahepatic Portosystemic Shunts in Irish Wolfhounds. *J Vet Intern Med* **23**(4):950-2