Selection for scrapie resistance decreased inbreeding rates in two rare sheep breeds in the Netherlands

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Introduction

Conservation of genetic diversity is important for the possibility to adapt to changing future demands in livestock next to cultural and historic reasons. In general breeders are constantly seeking genetic improvement. Selection for desirable characteristics, however, generally leads to a loss in genetic diversity in other traits. This loss occurs not only in selected traits, but in other traits as well. This is mainly due to the lower effective population size in selected populations. It is thus important to simultaneously select and manage genetic diversity.

An attempt to balance selection intensity and conservation of genetic diversity was made in the national program for breeding for scrapie resistance in the Netherlands. Scrapie is a fatal infectious neurodegenerative disease for which susceptibility is associated with the prion protein (*PrP*) gene. The *ARR* allele is associated with resistance to scrapie (Foster *et al.*, 2001). In the Netherlands a breeding program was started on a voluntary basis in 2001 and starting 2004 the use of *ARR/ARR* rams was obligatory.

In some rare breeds there were so few *ARR/ARR* rams that the risk of high inbreeding and associated loss of genetic diversity would be unacceptably high. Based on computer simulations predicting the inbreeding rates for several breeds exemptions on the obligatory breeding program were allowed (Windig *et al.* 2004). To evaluate whether the effect of scrapie selection on inbreeding matched initial expectations two of the breeds were reanalyzed in 2009. The "Zwartbles schaap" (Black-blazed sheep) had started selection in 2001 and fully conformed to the obligatory use of *ARR/ARR* rams in 2004. The "Melkschaap" (Friesian-Zealand Milksheep) was exempt from the obligatory use of *ARR/ARR* rams and allowed the use of heterozygous *ARR* rams after 2004. In this paper we analyze the ARR frequencies and associated inbreeding rates as an indication of loss in genetic diversity during the years of scrapie selection in both breeds.

Material and methods

Breeds. The Zwartbles schaap is mostly kept in small flocks. There are more then 5000 ewes used for breeding, of which around 4000 are registered in the herd book. Each year around 3000 lambs are born and registered in the herd book, many new born ram lambs that will not be used for breeding are never registered. The Melkschaap are kept increasingly on a commercial basis for cheese production, but only around 50% of the animals on professional

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farms are registered in the herd book. The size of the Melkschaap herd book increased from around 2000 lambs registered in 1997 to around 4000 lambs in 2008.

Statistical analyses. Selection for scrapie resistance was evaluated by tracing the *PrP* genotype, if known, of the father of each lamb registered in the herd book. The effect of selection was evaluated by counting allele frequencies in new born lambs. To evaluate the effect of selection on genetic diversity, average inbreeding levels per year cohort were calculated using pedigree data. Only lambs with at least 4 generations of known ancestors were used. Inbreeding rates were calculated from average inbreeding levels using $\Delta F = 1 - [(1 - F_t)/(1 - F_{t-x})]^{1/x}$ where F_t is the average inbreeding level of lambs born in year t and F_{t-x} the average inbreeding level of lambs born x years before year t. Effective population sizes were estimated with $N_e = 1/[(age_f+age_m)\Delta F]$, where age_f and age_m is the average age of the father, respectively mother, of the lambs at the time of birth (Wooliams and Toro 2007).

Results and discussion

Before selection the ARR frequency in the Zwartbles was around 17%. In the Melkschaap the frequency was only 9% (fig. 1). Consequently only three ARR/ARR rams were available for selection in the Melkschaap in 2001 versus 28 in the Zwartbles in 1999. Selection for scrapie resistance started earlier in the Zwartbles than in the Melkschaap. In 2001 over 40% of fathers had at least one ARR allele in the Zwartbles (fig. 2) while in the Melkschaap it took until 2003 to reach this percentage. In 2004 the Zwartbles followed the compulsory breeding program with exclusive use of ARR/ARR rams. The Melkschaap made use of the exemption for rare breeds and heterozygous ARR rams remained in use up to 2008. For the Zwartbles more than 99% of fathers after 2004 had at least one ARR allele, while for the Melkschaap this percentage was, presumably, reached in 2006, although about 10% of the fathers had not been typed.

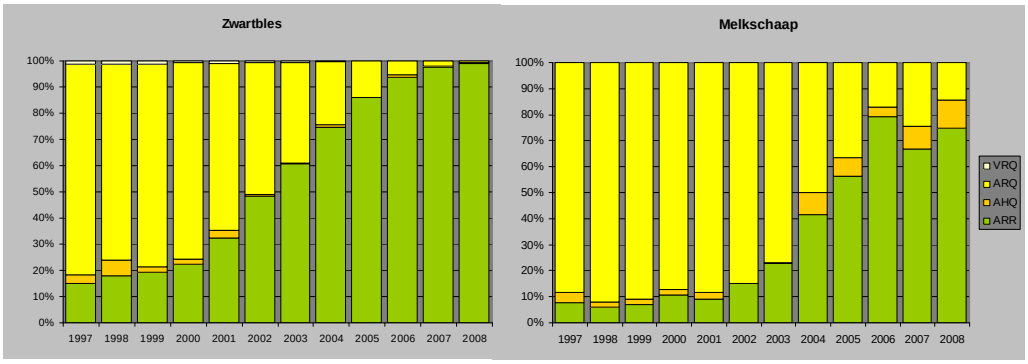

Figure 1: Allele frequencies of lambs in the Zwartbles and Melkschaap according to birth years.

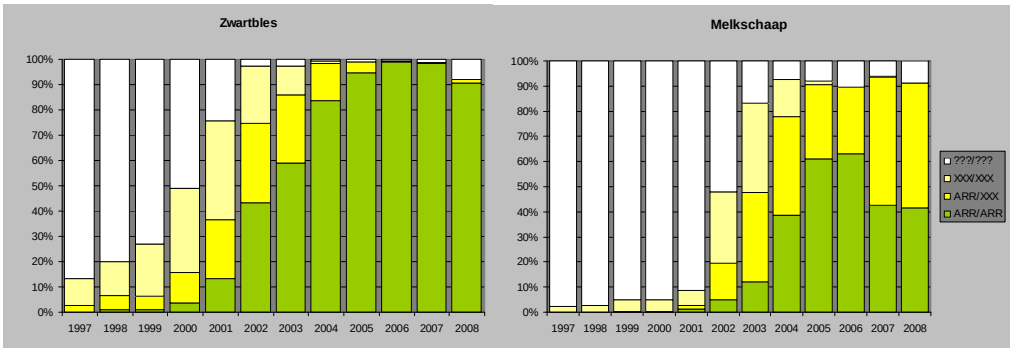

Figure 2: Genotypes of fathers siring lambs per birth year

Before the start of selection for scrapie resistance inbreeding levels increased in both herd books (fig. 3). Inbreeding rates per year were about 0.25% in both herd books (table 1). After the start of selection inbreeding levels decreased to negative values for both breeds, the decrease being stronger in the Zwartbles. Thus inbreeding levels did not increase due to selection for scrapie resistance but decreased. When selection ceased to be intense inbreeding rates returned to slightly under the level before selection.

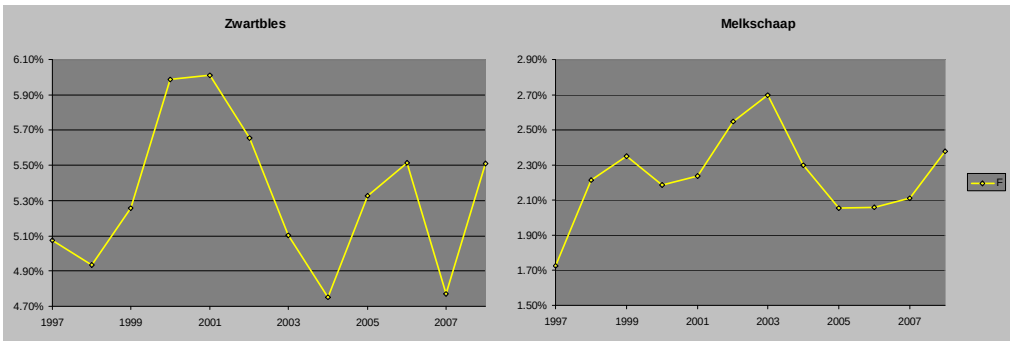

Figure 3: Average inbreeding level for new born lambs per year of birth.

Table 1: Inbreeding rates (on yearly basis) and effective population size (generation basis) in Zwartbles and Melkschaap in period before selection for scrapie resistance, and periods with more than 40%, respectively 90%, of fathers with at least 1 ARR allele.

Zwartbles			Melkschaap		
period	Inbreeding rate	Effective population size	period	Inbreeding rate	Effective population size
1997-2001	0.25%	80	1997-2003	0.24%	79
2001-2004	-0.44%	-	2003-2006	-0.28%	-
2004-2008	0.20%	100	2006-2008	0.19%	100

Discussion

Before the start of the obligatory breeding program for scrapie resistance there was great concern that this would lead to unacceptably high inbreeding levels in rare breeds. Interestingly, in the two breeds analysed here the contrary was observed. The explanation is that rams with the ARR allele had on average a low relatedness to the rest of the breed before the start of selection. Breeders of the Zwartbles confirmed that at the time of selection they used rams from other families which they would never have used otherwise because of bad conformation and low relatedness to the best and most popular rams. In the Melkschaap one of the three ancestral ARR rams was imported from Germany.

Before the start of selection computer simulations were performed to estimate the risk for high inbreeding levels Windig et al. 2004). For the Zwartbles the predicted rate with selection was estimated between 0.18 and 0.36%. This was, however, estimated assuming equal relatedness between all animals whether possessing the ARR allele or not. For the Melkschaap relationships of ARR and non-ARR animals were known and taken into account in the simulations. The prediction was that when using only homozygous rams the inbreeding rates would be between 0.76% and 1.56%, and when heterozygous rams were used as well between 0.09% and 0.31%. The latter regime was followed and actual inbreeding rates were negative. The explanation is that in contrast to the simulations matings in reality were not random with respect to ARR alleles. Non ARR animals were preferably mated to ARR animals leading to disassortive mating. Nevertheless, the conclusion that inbreeding rates could be acceptable when using heterozygous rams was met in practice. Whether inbreeding rates would have been unacceptably high when only homozygous rams would have been used cannot be proven. The prediction that with the use of heterozygous rams ARR frequencies would be around 75% by 2006 was close to reality. The inbreeding levels in the last years rose again to pre selection levels. The main cause is the use of popular rams. In the Melkschaap, for example, there was one ram with more than 500 offspring in the years 2005-2008. To keep inbreeding rates at a sustainable level measures such as a restriction of the number of offspring per ram or the number of sons per ram entered in herd book are needed.

Conclusion

Inbreeding levels decreased during the selection for scrapie resistance in both sheep breeds. The use of a small number of sires desirable for production, conformation or other traits for a prolonged time seems a bigger threat for diversity than a temporary breeding program for a different than usual trait.

References

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