Genetic Susceptibility to Porcine Reproductive and Respiratory Syndrome (PRRS) virus in commercial pigs in Italy

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Introduction

In the intensive pig industry, control of infectious diseases is a major production challenge. Not only infectious diseases cause great losses to the producer, but they are important also from the animal welfare perspective. Approaches applied to achieve disease eradication include various control measures designed to reduce infection pressure within the herd, e.g. management changes, medication and vaccination (Christensen and Mousing, (1992)). Additionally, drugs used to treat infectious diseases in pigs, if not properly applied, have the potential to remain as residues in meat destined for human consumption. For these reasons the prevention of infectious diseases is of great interest not only to the pig producer but also to the consumer. Evidence for genetic variation in pigs in response to different pathogens has already been reported, such as breed differences in incidence of respiratory and enteric diseases (Van Diemen *et al.*, (2002)) and in immune response (Henryon *et al.,* (2002), Petry *et al.,* (2007)). The identification of genetic variation might allow to use it in selective breeding program (Lewis *et al*., (2009a)). Moreover, advances in genomics of main livestock species, including pigs, will provide a powerful set of tools for understanding the genetic variation underlying economically important and complex phenotypes, such as susceptibility to metabolic and infectious diseases (Green *et al*., (2007), Tuggle *et al.*, (2007), Chen *et al.*, (2007)). In this new scenario Genome-Wide Association (GWA) studies are being used in livestock, as in humans, to map genes affecting complex traits (Goddard and Hayes, 2009) but prior to them heritability, defined as the proportion of variation in a particular trait that is attributable to genetic factors (Visscher *et al.,* (2008)), needs to be estimated in order not only to assess the genetic contribution to the disease outcome, but even to obtain a proper evaluation of SNPs across chromosomes and lines or breeds (Hassen *et al*., (2008)) and hence accurately predicting the response to artificial and natural selection.

Porcine Reproductive and Respiratory Syndrome (PRRS) represents one of the most economically important disease in pig populations worldwide and causes reproductive failure, abortions, stillbirths, interstitial pneumonia and decreased growth rate (Neumann *et al.*, 2005). The causative agent is a small envelope RNA virus (Arteriviridae family) that infects alveolar macrophages (Murtaugh *et al.*, (2002)) and induces apoptosis and virus persistence for several weeks (Mateu *et al.,* (2007)).

The goal of the present study was to estimate heritability of susceptibility to PRRS virus in commercial pigs in Italy.

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Material and methods

Source of Data. The data used were collected in the north of Italy and refer to the incidence of PRRS viremia in 18 commercial swine farms, spanning the period January 2006 - December 2008. The data were extracted from an existing database belonging to the MISAGEN project (Botti *et al.*, 2006), which included pedigree information, clinical symptoms, and health related phenotypes. The original dataset included records for the PRRS viremia measured by PCR in sera of 2908 weaning piglets from 4 breeds, namely *Large White* (n=1692), *Landrace* (n=621), *Duroc* (n=530) and *Pietrain* (n=65), representing 145 sires and 445 cows. PRRS viremia was defined as a binary trait based on the results of the traditional PCR: negative samples were coded as 0, positive samples as 1.
A contemporary group was defined as all pigs reared in the same herd, in the same year and whose samples were collected in the same season. Sampling season was categorized as season 1 (January to April), season 2 (May to August) and season 3 (September to December). A minimum of 10 piglets per sire and 15 piglets per contemporary group were required to estimate heritability. After editing the whole data set contained 2430 records, from 89 sires, 374 cows and 90 herd-year-season groups.

Statistical analyses. A nested half-sib design was used to estimate additive genetic variance by restricted maximum likelihood for PRRS viremia, using the Mixed procedure in SAS version 9.1 (SAS Institute Inc., Cary, NC). The fitted model was:

$$Y_{ijklm} = HYS_i + G_j + B_k + S_{l(k)} + D_{m(l)} + a_{cov} + e_{ijklm} \quad (1),$$

where Y is the trait, HYS_i is the fixed effect of the *i*th contemporary group, G_j is the fixed effect of *j*th gender class, B_k is the fixed effect of the *k*th breed class, $S_{l(k)}$ is the random effect of *l*th sire nested within *k*th breed class, $D_{m(l)}$ is the random effect of *m*th cow nested within *l*th sire, a_{cov} is the covariate for age at sampling and e_{ijklm} is the random error. Heritability was calculated as the ratio of $4\sigma_s^2 / (\sigma_s^2 + \sigma_d^2 + \sigma_e^2)$.

Results and discussion

Observed disease incidence was 36.4 %, with a decreasing trend over year 2006 and 2007 and a successive increase in year 2008 (Figure 1). Observed disease incidence per breed and sex is given in Table 1, with the *Pietrain* breed showing the highest % of positive piglets (60 %) and a close disease incidence in males and females. Contemporary group effect was statistically significant ($p < .0001$), while no difference were found within breed, sex or for age effect. The heritability of PRRS viremia on the observed scale was 0.096
Herd, year and season play a major role on PRRS viremia incidence, explaining most of the variation observed in the data, as expected since herd management and environmental conditions are known to be important factors in PRRS outbreaks (Evans *et al.*, (2008)). Some authors reported significant breed differences, highlighting a greater impact of PRRS virus on the *Meishan* line than on *Landrace*, *Large White*, *Pietrain*, and *Duroc* breeds (Lewis *et al.*, (2009b)). No breed differences was found in the present study even if the *Pietrain* breed showed the highest % of positive piglets. However, only 45 records were available for the *Pietrain* breed. In order to test their possible confounding effect they were removed from the data and the same model as (1) was fitted. Results (not shown) confirmed the not

significant breed effect and showed that the few *Pietrain* observation had no impact on variance components estimation.

Trait heritability was low, as most of the fitness related traits (Visscher *et al.*, (2008)). No previous findings are available in the literature because host genetic variation was analyzed mainly by using immune response differences both *in vitro* or *in vivo* (Lewis *et al.*, (2007)) and by using alternative phenotypes (Lewis *et al.*, (2009)), e.g. number of mummified pigs. However, even if a low heritability means that a small proportion of the observed variation is caused by variation in genotypes, it does not mean that the additive genetic variance is small. Using the additive genetic coefficient of variation ($CV_A = \sigma_A/\text{mean}$, Houle *et al.*, (1992)) we obtain a value of 36 % for genetic susceptibility to PRRS.

Variance components were obtained using a nested half-sib design and a linear model (LM). The former was chosen mainly because of its implementation simplicity as well as because it provides variance estimates that are not biased by common-environment and dominance variances. Moreover, estimates were obtained by REML, which is quite robust to unbalanced design and missing cells. Even if threshold models have been shown to be theoretically better than linear models for estimation of variance components for binary traits, a previous work did not find any significant differences between the two methodologies (Kadarmideen *et al.*, (2000)).

Table 1: Percentage of piglets positive for PRRS viremia by breed and sex

Trait		Number of piglets	
		Total	% Positive
Breed			
	Large White	1,447	36.8
	Landrace	537	33.7
	Duroc	401	36.9
	Pietrain	45	60.0
Sex			
	Males	1,236	36.7
	Females	1,194	36.4

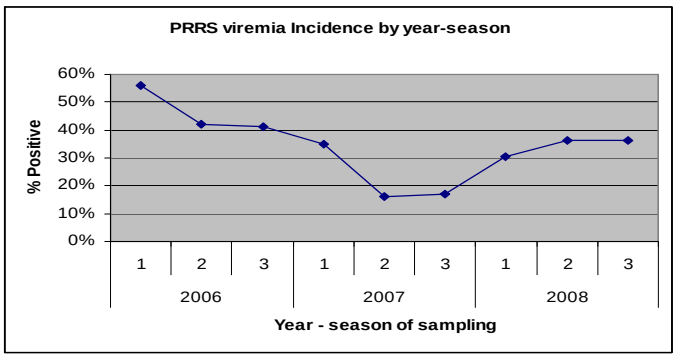

Figure 1: Proportion of piglets positive to PRRS viremia across year and season. Season 1 (January to April), season 2 (May to August) and season 3 (September to December)

Conclusion

This study demonstrates that susceptibility to PRRS, analyzed as a binary trait, has a genetic component, with an additive genetic coefficient of variation of 36 %. Additional investigation fitting a threshold in place of a linear model could be advisable but an unbalanced design or miss cells might lead to misleading results. Herd, year, season and their respective interaction have a large effect on the observed variation, stressing the need for control measures designed to reduce infection pressure within the herd.

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