Genetic Correlations Between Susceptibility To *Mycobacterium Bovis* Infection And Performance In Irish Holstein Friesian Dairy Cows

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Introduction

Mycobacterium bovis is the principal agent of bovine tuberculosis (TB). In Ireland, a TB eradication policy was introduced in 1954, to reduce the then estimated 17% animal incidence of bovine TB. Progress was rapid during the initial stages of the program, leading to a considerable reduction in the incidence of the disease in cattle by the mid-1960s. However, since then progress has stalled; animal incidence of TB was 0.33 % in 2004 (Good (2007)). The failure of Ireland, and some other countries, to reach TB-free bovine herd status is due to a range of factors relating to ongoing wildlife-to-cattle, and cattle-to-cattle transmission (More and Good (2007)). Two recent studies have independently demonstrated that genetic variation exists in two measures of *M. bovis* infection: abattoir confirmed *M. bovis* infection and responsiveness to the single intradermal comparative tuberculin test (SICTT; Bermingham et al. (2009); Brotherstone et al. (2010)) which indicates that genetic improvement is possible. Furthermore, a near unity genetic correlation between susceptibility to responsiveness to the SICTT and resistance to abattoir confirmed *M. bovis* infection has been estimated in Irish Holstein-Friesian dairy cows (Bermingham et al. (2009)), suggesting that indirect selection for increased resistance to confirmed *M. bovis* infection is possible using routinely recorded SICTT data.

A strong negative genetic correlation between milk yield and susceptibility to confirmed *M. bovis* infection has been recently estimated in UK dairy cattle, indicating that selection for increased resistance to *M. bovis* infection would not conflict with improving milk yield of lactating dairy cows (Brotherstone et al. (2010)). Nevertheless, the estimates of the genetic correlations reported in the literature between susceptibility to different diseases and performance are inconsistent (Ingvartsen et al. (2003)). The objective of this study, therefore, was to estimate the genetic correlations between two measures of *M. bovis* infection and economically important traits to determine the impact of current selection pressures on responses in genetic resistance to *M. bovis* infection in the Irish Holstein-Friesian dairy herd.

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Material and methods

Individual animal *M. bovis* infection status in Ireland is primarily based on the SICTT, which involves injecting *M. bovis* purified protein derivative (PPD) into the neck of each animal, and comparing the reaction induced to that produced by *Mycobacterium avium* PPD (a measure of sensitisation to environmental mycobacteria). Susceptibility to responsiveness to the SICTT in this study was dichotomised as standard reactors (animals with a *M. bovis* PPD reaction 4 mm or greater than the *M. avium* PPD reaction) and non reactors (animals with a *M. bovis* PPD reaction equal to the *M. avium* PPD reaction). Post-mortem examination of every animal at slaughter for tuberculous lesions is also an integral part of the ongoing TB eradication scheme in Ireland. *M. bovis* infection is confirmed through histopathology or culture. Susceptibility to abattoir confirmed *M. bovis* infection in this study was dichotomised as lesioned (an animal with an abattoir confirmed tuberculous lesion following the SICTT) or non-lesioned (a non-reactor with no subsequently abattoir confirmed *M. bovis* infection). A total of 2,094,750 animal SICTT results from 17,213 positive herd-tests (herd tests with at least 1 *M. bovis* standard reactor) in 5,905 herds, and 21,889 positive abattoir animal lesion records from November 2000 to December 2007, were obtained from the Irish Department of Agriculture Fisheries and Food disease control and eradication databases.

An attempt was made to include only animals that had a high likelihood of being exposed to *M. bovis*, by dividing the data into episodes using SICTT records at the herd level. A SICTT responsiveness episode was defined as a herd restriction initiated by 2 or more standard reactors (the likelihood of two false positive SICTT is very low), with at least one of the cows being home bred. An abattoir confirmed *M. bovis* infection episode was defined as a herd restriction initiated by an abattoir confirmed lesion. The criterion of a home-bred TB case within each episode was not implemented, as this requirement resulted in excessive loss of abattoir confirmed *M. bovis* infection records. Each episode was terminated by two consecutive clear herd tests. Only Holstein-Friesian animals were retained. Animals with no known sire, that calved outside the normal age for a given parity, that had inconclusive SICTT results, or that moved into the herd within 6 weeks of the SICTT (as it takes 3-6 weeks to develop a positive reaction to the test post infection) were discarded. Only episodes with at least one standard reactor (case of abattoir confirmed *M. bovis* infection) and 10 or more animals were retained. Following all edits 15,182 cow SICTT responsiveness records and 13,791 abattoir confirmed *M. bovis* infection cow records remained.

A total of 3,642,006 first to third parity 305-day milk, fat, and protein yield and somatic cell score (SCS), 6,495,139 first to fifth parity calving dates and calving interval (CI; defined as the number of days between consecutive calvings), and 86,814 first parity body condition score (BCS) records were extracted from the Irish Cattle Breeding Federation (ICBF) database for cows calving between 1985 and 2007. Survival from lactation 1 to 2, 2 to 3 and 3 to 4 was obtained for each cow. Cows of unknown parity and less than 15 months of age, with CIs less than 300 or greater than 800 days, and cows with an age at calving greater than 22 months from the parity median were removed. Contemporary groups of herd-year-season of calving with less than 5 records and paternal half sib group of fewer than 5 progeny records were removed. Following all edits 105,064 cows had information on production, 112,337 had information on CI, 95,239 had information on survival, and 57,250 had information on BCS. Pedigree information of each animal was traced back four generations.

Genetic and residual covariance components between the measures of susceptibility to *M. bovis* infection and performance were estimated using bivariate linear-linear (which ignored the binary nature of the *M. bovis* infection trait measures data) and threshold-linear (with a logit link function, which assumed an underlying distribution for the susceptibility to the *M. bovis* infection trait measures) sire models in ASREML (Gilmour et al. (2009)). The likelihood ratio test was used to determine if the genetic correlation between the measures of *M. bovis* infection and performance traits differed from zero. The t-test was used to test the difference between the correlation coefficients estimated between the *M. bovis* infection trait measures and performance traits from the linear-linear and threshold-linear models.

Results and discussion

The heritability from the linear sire model for susceptibility to abattoir confirmed *M. bovis* infection (0.06 ± 0.02) and responsiveness to the SICTT (0.02 ± 0.01), were similar to those reported by Bermingham et al. (2009) although the present study contained 46% and 23% more records, respectively. Estimates of heritability for all performance traits in this study are within the range of estimates from the literature (Ingvartsen et al. (2003); Tsuruta et al. (2005)). Genetic correlations estimated using the linear-linear sire model between the measures of *M. bovis* infection and the performance traits were similar to those estimated with the threshold-linear sire model ($P>0.05$). Two earlier studies (Heringstad et al., 2005; Negussie et al., 2008) have also reported similar genetic correlations from linear-linear and threshold models. Susceptibility to abattoir confirmed *M. bovis* infection was not genetically correlated with performance (Table 1). Susceptibility to responsiveness to the SICTT was positively genetically correlated with second parity fat production and BCS, and negatively correlated with first parity SCS and third parity survival. Hence, selection for increased survival may indirectly reduce susceptibility to *M. bovis* infection, while selection for reduced SCS and increased fat production and BCS may increase susceptibility to *M. bovis* infection within the national Holstein-Friesian dairy herd.

Susceptibility to the *M. bovis* infection trait measures was not genetically correlated with milk yield. An Irish phenotypic study has however recently shown that SICTTresponders produced significantly less milk yield than nonreactors (Boland et al. (2009)). However, genetic and phenotypic correlations with opposing signs have been reported (Koivula et al. (2005)). A recent U.K. study has nevertheless documented a negative genetic correlation between susceptibility to abattoir confirmed *M. bovis* infection and milk yield at the genetic level (Brotherstone et al. (2010)). The different results from the UK and Ireland may have been a result of differences in genetic background of respective cow populations, or previous selection/TB eradication practices that may have unconsciously favoured particular clinical/non-clinical genotypes. The inconsistencies between the UK and Irish studies need to be resolved before any definitive conclusions can be drawn for the dairy industry.

Conclusion

The results of this study based on large datasets and different statistical approaches suggest that selection for increased survival may indirectly reduce susceptibility to *M. bovis* infection, as measured by responsiveness to the SICTT, while selection for reduced SCS and increased fat production and BCS may increase susceptibility to *M. bovis* infection within the national Holstein-Friesian dairy herd.

Table 1: Genetic correlations (standard errors as subscript of coefficients) between abattoir confirmed *M. bovis* infection and responsiveness to the single intradermal comparative tuberculin test (SICTT) and performance traits estimated using the sire linear-linear models

Trait	Abattoir confirmed *M. bovis* infection			Responsiveness to the SICTT		
	Parity 1	Parity 2	Parity 3	Parity 1	Parity 2	Parity 3
Milk	$-0.31_{0.18}$	$0.06_{0.18}$	$-0.05_{0.20}$	$0.23_{0.14}$	$0.24_{0.14}$	$0.13_{0.16}$
Fat	$-0.13_{0.18}$	$0.21_{0.17}$	$0.09_{0.20}$	$0.32_{0.14}$	$0.39^{*}_{0.13}$	$0.23_{0.15}$
Protein	$-0.18_{0.18}$	$0.21_{0.18}$	$0.01_{0.20}$	$0.16_{0.15}$	$0.32_{0.14}$	$0.06_{0.16}$
SCS	$0.02_{0.19}$	$-0.05_{0.19}$	$-0.24_{0.22}$	$-0.34^{*}_{0.14}$	$-0.11_{0.15}$	$-0.14_{0.17}$
CI	$-0.30_{0.21}$	$-0.21_{0.26}$	$-0.67_{0.22}$	$-0.07_{0.18}$	$0.00_{0.22}$	$-0.18_{0.29}$
Survival	$0.44_{0.24}$	$-0.15_{0.28}$	$-0.49_{0.29}$	$-0.08_{0.22}$	$-0.17_{0.23}$	$-0.62^{*}_{0.22}$
BCS	$0.13_{0.19}$			$0.36^{*}_{0.14}$		

Significance of the difference from zero; * $P < 0.05$

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