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Inheritance of pulmonary arterial pressure in Angus cattle and its correlation with growth

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ABSTRACT: Pulmonary arterial pressure (PAP) is an indicator of resistance to blood flow through the lungs and when measured at high altitude is a reliable predictor of susceptibility of an animal to brisket disease, a noninfectious cardiac pulmonary condition. (Co)-variance components for PAP, birth weight, and adjusted 205-d weaning weight were estimated from 2,305 spring-born, registered Angus cattle from a Colorado ranch at an elevation of 1,981 m. A single measure of PAP was collected after weaning on animals born from 1984 to 2003. The same licensed veterinarian measured every animal. Multitrait animal models with and without PAP maternal effects were fitted for a pedigree including 132 sires and 793 dams. The interaction of year × sex was a significant fixed effect (P < 0.05) for PAP, but age of dam was not. Age at PAP testing was a significant (P < 0.1) linear covariate for PAP, and scores increased 0.012 ± 0.007 mmHg·d⁻¹ of age. Heritability of PAP direct was 0.34 ± 0.05. Maternal heritability converged to a boundary at 0.0, and the model with maternal genetic effects for PAP was not significantly better than a model with only direct effects. Phenotypically, PAP was uncorrelated with birth or weaning weights. Genetically, PAP appeared to have positive, unfavorable relationships with direct effects for birth (0.49 ± 0.12) and weaning weight (0.50 ± 0.18). Positive correlations imply sires whose offspring exhibited resistance to brisket disease had lower weights and gains. A model that evaluated PAP in females and males as different traits had heritability estimates for each sex of 0.38 ± 0.07 and 0.46 ± 0.09, respectively, with a genetic correlation of 0.64 ± 0.12 between the sexes and was not significantly better than the model assuming homogeneity by sex and a unit genetic correlation between sexes. The results suggest that PAP is moderately heritable in spring-born Angus cattle acclimatized and tested at high altitude, and selection for low PAP scores would be effective. Selection for growth at low altitude will produce cattle less suited to high altitude.

Key words: cattle, growth, heritability, maternal effect, pulmonary arterial pressure

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INTRODUCTION

High altitude or brisket disease is characterized by right ventricular hypertrophy and edema of the chest and brisket in domestic cattle at altitudes above 1,500 m. The incidence and severity of the disease increase with altitude and ultimately lead to death (Puntriano, 1954; Alexander and Jensen, 1959). First reported in 1915 (Glover and Newsom, 1915), this noninfectious cardiopulmonary condition occurs in 0.5 to 5% of cattle native to high altitudes and 10 to 40% of cattle adapted to low altitude and moved to higher altitudes for pasture grazing (Will and Alexander, 1970; Salman et al., 1990). Heritability estimates for PAP from nonrefered sources range from 0.40 to 0.46 (LeValley, 1978; Schimmel, 1981; Enns et al., 1992), suggesting pulmonary arterial pressures (PAP) may be reduced in successive generations by selection. This in turn would be expected to reduce the incidence of brisket disease.

Research conducted by Schimmel and coworkers determined PAP were positively correlated with preweaning performance in heifer calves and negatively correlated with postweaning performance in feedlot bulls (Schimmel et al., 1980; Schimmel and Brinks, 1982, 1983). Correlations of PAP with growth are especially...
important, because genetic merit for direct effects on 
weaning and yearling weights in the national popula-
tion of registered Angus cattle has been increasing over 
the last 3 decades at 1.5 and 2.8 kg·yr⁻¹, respectively 
(American Angus Association, 2007). Darling and Holt 
(1999) found coefficients from parent-offspring regres-
sion of PAP were different for sire-daughter compared 
with sire-son, dam-daughter, and dam-son compara-
tions. Possible explanations include maternal effects or 
different inheritance of PAP for male and female calves. 
The objectives of this study were to compare alternative 
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MATERIALS AND METHODS

Animal Care and Use Committee approval was not 
obtained for this study, because data were obtained 
from existing databases.

Data Source

A database of PAP scores from a Colorado ranch located 
at an elevation of 1,981 m was made available by 
the owner. Body weights and pedigree information 
from that ranch were provided by the American Angus 
Association. Both data sources were provided electroni-
cally in 2004. Body weights had been collected from 
2,305 spring-born, registered Angus cattle born between 
1984 and 2003. Cattle included 1,088 bulls, 1,150 
heifers, and 67 steers that were AI or natural-mated progeny of 132 sires and 793 dams. Average progeny 
per sire and dam were 16 and 2, respectively.

Adjusted Weaning Weight

Adjusted 205-d weaning weight (WW) was calculated as 
birth weight (BWT) plus 205 × ADG from birth to 
weaning (Beef Improvement Federation, 2002), with no 
adjustment for age of dam. No adjustments were made to 
BWT.

Measurement of PAP

A single measure of PAP from each calf was collected 
at weaning in November of each year, except 2003, 
when PAP was measured in December. The same li-
censed veterinarian experienced in PAP measurement 
collected scores on an average of 115 animals·yr⁻¹ using 
procedures described by Ahola et al. (2006). In brief, 
a catheter was inserted into either jugular vein via 
venipuncture and threaded through the right atrium and 
ventricle to the pulmonary artery. Systolic and 
diastolic blood pressures were measured and averaged 
using a cardiac monitor (Hewlett-Packard, Grady Medi-
cal Systems, Winchester, CA). Age at the time of PAP 
testing averaged 277 d, ranged from 171 to 343 d with 
a SD of 28 d, and was used as a linear covariate for PAP.

Multivariate Models for PAP

Three multivariate models were compared, which dif-
fered in the nature of the random effects for PAP but 
used commonly accepted model equations for WW and 
BWT. Fixed effects fitted for growth traits were identi-
ﬁed from previously published reports and included 
contemporary group effects deﬁned as management 
group × age of dam × year × sex subclasses. Fixed effects for 
PAP included age of dam, contemporary group de-
fined as year × sex subclasses, and the covariate age at 
measurement. These were tested for signiﬁcance in a 
single-trait mixed model using a conditional Wald sta-
tistic in ASREML (Gilmour et al., 2006). Significant 
ﬁxed effects were subsequently ﬁtted for PAP in multi-
variable models including growth traits.

The model equations for growth traits included direct 
(D superscript) and maternal (M superscript) effects 
and were 

\[ y_{BWT} = cg_{BWT} + u_{BWT}^D + u_{BWT}^M + e_{BWT} \]

and 

\[ y_{WW} = cg_{WW} + u_{WW}^D + u_{WW}^M + e_{WW} \]

where \( cg \), and \( e \) denote the 
temporary group and residual effects for trait \( i \). 
Model 1 included the 2 growth trait equations and a 
maternal model equation for PAP, \( y_{PAP} = cg_{PAP} + \beta a_{PAP} + \beta u_{PAP}^D + \beta u_{PAP}^M + e_{PAP} \). The coefficient \( \beta \) represented the regression of PAP on age at PAP measurement, \( a_{PAP} \). 
Model 2 included the 2 growth trait model equations 
and 1 equation for PAP measurements on males 
(PAPM) and another for measurements on females 
(PAPF), \( y_{PAPM} = cg_{PAPM} + \beta a_{PAPM} + \beta u_{PAPM}^D + \beta u_{PAPM}^M + e_{PAPM} \), and 
\( y_{PAPF} = cg_{PAPF} + \beta a_{PAPF} + \beta u_{PAPF}^D + \beta u_{PAPF}^M + e_{PAPF} \). These equations for PAP did not include maternal effects. A distinct 
regression coefficient, \( \beta_i \), was fitted for age at PAP mea-
measurement, \( a_{PAP} \), where \( i \) reflects the sex of the animal with the 
PAP record. Model 3 was the simplest model 
for PAP and included the 2 growth trait model equations 
and a model equation for PAP that ignored mater-
nal effects and did not distinguish random direct and 
residual effects according to the sex of the animal with 
the PAP record, \( y_{PAP} = cg_{PAP} + \beta a_{PAP} + u_{PAP}^D + u_{PAP}^M + e_{PAP} \).

The residual variance-covariance matrices for models 
1 and 3 were constructed from a matrix \( R_0 \) of order 3 
and included 6 parameters. The corresponding matrix 
for model 2 had order 4 and included 9 parameters, not 
counting the residual covariance between PAPM and 
PAPF, because no individual could be observed for both 
the male and female definition of the trait.

The genetic variance-covariance matrices were con-
structed from a matrix \( G_0 \) that for model 1 had order 
6 \((u_{BWT}^D, u_{BWT}^M, u_{WW}^D, u_{WW}^M, u_{PAPM}^D, u_{PAPM}^M)\), model 2 had order 6 
\((u_{BWT}^D, u_{BWT}^M, u_{WW}^D, u_{WW}^M, u_{PAPM}^D, u_{PAPM}^M)\), and model 3 had order 
5 \((u_{BWT}^D, u_{BWT}^M, u_{WW}^D, u_{WW}^M, u_{PAP}^D)\). The corresponding 
number of genetic parameters was 21, 21, and 15, mak-
ing a total of 27, 30, and 21 variance parameters in each of the 3 models.

Models were compared by likelihood ratio test, as-
suming that the genetic and residual effects followed a 
multivariate normal distribution with zero covariance 
between genetic and residual effects. Twice the absolute
difference, after convergence, in ASREML-estimated likelihood between the full and reduced models was compared with tabulated $\chi^2$ values with degrees of freedom determined by the difference in number of parameters between the models. The significance of maternal effects for PAP was obtained from the likelihoods for models 1 and 3. This test had 6 df, the difference in number of parameters between the 2 models. The significance of fitting PAP as different traits by sex could not be obtained by comparing likelihoods of models 1 and 3, because these have different fixed effects and ASREML does not compute the contribution of fixed effects to the likelihood. Instead, model 3 was approximated by parameterizing model 2 using converged estimates of variance parameters from model 3 and assessing the likelihood without iteration. The genetic correlation between male and female effects could not be parameterized to unity, because this would result in a singular genetic variance-covariance matrix. Accordingly, it was fixed as 0.99, arbitrarily close to the boundary of the parameter space. This test had 9 df.

Variance components were estimated using significant fixed effects for PAP and the most appropriate multivariate model. Functions of estimated components, such as heritabilities and genetic and phenotypic correlations, were obtained from converged variance components using ASREML procedures.

**RESULTS AND DISCUSSION**

Average BWT and WW were 36.6 ± 0.1 kg and 224.1 ± 0.6 kg, respectively. Measurements of PAP were collected when calves were 277 ± 0.6 d of age, and scores averaged 39.8 ± 0.2 mmHg. Previously reported mean PAP scores were slightly lower, ranging from 32.1 to 38.6 mmHg in Angus bulls and heifers, but were observed at slightly higher altitudes of 2,070 to 2,316 m (Schimmel et al., 1980, 1981; Schimmel and Brinks, 1985). The hypobaric chamber mimicked conditions of inclement weather, or both, is more common than in summer (Jensen et al., 1976a,b; Busch et al., 1985). Calves exposed to colder temperatures in a temperature-controlled hypobaric chamber developed pulmonary hypertension, and exposure to high altitudes exacerbated this condition further (Busch et al., 1985). The hypobaric chamber mimicked conditions calves may experience when moved to higher-altitude pastures in midsummer. Alexander and Jensen (1959) and Alexander et al. (1960) observed variation in susceptibility of calves to brisket disease when dams were moved to higher elevations prepartum. Subsequent studies at an altitude of 1,524 m observed variation in postpartum survival among those calves with elevated PAP at birth. Some died within 10 d, whereas others exhibited a gradual decrease then stabilization in PAP scores over the same time frame (Will et al., 1975a,c; Stenmark et al., 1987). These results suggested there may be both individual and maternal influence on PAP.

In the current study, greater PAP scores did not appear to be adversely phenotypically associated with WW. Every animal whose details were provided for...
analysis had a WW. Colorado ranchers usually move cows and calves before weaning to grazing pastures at higher altitudes in June or July, and susceptible calves that did not exhibit symptoms at birth may have developed brisket disease (Will et al., 1975a,b) and died before weaning with no birth information being entered into the database. The extent of such bias cannot be determined from these records.

Alexander and Jensen (1963) observed a phenotypic correlation between chronic hypoxia and hypertrophy of the smooth muscle located within pulmonary arteries and arterioles. Comparison of domestic cattle and other Bos species residing at high altitudes indicated the latter do not experience brisket disease, even though these animals reside at altitudes of 3,200 m or higher (Anand et al., 1986; Durmowicz et al., 1993). Durmowicz et al. (1993) evaluated the response of the native high-altitude yak (Bos grunniens) and determined that at rest at 730 m the yak had PAP scores of 24 mmHg, lower than 29 mmHg for yearling steers residing at 1,600 m and 24 mmHg for cattle less than 1 yr of age at sea level. Durmowicz et al. (1993) also observed that induced hypoxia elevated PAP, but a vasoconstrictor agent such as norepinephrine caused greater vasoconstriction response and higher PAP than hypoxia. Also, acetylcholine and sodium nitroprusside caused vasodilation, lowered PAP, and increased cardiac output.

Comparison of domestic cattle and yak artery and arterioles indicated the yak had less vascular smooth muscle, and endothelial cells were longer, wider, and rounder. Histological differences may influence pulmonary vascular tone and reactivity and allow the yak to adapt to hypoxic conditions better than cattle (Durmowicz et al., 1993). Anand et al. (1986) mated adapted high-altitude yak sires with domestic cows, and the F1 progeny had PAP and pulmonary arterial resistance measurements similar to yak sires; however, backcrossing F1 females with domestic bulls created backcross progeny with segregated PAP scores representative of either the resistant yak or susceptible domestic cow. Anand and coworkers (1986) concluded the F1 and some backcross progeny retained the hypoxic vasoconstrictor response of the high-altitude yak. Will et al. (1975a) observed a similar result in which progeny of sires resistant to high-altitude pulmonary hypertension and brisket disease had calves that were resistant and had lower PAP scores than progeny of susceptible sires.

Regulation of variation in the vasoconstrictor response by a single locus may be plausible; however, the challenge will be to determine where the locus is and what gene or genes are influenced by that locus. Comparison of smooth muscle in the small pulmonary arteries and arterioles indicated a negative relationship between the amount of smooth muscle and hyporesponsiveness (Tucker et al., 1975). Therefore, smooth muscle structure may be useful to identify proteins responsible for regulation of pulmonary hypertensive reactivity and expression of brisket disease. Potential candidates include plasminogen activator, endothelial NO synthase, and hypoxia-inducible factor-1.

Plasminogen activator is a protein associated with repair of the endothelial cells of veins and capillaries. Astrup et al. (1968) observed greater mean levels of this protein in Bos indicus vs. Bos taurus cattle, suggesting B. indicus are less susceptible to brisket disease and are able to recover more quickly if inflicted. Polymorphisms induced in the endothelial NO synthase gene resulted in mice that were more reactive to mild hypoxia and developed pulmonary hypertension more quickly than mice lacking the polymorphisms (Steudel et al., 1997). Levels of hypoxia-inducible factor-1 were shown to influence expression of genes that modify vascular tone in response to low oxygen tension (Ke and Costa, 2006). Variation in pulmonary hypertensive reactivity is present among many species, and other candidate genes may be identified using genomes of the hyper-responsive porcine, moderately responsive ruminant, hyporesponsive ovine, or nonresponsive canine (Tucker et al., 1975).

Table 1. Heritability (on diagonal) and genetic correlations (above diagonal; ±SE) among pulmonary arterial pressure (PAP), birth weight direct and maternal (BWT and BWTM), and weaning weight direct and maternal (WWD and WWM) for spring-born, registered Angus cattle

<table>
<thead>
<tr>
<th>Trait</th>
<th>PAP</th>
<th>BWTD</th>
<th>BWTM</th>
<th>WWD</th>
<th>WWM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>0.34 ± 0.05</td>
<td>0.49 ± 0.12</td>
<td>0.01 ± 0.17</td>
<td>0.51 ± 0.18</td>
<td>−0.05 ± 0.14</td>
</tr>
<tr>
<td>BWTD</td>
<td>−</td>
<td>0.45 ± 0.08</td>
<td>−0.12 ± 0.18</td>
<td>0.36 ± 0.18</td>
<td>0.09 ± 0.15</td>
</tr>
<tr>
<td>BWTM</td>
<td>−</td>
<td>−</td>
<td>0.14 ± 0.04</td>
<td>0.33 ± 0.26</td>
<td>0.15 ± 0.17</td>
</tr>
<tr>
<td>WWD</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>0.16 ± 0.06</td>
<td>−0.44 ± 0.18</td>
</tr>
<tr>
<td>WWM</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>0.26 ± 0.05</td>
</tr>
</tbody>
</table>

Table 2. Phenotypic (below diagonal) and residual (above diagonal) correlations (±SE) and phenotypic SD (on diagonal) for pulmonary arterial pressure (PAP), birth weight (BWT), and weaning weight (WW) for spring-born, registered Angus cattle

<table>
<thead>
<tr>
<th>Trait</th>
<th>PAP</th>
<th>BWT</th>
<th>WW</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>8 mmHg</td>
<td>−0.17 ± 0.06</td>
<td>−0.13 ± 0.05</td>
</tr>
<tr>
<td>BWT</td>
<td>0.10 ± 0.03</td>
<td>4 kg</td>
<td>0.28 ± 0.06</td>
</tr>
<tr>
<td>WW</td>
<td>0.02 ± 0.03</td>
<td>0.35 ± 0.04</td>
<td>26 kg</td>
</tr>
</tbody>
</table>
Regardless of the underlying causes of variation, single measures of PAP collected in spring-born registered Angus cattle were found to be moderately heritable but had unfavorable genetic correlations with direct effects on growth. Selection for growth based on performance recorded at a low altitude would be expected to increase PAP scores and susceptibility to brisket disease at high altitude. Selection for performance at high altitude should consider PAP along with growth and other economically relevant traits recorded in high-altitude conditions.

LITERATURE CITED


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