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The role of gene banks as a safe guard in scrapie genotype eradication schemes

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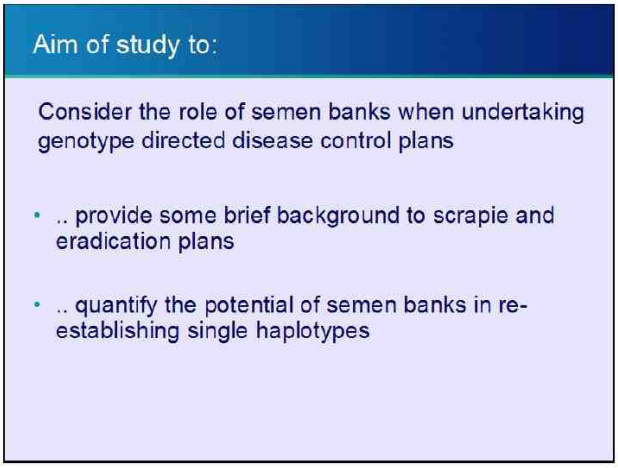
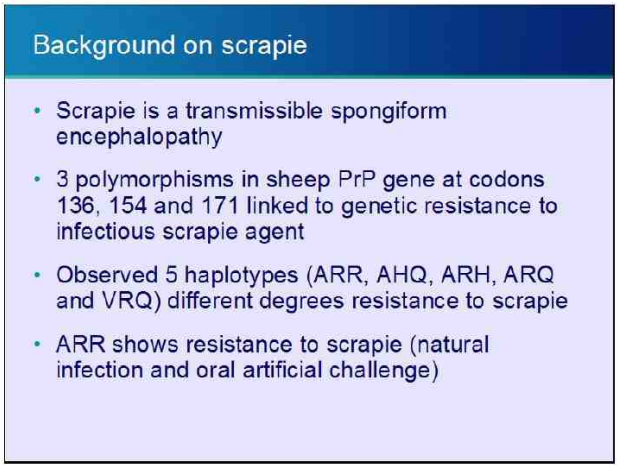




Risks inherent in scrapie plan

1. That a new TSE emerges to which the favoured haplotype (ARR) is susceptible
2. That attributes are lost from breeds through linkage with the removed haplotypes
3. That variation is lost in breeds through selection on a narrow proportion of the population

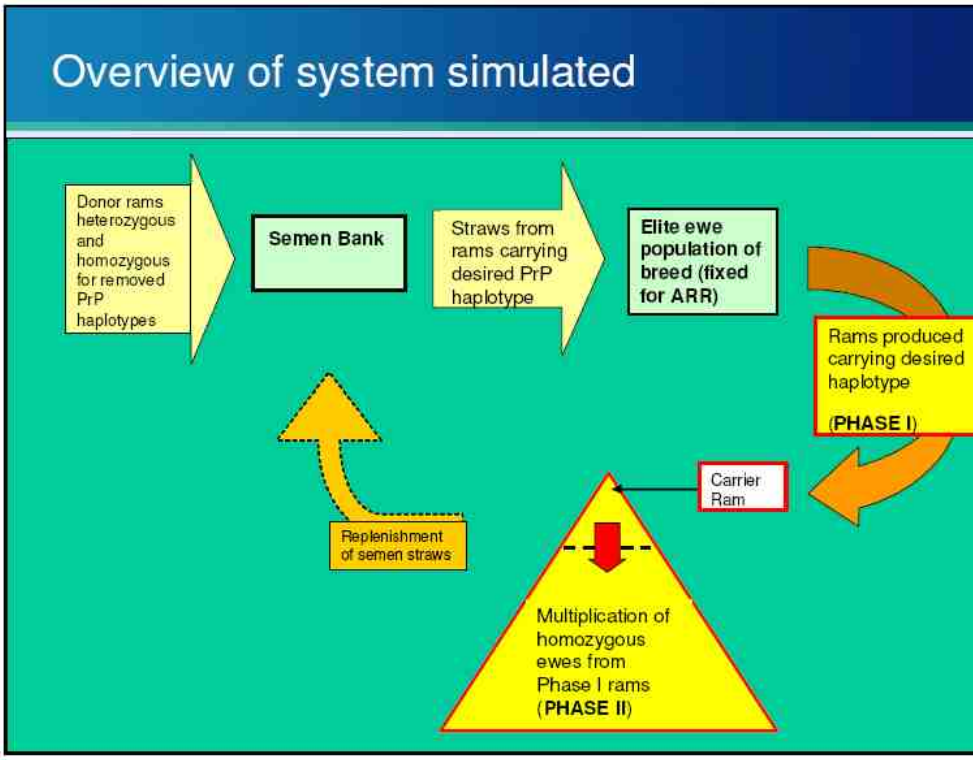
This study considers risks 1 and 2

Addressing Risks 1 and 2

1. One of the removed haplotypes may confer resistance to a new TSE
2. If removed haplotype had pleiotropic effect on or was linked to genes controlling another trait may want to restore
3. Most extreme case is total reversal of prp haplotype frequency to fixation of one of removed haplotypes

Semen Archive

- Intended to provide a collection of semen representing all 4 removed prp haplotypes for all breeds in plan
- Would allow experimentation initially to investigate remove haplotypes
- This study considers restorative potential of gene bank in addressing the previously described risks
- Capacity to reverse removal of haplotypes (full reversal at extreme)



Assumption that existing population of sheep fixed ARR homozygous

Phase 1

- Use bank straws to mate to existing population of sheep at top of breeding pyramid
- Interested in how many carrier males generated
- Depends on whether donor rams were hom or het for haplotype
- Non-limiting environment for phase 1

Phase 2

- Carrier rams from phase 1 introduced to elite breeders of sheep population
- Natural mating is used
- Driving parameters are:
    - Number viable breeding offspring per litter (male and female)
    - Mating ratio of ewes per ram
- Series of mating rules followed to maximise speed of increase of haplotype frequency
- Age over which rams and ewes breeding for considered.

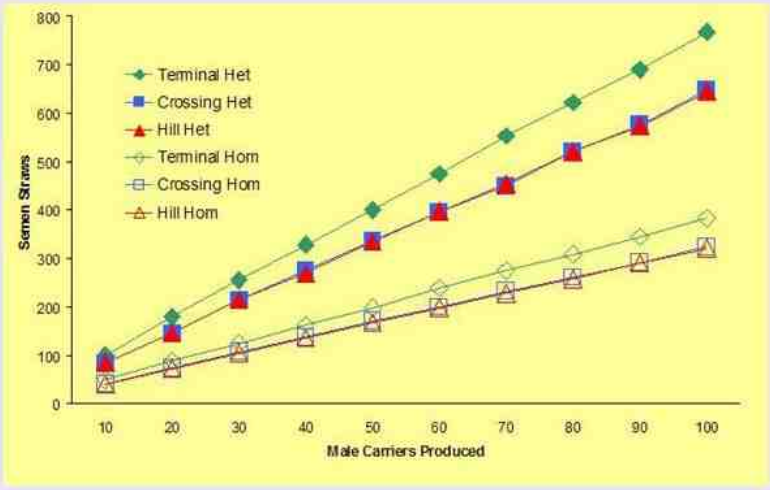
Parameter Values (3 Breed Types)

Phase	Parameter	Terminal	Crossing	Hill
I	Breeding offspring per AI pregnancy	1.0	1.2	1.2
II	Male breeding offspring/natural mating	0.125	0.15	0.1
	Female breeding offspring/natural mating	0.5	0.6	0.4
	Mating ratio ewes:rams	25:1	20:1	40:1

In phase 1 non-limiting environment (i.e. sheep not on poor hill ground). Hill breed considered to have high fertility in such environment

In phase 2 natural mating in natural environment with breed specific mating parameters, driven by structure of industry. Higher selection considered in males for traits other than prp genotype status.
Mating ratio driven by industry structure.

Phase I - Results



Straws required to produce carrier males of desired haplotype given hom and het donors of straws for hill, crossing and terminal sire breeds types

We see that if heterozygous donors contribute to the bank then twice as many straws are required. However a heterozygote accounts for the banking of more than one haplotype so this may not be an issue.

Terminal breed type required most straws to produce given number of carrier rams in phase 1.

Hill and crossing breed types had the same requirement.

Phase II - Results

Number of female homozygotes, produced annually in Phase II, from 1 initial carrier ram, introduced in year zero

	Breed Type		
Year	Terminal	Crossing	Hill
3	1	1	1
5	12	14	16
7	99	107	175
9	699	731	1674
Doubling Time* (Years)	0.71	0.72	0.61

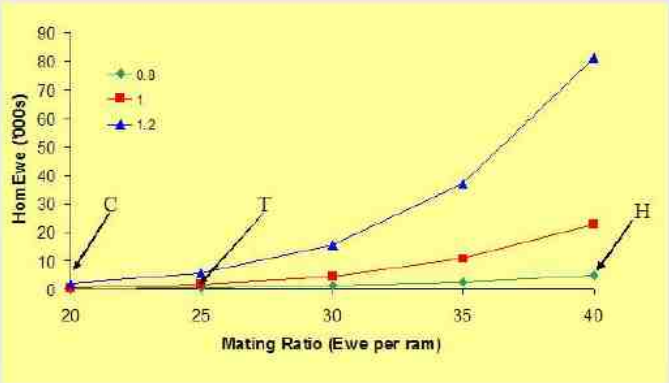
* Doubling time = ln(2)/r where r = rate of increase in HomEwe calculated as the regression coefficient of ln(HomEwe) on year.

In Phase 2 Hill breeds had lowest doubling time, i.e. time for number of homozygous breeding ewes to double.

Similar for terminal and crossing breeds.

Largely driven by mating ratio which can be manipulated by management.

Phase II Results – Varying Mating ratio and viable breeding animals produced per litter



Effect of mating ratio (x axis) and viable offspring (0.8, 1.0 and 1.2) on the number of female homozygotes (HomEwe) produced from 1 initial carrier male, introduced in year zero, after 10 years of multiplication.
C = Crossing, T = Terminal and H = Hill.

To investigate driver in phase 2 looked at varying viable breeding litter size and mating ratio.

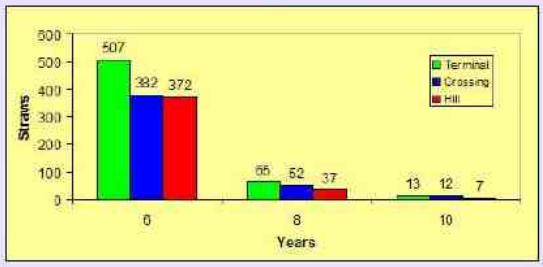
See that crossing and terminal breeds could easily increase capacity over hill breeds by increasing mating ratio.

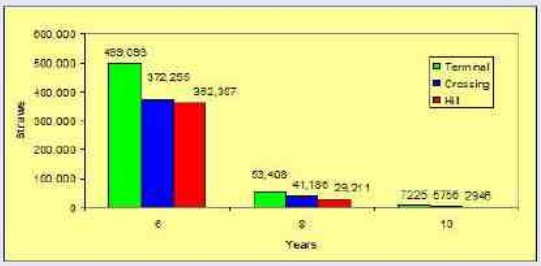
Combined Results

500 homozygous ewes

Number of straws required in the bank to produce the given number of homozygous ewes in the given time

500,000 homozygous ewes





Combining phases 1 and 2 we see that realistically more than 6 years are required to reverse the haplotype from ARR to another if 500 ewes required.

Need at least 10 years to achieve for 500,000 ewes.

Conclusions

- Highlighted need for rigorous planning
  - Long term proposition
  - Need to understand what capacity is for planning
  - May need to adopt different approaches to breeding program in event of needing rapid re-introduction