Genetic studies of bloat susceptibility in cattle

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ABSTRACT

Bloat costs the dairy industry about $50 million per year and one of the possible long-term solutions is to breed cattle with reduced susceptibility. Studies on two herds established at Ruakura in 1972/73, and selected divergently for high susceptibility (HS) or low susceptibility (LS) to bloat, have shown that: (1) bloat score on any single day of serious challenge has a heritability of 0.19±0.04; (2) the within-animal repeatability of scores across days is 0.44±0.02; (3) divergence of bloat score between herds has now reached 2.75 genetic standard deviations; (4) the recent response rate in the HS herd has been approximately linear whilst the LS response has reached a plateau; (5) 70% of the HS herd and 3% of the LS herd are at risk of death from bloat if left untreated. Alternative definitions of the bloat syndrome have been investigated; one of these (maximal bloat score) has a heritability of 0.30±0.06. Using this and other definitions, a mixed-inheritance segregation analysis was undertaken, which led to the conclusion that a major gene for susceptibility is segregating as an autosomal recessive. The implication is that the use of non-carrier AI sires in industry could minimise the bloat problem in one generation, by removing all homozygous bloat-susceptible progeny from the population.

Keywords: cattle; bloat; susceptibility; genetics; heritability.

INTRODUCTION

Bloat costs the dairy industry about $50 million per year, for bloat deaths, lost production, treatment costs and extra labour. One of the possible long-term solutions is to breed cattle with reduced susceptibility to bloat. The problem has been of serious concern for many years (e.g. Clifford, 1964), and records on susceptibility used to be collected from daughters in the New Zealand Dairy Board's (NZDB) young sire proving scheme (SPS). However, as the prevalence of drenching or other anti-bloat treatments increased in the industry, the validity of collecting comparative bloat scores in industry SPS herds became suspect. Data published by Morris (1991) suggested that any SPS summary for bloat was probably invalid if collected on daughters tested in the lactation of 1971/72 or later (i.e. 1968-intake bulls or subsequent bulls).

Alternative methods of evaluating the bloat genetics of young sires are by scoring their phenotypes directly or through the use of genetic markers. Bloat score on a single day is heritable (results are given below), but the required testing procedures are expensive on labour and can put the lives of otherwise-valuable animals at risk. Selection on bloat score has, however, been achieved successfully in our experimental herd at Ruakura (as described below), and the resulting herds of high susceptible (HS) and low susceptible (LS) cattle have recently provided the resources for us to begin searching for genetic markers and candidate genes for bloat susceptibility. The ultimate aim is to assist the dairy industry to identify bloat susceptible animals, so that these animals may be culled or used less frequently as parents in the national herd. Progress in breeding the divergent herds and in studying bloat susceptibility genetics is described below.

MATERIALS AND METHODS

Herd establishment and bloat scoring

The HS and LS herds at Ruakura were set up in 1972/73 as an interdepartmental project involving NZDB, the Ministry of Agriculture & Fisheries and the Department of Scientific and Industrial Research (Reid *et al.*, 1972). Details of the establishment and early years were given by Morris *et al.* (1991), but briefly the foundation cows were mainly Friesians (F), Jerseys (J) and FxJ crosses from identical twin pairs, scored for bloat and allocated on score to herd (or in some cases with pairs allocated one to each herd). There were four years of outside inseminations using NZDB bulls (1 per herd per year; 1972 and 1974, J; 1973 and 1975, F), followed by matings each subsequent year to HS and LS bulls bred in the project. Data are reported here from calves born over the 23 years, 1973-95, consisting of 901 animals by 99 sires. In early years, animals were scored for bloat repeatedly at about six months of age, and again at 12 and 18 months of age, and as lactating cows. Animals were scored on white clover/ryegrass or red clover pastures. The majority of scores on the data file refer to repeated 6-month scores, and analyses here are restricted to these. Scores (Johns, 1954) consisted of 0 (no bloat), 1 = mild boat, 2 = moderate bloat, 3 = severe bloat, 4 = urgent treatment required to prevent death. From a score of 1.0 upwards, half-units were used. Only the scores from all animals on "qualifying half-days" were included, and Cockrem *et al.* (1983) defined "qualifying" occasions as those when at least 20% of the HS animals had a score of at least 2.5 (since reduced to a threshold of at least 2.0 from about 1988, as a result of tighter ethics controls requiring earlier intervention to treat bloating animals).

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Data analyses

Individual scores on 204 qualifying half-days at about 6 months of age over 23 years were analysed (n = 4340 records), using an animal-model restricted maximum likelihood (REML) programme (Johnson and Thompson, 1995). These results supersede results from Morris *et al.* (1991), based on mean scores per animal over qualifying half-days at the same age.

The model was a repeatability REML, accounting for contemporary group as the fixed effect (i.e. year of birth x qualifying half-day group), and with random effects for error and for animal (additive genetic term and permanent environment term). This model and a single-record-per-animal model were applied to various definitions of the bloat score data, described below. The same data were also used as input to a Bayesian mixed polygenic-major gene model called 'MAGGIC' (Janss *et al.*, 1995), developed in Holland to test for evidence of a segregating autosomal major gene. In this type of analysis, much depends on the definition of the trait:

Bloat score definitions applied to each animal

(1) Maximum score (MAX1): the highest score over all qualifying half-days. (2) Mean of the two highest scores (MAX2) on qualifying half-days. (3) At risk of death, or not (D1): a binomial indicating whether any score had been at least 1.5. (4) The proportion of scores on qualifying half-days which were at least 1.5, and thus with the animal being at risk of death (PRD1). (5) Repeated records (REP): records on all qualifying half-days. (6) Standardised repeated records (STR): REP data expressed for each animal as the deviation of REP from the mean of the year x sex group, and standardised by dividing by the standard deviation of the HS animals in that year x sex group. The decision to use the HS standard deviation was not clear-cut but it was made because many LS animals had all zero scores. Definitions 1 to 4 led to single records per animal, whereas definitions 5 and 6 provided multiple records per animal.

RESULTS

Table 1 shows the parameter values and the estimated herd difference achieved by 1995. Heritabilities for traits 1 to 4 ranged from 0.20 to 0.32, whilst the single-record heritabilities for the repeated traits 5 and 6 were 0.19 and 0.18. There was evidence of reasonably good repeatabilities among days for these two traits (0.44 and 0.43). Divergence between the two herds had been achieved by 1995, whatever the criterion (1.20 to 1.78 phenotypic standard deviations (σ_p); 2.65 to 3.44 genetic standard deviations).

Other evidence for a major gene (b) segregating for bloat, and recessive for susceptibility, includes the following points. (1) Genetic progress in the LS herd has ceased since 1984 (the heritability in the LS herd from 1988 to 1994 has fallen to 0.02±0.11, and the herd presumably now contains ++ and b+ animals with similar phenotype). In contrast, progress in the HS herd is continuing, with no fall in heritability, presumably as bb and b+ phenotypes are separated. (2) There is a discontinuous distribution of mean bloat scores in the two herds, consistent with two separate phenotypes. This is unlikely with polygenic inheritance after only 6 generations. Based on D1, 70% of HS animals in the 1992-94 calf crops were at risk of death from bloat if left untreated, compared with 3% of the corresponding LS herd animals. (3) Heterosis data (not described here) were consistent with the first crosses being more resistant than predicted from their parent herds (i.e. b is at least partially recessive for susceptibility). (4) Finally, amongst the NZDB F bulls, one foundation HS bull and one foundation LS bull had breeding values in the selection experiment which were as elite in 1974 and 1976 as the corresponding herd means 18 years (5 generations) later. This is possible but rather unlikely under quantitative genetics inheritance. Definitive evidence should come when scores from adequate numbers of back-cross progeny by first-cross (b+) sires are obtained.

Results from gene-segregation programme

Table 2 shows the parameter values from the same six trait definitions as above, using the 'MAGGIC' programme. All traits provided evidence of a major gene, apart from D1, using the t test for a . Discarding MAX2 as well, whose parameters had high standard errors (see last 2 rows of the Table), we were left with four traits, MAX1, PRD1, REP and STR. All four showed that d was approximately equal to -a (indicating complete dominance for resist-

TABLE 1: Results from the restricted maximum likelihood analyses for bloat susceptibility score, using six definitions of the trait : 1973-95 calf crops (901 animals).

Parameter[a]	MAX1	MAX2	D1	PRD1	REP	STR
Records per animal	1	1	1	1	4.8	4.8
Mean	1.65	1.42	0.60	0.37	0.96	-0.00
Heritability	0.30±0.06	0.32±0.06	0.20±0.05	0.26±0.06	0.19±0.04	0.18±0.04
Repeatability	-	-	-	-	0.44±0.02	0.43±0.02
σ_p	0.86	0.79	0.41	0.31	0.86	0.86
CV[b]	0.52	0.55	0.67	0.84	0.89	-
Herd difference[c]	1.71	1.78	1.54	1.35	1.20	1.33

[a] For trait definitions, see text; σ_p = phenotypic SD

[b] Coefficient of variation = σ_p/mean

[c] σ_p units for the herd difference up to 1995

TABLE 2: Comparison of parameters from the major gene analyses using six definitions of bloat susceptibility score.

Parameter[a]	MAX1[b]	MAX2	D1	PRD1	REP	STR
σ_p	0.85	0.74	0.46	0.34	0.95	0.95
a/σ_p	0.73	0.51	0.00	0.79	0.60	0.55
d/σ_p	-0.70	-0.09	0.63	-0.87	-0.64	-0.73
$\sigma^2_{genetic}/\sigma^2_p$	0.32	0.35	0.89	0.64	0.42	0.44
$\sigma^2_{major\ gene}/\sigma^2_{genetic}$	0.83	0.47	0.99	0.86	0.80	0.78
t test: a/se(a)	6.9	2.4	-	11.0	9.9	8.6
d/se(d)	3.9[c]	2.9	74	9.1	8.4	9.2

[a] σ_p = phenotypic standard deviation; a = additive allelic effect; d = dominance effect.

[b] For trait definitions, see text. Three separate runs were averaged for each trait. MAX1, PRD1, REP and STR were run for 200 000 cycles, whilst the other two were run for 50 000 cycles

[c] This row was calculated regardless of sign.

ance). The value of a/σ_p was higher for MAX1 than for REP or STR because MAX1 was an intentional choice of extreme scores only. However, a/σ_p was as high for PRD1 as for MAX1. Amongst the four traits, PRD1 had the largest genetic variance ($\sigma^2_{genetic}$) as a ratio of phenotypic variance. For PRD1, REP and STR, but not MAX1, this ratio exceeded the heritability from the polygenic model assumed in Table 1. In addition, the variance attributable to the major gene accounted for at least 75% of the genetic variance in these four traits, a fact which would not be accounted for in the REML analyses. There seemed to be a similar fit of REP and STR to the data, based on $\sigma^2_{major\ gene}/\sigma^2_p$ (not shown). However, the MAGGIC programme works with outliers, and there was a concern with STR of adjusting away some legitimate outliers by standardising variances for each year.

There seemed to be no clear-cut first-choice trait. However, the four together were all suggestive of a major gene segregating, and average absolute values of a/σ_p and d/σ_p were similar at 0.67 and 0.74 respectively (with d negative, indicating that the resistance (or '+') allele is dominant and the susceptibility (or 'b') allele is completely recessive).

DISCUSSION

Results presented here show a relatively high genetic variance for a disease trait, and the 'MAGGIC' analyses are consistent with a major gene having a dominant (resistance) allele and a completely recessive (susceptibility) allele. A similar computer programme from Armidale, NSW ('FINDGENE' : Kerr and Kinghorn, 1996) has been used with the same data and has led to a similar conclusion. Bloat scores from back-cross progeny by first-cross sires will be necessary to confirm the putative major gene and its mode of action. For industry use, it is expensive to test animals for the bloat phenotype, and it would be more convenient to use a closely linked genetic marker, if this could be developed. These two objectives are the subject of a current project proposal being developed at Ruakura.

It may be possible to short-circuit the genotyping required to locate a linked marker, through a candidate gene (bSP30, or bovine salivary protein, of size 30 kDaltons). Its protein has been isolated from the parotid salivary gland (Rajan *et al.*, 1996), and its concentration is negatively correlated with bloat susceptibility. A similar protein is already mapped in rodents.

We believe that prospects are good for providing the New Zealand dairy industry with a means of removing bloat susceptible cattle. Carrier sires could be identified using a marker, and these sires could be withheld from the teams of widely used proven sires available for commercial use. Bull dams could also be tested, so that the cost of culling young carrier sires could be minimised.

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