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Genetic Control of Immune Response to Pseudorabies and Atrophic Rhinitis Vaccines: II: Comparison of Additive Direct and Maternal Genetic Effects

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Abstract

Data from 52 litters farrowed in two seasons of a cross-fostering experiment were analyzed to estimate variances and covariances for additive direct and maternal genetic effects on immune response to pseudorabies virus and B. bronchiseptica vaccine. Twenty purebred boars and 44 sows of the Duroc, Landrace and Yorkshire breeds were used. Immune response was measured after vaccine challenge. A modified-live pseudorabies (PR) vaccine was administered to piglets at 28 d of age; response was measured by log, serum neutralization titers at 56 d. An inactivated B. bronchiseptica bacterin was administered at 28, 42 and 112 d. Antibody levels were measured relative to positive and negative controls at 28, 56 and 119 d by using an enzyme-linked immunosorbent assay (ELISA). Results from this study for heritability were .18 ± .09 for PR titer and .15 ± .07 and .52 ± .15 for 56- and 119-d ELISA values, respectively. The variability due to nurse environment (maternal genetic variance and common environmental variance) as a percentage of phenotypic variance was 11.1% for PR titers and 29.6 and 8.8% for 56- and 119-d ELISA values, respectively. The heritabilities estimated in this study indicate that, if improved immune response to vaccines is desired, selection may be useful. However, the importance of maternal environment would make early selections less accurate than selections based on immune response measured later in life.

Keywords

Immune Response, Pigs, Maternal Effects, Heritability, Aujeszky Virus, Rhinitis

Disciplines

Agriculture | Animal Sciences | Biochemistry, Biophysics, and Structural Biology | Genetics | Other Veterinary Medicine

Comments

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GENETIC CONTROL OF IMMUNE RESPONSE TO PSEUDORABIES AND ATROPHIC RHINITIS VACCINES: II: COMPARISON OF ADDITIVE DIRECT AND MATERNAL GENETIC EFFECTS[1,2]

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ABSTRACT

Data from 52 litters farrowed in two seasons of a cross-fostering experiment were analyzed to estimate variances and covariances for additive direct and maternal genetic effects on immune response to pseudorabies virus and B. bronchiseptica vaccine. Twenty purebred boars and 44 sows of the Duroc, Landrace and Yorkshire breeds were used. Immune response was measured after vaccine challenge. A modified-live pseudorabies (PR) vaccine was administered to piglets at 28 d of age; response was measured by $\log_2$ serum neutralization titers at 56 d. An inactivated B. bronchiseptica bacterin was administered at 28, 42 and 112 d. Antibody levels were measured relative to positive and negative controls at 28, 56 and 119 d by using an enzyme-linked immunosorbent assay (ELISA). Results from this study for heritability were .18 ± .09 for PR titer and .15 ± .07 and .52 ± .15 for 56- and 119-d ELISA values, respectively. The variability due to nurse environment (maternal genetic variance and common environmental variance) as a percentage of phenotypic variance was 11.1% for PR titers and 29.6 and 8.8% for 56- and 119-d ELISA values, respectively. The heritabilities estimated in this study indicate that, if improved immune response to vaccines is desired, selection may be useful. However, the importance of maternal environment would make early selections less accurate than selections based on immune response measured later in life.
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Introduction

Immune response to pathogens is a natural mechanism to protect the piglet early in life. The immunological immaturity of the piglet makes transfer of maternal antibodies through the colostrum an important mechanism of conferring disease resistance to very young piglets. Maternal antibodies may be produced by vaccination of the sow or exposure of the sow to naturally occurring pathogens. The relative importance of maternal antibodies vs the immune competence of the piglet itself has not been well studied. This question is important because livestock disease costs producers and consumers millions of dollars every year from mortality, veterinary costs, product contamination and subclinical infections.

Humoral immune response is a primary component of disease resistance (Gavora and Spencer, 1983; Buschmann et al., 1985; Warner et al., 1987). However, a complicating factor in the study of the humoral immune response is the maternal influence due to antibody transfer via the dam's colostrum. Intestinal absorption of colostral antibodies ceases in the baby pig 24 to 36 h after birth (Speer et al., 1959; Miller et al., 1962; Chidlow and Porter, 1979). This passive immunity is gradually replaced by the young pig's own active antibody production (Jakobsen and Moustgaard, 1950; Nordbring and Olsson, 1957). Immune colostrum interference with active antibody production in pigs for about the first 3 wk reduces the importance of the genetics of a pig in the early stage of immunity development (Hoerlein, 1957; Segre and Kaeberle, 1962a,b; Kaeberle, 1968; Huang, 1977; Takahashi et al., 1984).

The objective of the research presented here was to estimate and compare the direct additive

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and maternal genetic effects on the humoral immune response.

Experimental Procedure

Sows and boars of the Yorkshire, Duroc and Landrace breeds were mated in a three-breed diallel crossbreeding design, which yielded nine groups of sire breed by dam breed combinations. Twenty purebred boars and 44 purebred sows were used to produce 496 pigs from 52 litters in two seasons. Description of the animals and facilities is given by Meeker et al. (1987).

All the sows in this project tested negative to pseudorabies (Aujeszky virus) by a serum neutralization (SN) test. No clinical signs of atrophic rhinitis existed in this herd. All sows had antibody levels for B. bronchiseptica lower than the positive control. Sows were not immunized with either pseudorabies (PR) vaccine or B. bronchiseptica bacterin.

Cross-fostering of piglets within breed group combinations was used to investigate maternal effects on immune response. Separation of the nursing period and prenatal maternal effects was critical and was accomplished by cross-fostering pigs before they nursed for the first time. Estrous synchronization was used to increase the probability that sows within a breed combination farrowed at the same time. However, all farrowing were within a 3-wk period in each season and the order in which breed combinations were farrowed was different for each season. The synchronization was produced by breeding the sows over a 30-d period, followed by administration of prostaglandin $F_{2\alpha}$[7] to cause simultaneous abortions in sows assigned to farrow at the same time. Two 10-mg doses of prostaglandin were given intramuscularly 16 h apart to sows 10 to 53 d pregnant (Meeker et al., 1985). The sows expressed estrus 5 to 11 d later and were bred to the assigned boar at that time. Breed differences in time between injection of prostaglandin and return to estrus have been reported (Meeker et al., 1985).

At farrowing, two sows of the same breed mated to the same breed of boar and farrowing within 12 h of each other formed a cross-fostering pair. One-half of the male and female piglets of each litter were chosen at random to be fostered on the other sow of the pair. Pigs were separated from their mother immediately after birth and not allowed to nurse or receive colostrum until after assignments were made. The pigs were then placed on their assigned nurse sow at the same time. All litters were denied the opportunity to nurse for the first 6 to 12 h, so that nursing was reasonably standardized for all litters.

All pigs were immunized at 28 d of age with PR vaccine and B. bronchiseptica bacterin via separate intramuscular shots in separate hams. Bordetella bronchiseptica bacterin was again administered in 42 and 112 d of age. Immediately before the 28-d immunization, blood samples were taken from all pigs and dams. Blood samples were collected from all pigs again at 56 and 119 d. The pigs were weaned at 42 d, simultaneously with the second B. bronchiseptica immunization. Blood samples were collected with glass capillary tubes from the orbital venous sinus by using the technique described by Huhn et al. (1969) for 28- and 56-d-old pigs. A modification of the technique for pigs standing in the upright position was developed and used to bleed sows and 119-d-old pigs.

The immunogens used were a chemically inactivated, adjuvanted culture of B. bronchiseptica[8], and a modified-live pseudorabies virus vaccine[9]. The immunogens were used according to the manufacturer's recommendations.

Ten milliliters of blood were collected from the pig and dams at the designated time in the vaccination and bleeding schedule. The blood was allowed to clot at room temperature, and the clots were removed after contraction. The samples were then centrifuged twice to produce serum. The sera were stored in aliquots at −20 C until assayed. The assay procedures are described in Meeker et al. (1987).

The immune response traits measured in this experiment were response to PR vaccine at 56 d of age, response to B. bronchiseptica vaccine at 56 d of age (secondary response) and response to B. bronchiseptica vaccine at 119 d of age (memory response).

Data from the 26 cross-fostered pairs were analyzed to estimate variances and covariances for additive direct and maternal genetic effects on immune response. The following model was used:

[7] Lutalyse, dinoprost tromethamine injectable, The Upjohn Co., Kalamazoo, Michigan.

[8] Rhinobac, Norden Labs., Lincoln, NE.

[9] PR-VAC, Norden Labs., Lincoln, NE.

$$Y_{ijkl} = \mu + P_i + D_{ij} + N_{ik} + DN_{ijk} + e_{ijkl},$$

where

μ = overall mean,
P_i = random effect of i^{th} cross-fostering pair,
D_{ij} = random effect of j^{th} dam in the i^{th} pair with mean 0 and variance σ^2_D,
N_{ik} = random effect of k^{th} nurse in i^{th} pair with mean 0 and variance σ^2_N,
DN_{ijk} = random effect of dam x nurse interaction within i^{th} pair with mean 0 and variance σ^2_{DN} and
e_{ijkl} = random error with mean 0 and variance σ^2_e.

The observed mean squares were equated to their expectations and then solved for the variance components as described for Henderson's Method III (Henderson, 1953).

The phenotypic variance (σ^2_P) was partitioned as follows (Willham, 1963; Rutledge et al., 1972):

dam variance (σ^2_D) = cov (full-sibs reared by different nurses) = 1/2 direct additive genetic variance;

nurse variance (σ^2_N) = cov (unrelated individuals reared by the same nurse) = maternal genetic variance + common environmental variance;

dam x nurse interaction variance (σ^2_{DN}) = cov (full-sibs reared by their own dam) − $\sigma^2_D - \sigma^2_N$ = direct-maternal genetic covariance;

within variance (σ^2_e) = $\sigma^2_P - \sigma^2_D - \sigma^2_N - \sigma^2_{DN}$ = 1/2 direct additive genetic variance + residual variance.

Heritabilities were estimated as $h^2 = 2\sigma^2_D/\sigma^2_P$. Standard errors of heritabilities were approximated by using the method described by Dickerson (1969).

Results and Discussion

Estimates of variance components for the immune response traits are shown in table 1. Components of variance are expressed as a percentage of phenotypic variance in table 2.

The immune response to PR vaccine was measured only once, so changes in importance of the dam and nurse variance components over time cannot be noted. Measured at 56 d, the dam and nurse variance components were both important (table 1), though the nurse component was larger.

The variance component for nurse was relatively large compared with dam variance for response to B. bronchiseptica vaccine measured at 56 d (table 1), and was relatively small for response measured at 119 d. The variance component for dam was relatively large for response at 119 d. These data show that immune response to B. bronchiseptica vaccine is influenced by maternal environment during the nursing period and for a time after weaning. It is likely that by 119 d the pigs have been separated for sufficient time from their maternal environment so that the additive direct genetic component became much more important as a factor influencing the pigs' immune response. The pig's genetic ability to respond to the vaccine is not fully expressed until the maternal influence is removed.

Heritability estimates are in table 3. The heritability estimate of PR titer at 56 d was .18 ± .09 and higher than the paternal half-sib estimate of .05 ± .20 found by Rothschild et al.

TABLE 1. VARIANCE COMPONENT ESTIMATES FOR HUMORAL IMMUNE RESPONSE TO PSEUDORABIES (PR) AND B. BRONCHISEPTICA VACCINES

Trait	Component				
	σ^2_D	σ^2_N	σ^2_{DN}	σ^2_e	σ^2_p (total)
PR vaccine titer[a]	.96	1.18	−.07	8.60	10.67
B. Bronchiseptica[b] vaccine titer					
at 56 d	.0061	.0236	.0004	.0497	.0798
at 119 d	.0239	.0082	−.0013	.0620	.0928

[a]Units = $(\log_2$ PR vaccine titer$)^2$.

[b]Units = (ELISA value)^2.

TABLE 2. VARIANCE COMPONENTS OF HUMORAL IMMUNE RESPONSES AS A PERCENT OF PHENOTYPIC VARIANCE

Component	PR titer[a]	ELISA value[a]	
	56 d	56 d	119 d
σ^2_D	9.0	7.6	25.8
σ^2_N	11.1	29.6	8.8
σ^2_{DN}	− .7	.5	− 1.4

[a]Percent of σ^2_p.

(1984b). The estimate of B. bronchiseptica response was .15 ± .07. That estimate is similar to the estimate of .10 ± .12 by Rothschild et al. (1984a), although the present estimate reflects the heritability of IgG response, whereas Rothschild et al. (1984a) measured heritability of preferentially measured IgM response. No estimates of immune response to B. bronchiseptica vaccine measured as late as 119 d have been presented previously. The heritability estimate of response at 119 d was .52 ± .15, and is considerably higher than estimates early in life. This estimate of heritability is much closer to the estimates of .29 ± .24 and .45 ± .29 by Edfors-Lilja et al. (1985) for IgG response to two E. coli antigens. This higher estimate also reflects the lack of maternal influence later in life.

In previously reported cross-fostering research on swine production traits (Cox and Willham, 1962; Ahlschwede and Robison, 1971), the cross-fostering took place after the piglets had received colostrum. Therefore, these studies combined the period in which the piglets received colostrum with prenatal environment. In the present study of maternal effects on immune response, cross-fostering took place before the pigs received colostrum. Thus, the colostrum nursing period was included with the postnatal environment. Although the sows had not been vaccinated to the two antigens being studied, high levels of other, non-specific antibodies were assumed present in the colostrum. Thus, our studies show that the mere presence of maternal antibodies can depress the immune response of the pig, in agreement with the previous study of Kaeberle (1962). The procedure used here did not separate the prenatal environment from the genetics of the litter, but this is probably not important in this study because it is generally believed that maternal antibodies do not cross the placental barrier in swine (Myers and Segre, 1963; Kim et al., 1964, 1966).

Dam × nurse interaction variance estimates, which are reflective of the direct and maternal genetic covariance, were generally negative but close to 0 for the humoral immune response (table 2). The expectation of this variance component is a covariance, and, therefore, negative results can occur. Henderson's Method III is also known to permit negative estimates.

TABLE 3. HERITABILITIES AND STANDARD ERRORS OF IMMUNE RESPONSE TRAITS

Item	PR titer[a]	ELISA value[b]	
	56 d	56 d	119 d
h^2	.18	.15	.52
SE	.09	.07	.15

[a]As measured by SN $\log_2$ titers.

[b]B. bronchiseptica immune response.

Negative covariance estimates between direct and maternal genetic components are common to many production traits in swine (Cox and Willham, 1962; Ahlschwede and Robison, 1971; Jungst and Kuhlers, 1984). This negative covariance for our study can be explained for immune responses. While a sow may genetically pass the ability for immune response to her pigs, her own ability to respond allows her to pass maternal antibodies to the pigs that she nurses.

Conclusions

Direct additive gene action seems to be important in immune response to pseudorabies and B. bronchiseptica vaccines, but postnatal maternal genetic influences and common environment have important effects on immune traits measured early in the life of young pigs. Covariances among direct and maternal effects were negative or 0. Heritability for response to B. bronciseptica vaccine was higher later in life when the maternal environment was less important to the pig. The heritabilities estimated in this study indicate that selection may be effective for increasing immune response to vaccines. The importance of maternal environment, however, would make early selections less accurate than selections based on immune responses measured at 119 d.

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