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## Relationship between resistance to a *Pasteurella Multocida* experimental infection and production traits in rabbits

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### Abstract

Nine hundred and fifty five rabbits were inoculated at 6 weeks of age with a pyogenic strain of *Pasteurella multocida* and were scored for resistance from 0 to 4 by taking into account post-mortem examinations. Fifty five sires having at least 10 inoculated offspring produced also 9943 rabbits tested for health and growth and 1468 females tested for reproduction in commercial farm conditions. Total number born and number born alive per litter were significantly lower in daughters of resistant sires (-0.27 and -0.41). Prevalence of digestive diseases and infectious diseases were significantly lower in the resistant growing rabbits than in the susceptible ones (-1.7 point and - 3.0 points, respectively). This result suggests that resistance to pasteurellosis assessed by an experimental infection is favorably correlated to resistance to other infectious diseases.

### Introduction

Pasteurellosis is one of the most common bacterial infection in commercial rabbit farms. The RELAPA project (Genomics for the Genetic Resistance of Rabbits to Pasteurellosis) aims at identifying genomic regions associated with the resistance to pasteurellosis. To establish a successful commercial breeding program to improve resistance to pasteurellosis, we need to evaluate the relationship between this trait and resistance to other diseases and production traits. This study aims at comparing production and health traits of growing rabbits and breeding does raised in commercial farms and produced from the resistant and susceptible sires having offspring tested through experimental inoculation with *Pasteurella multocida* in the RELAPA project.

### Materials & Methods

#### *Sires evaluation.*

In the RELAPA program, 955 crossbred rabbits were inoculated at 6 weeks of age with a pyogenic strain of *Pasteurella multocida* and the response to inoculation was assessed during the following 14 days, the animals being sacrificed after 14 days (Shrestha *et al.*, 2018). These crossbreeds are progenies from six sire lines (two lines each from breeding companies Eurolap,

Hycole, and Hypharm) and one dam line (INRA 1777). The rabbits were scored for resistance to pasteurellosis from 0 to 4, by taking into account scores for extent of abscesses (0 to 4), scores of *P. multocida* presence (0 to 4), and status of the rabbits (dead/alive) at the end of the experiment. (Shrestha *et al.*, 2018). Among the sires used for RELAPA, 55 having produced at least 10 inoculated animals were classified as resistant (28 sires) or susceptible (27 sires) according to the mean resistance value of their inoculated offspring (Table 1).

**Table 1. Means and standard deviation of the resistance score of resistant and susceptible sires calculated from their inoculated offspring score**

Group of sire	N	Mean resistance score	Standard deviation of resistance score
Resistant	28	1.57	0.16
Susceptible	27	2.03	0.26

***Animals and measured traits.***

The 28 resistant sires produced 4991 growing rabbits (RG) and 884 breeding does (RD) while the 27 susceptible sires produced 4952 growing rabbits (SG) and 712 breeding does (SD). Growing rabbits and does were raised in six commercial farms belonging to the three breeding companies partners of the RELAPA project. The does were raised in conventional housing, inseminated for the first time at 19 weeks of age and then every 42 days. Females produced 6676 litters, or 4.2 litters per female on average. For each insemination, fertility was scored one (AI followed by a kindling) or zero (AI not followed by a kindling). For each litter, the number born alive and dead has been recorded. Stillbirth is calculated as the difference between the total number born and the number born alive divided by total number born. Nest mortality was calculated as the difference between the litter balance after adoption and the number of weaned rabbits divided by the litter balance.

The rabbits were weighed at weaning and at the end of the test. The weaning age ranged from 28 to 35 days, while the age of the end of fattening ranged from 66 to 70 days depending on the rearing farm. Mortality and clinical signs of diseases occurring in growing rabbits were recorded at the end of the test. The most likely cause of death of rabbits that died before the end of the test was also recorded. Disease traits were coded as 0 (absence) or 1 (disorder= morbidity or mortality). They were the following: 1) digestive disease, which includes diarrhea, bloated abdomen, and any form of digestive symptoms, 2) respiratory diseases which includes nasal discharge, pneumonia, 3) all infectious diseases, which combines digestive and respiratory diseases, abnormal low weights and other clinical signs of infectious origin. The basic statistics of growth and disease traits are given in Table 2.

**Table 2. Number of animals, mean and standard deviation (Std) for growth and reproduction traits.**

Trait	Number of animals	Mean	Standard deviation
Weaning weight (g)	8025	866	232
Final weight (g)	7477	2292	258
Fertility (0/1)	6676	0.87	-
Total number born / litter	5798	10.80	3.10
Number born alive / litter	5798	10.09	3.57
Stillbirth (%)	5137	7.35	-
Nest mortality (%)	5069	9.81	-

The total prevalence of digestive, respiratory, infectious diseases and mortality recorded during the growing period are given in Table 3.

**Table 3. Mean prevalence (in %) of digestive, respiratory, all infectious diseases and mortality (%) recorded during the growing period.**

Trait	Mean
Digestive diseases	8.7
Respiratory diseases	7.1
All infectious diseases	21.3
Mortality	5.3

### ***Statistical analysis.***

The growth performances were analyzed with the PROC MIXED procedure of the SAS software (2008). The significant fixed effects ( $P < 0.05$ ) retained in the model were: the sire's resistance group ( $n = 2$ ), the combined effect batch \* genotype ( $n = 30$ ), the litter size at birth ( $n = 12$ ), the litter size at weaning ( $n = 10$ ), the parity of the birth litter ( $n = 4$ ). The effect of weaning age was added to the weaning weight model while the end of fattening age effect was added to the final weight model. Health traits were analysed with the same procedure and the same fixed effects but without the litter size and the parity of the birth litter, which were not significant for this model. The random common environment of the litter effect was added for growth and health traits to the model.

The reproduction performances were analyzed with the PROC MIXED procedure of the SAS software (2008). The fixed effects retained in the model were: the sire's resistance group ( $n = 2$ ), the combined effect year \* season \* farm ( $n = 26$ ), the combined effect parity \* physiological stage (lactating or not) ( $n = 9$ ). The random effect of the female was added to the model to take into account the repetition of female performances.

### ***Ethics.***

All experiments were conducted in accordance with the guidelines of the Directive 2010/63/EU of the European Parliament and of the Council and were approved by the ethical review board (APAFIS#3866-2016020113447262).

## **Results and Discussion**

Differences in least squares means of traits are presented in table 4. Weaning and final weight were not significantly higher in RG than in SG (+7 g,  $P=0.26$  and +14 g,  $P=0.10$  respectively). However Shrestha *et al.* (2018) estimated a favorable genetic correlation between resistance to pasteurellosis and average daily gain from birth to weaning recorded in inoculated animals of the same experiment. A moderate and favourable correlation between natural resistance to infectious diseases and weaning weight was also observed in another study carried in a commercial population ( $-0.34 \pm 0.12$ ) (Gunia *et al.*, 2018). All together these findings suggest that breeding for pasteurellosis resistance is not detrimental to breeding for growth traits. On the contrary, total number born and born alive were significantly lower in litters of RD than in litters of SD ( $-0.27$ ,  $P=0.02$  and  $-0.41$   $P=0.003$ ). These results suggest that breeding for resistance to pasteurellosis could decrease the prolificacy of does. However birth and nest mortality were not significantly different between litters of RD and SD.

**Table 4:** Differences in least squares means between offspring of resistant and susceptible sires for growth, diseases and reproduction traits, *P* value of the sire group effect and standard error of least square means (LSM) differences.

Trait	Difference resistant-susceptible	<i>P</i> value	Standard error of LSM difference
Weaning weight (g)	7	0.264	6
Final weight (g)	15	0.106	9
<b>Digestive diseases (%)</b>	<b>-1.673</b>	<b>0.031</b>	<b>0.776</b>
Respiratory diseases (%)	-0.698	0.284	0.652
<b>Infectious diseases (%)</b>	<b>-2.991</b>	<b>0.008</b>	<b>1.121</b>
Mortality (%)	-1.084	0.066	0.588
Fertility (0/1)	0.003	0.708	0.008
<b>Total number born / litter</b>	<b>-0.270</b>	<b>0.023</b>	<b>0.119</b>
<b>Number born alive / litter</b>	<b>-0.410</b>	<b>0.003</b>	<b>0.137</b>
<i>Stillbirth (%)</i>	<i>1.547</i>	<i>0.056</i>	<i>0.809</i>
Nest mortality (%)	-0.901	0.706	0.202

Prevalence of digestive diseases and infectious diseases were significantly lower in RG than in SG (-1.7 point,  $P=0.03$  and - 3.0 points,  $P=0.008$  respectively). This interesting result suggests that resistance to pasteurellosis assessed by an experimental infection using a single strain of *Pasteurella multocida* is favorably correlated to resistance to other infectious diseases. Gunia *et al.*, (2015) demonstrated that a composite trait grouping all disease syndromes was heritable in rabbit. However, there was almost no genetic correlation between digestive and respiratory disease traits. This result can be partly explained by the fact only one syndrome was recorded per animal. The difference in prevalence of respiratory disease between RG and SG is not significant (-0.70 point,  $P=0.28$ ). This could be explained by a lack of homogeneity in the recording of the trait between the different farms: some breeders considered only true respiratory symptoms (nasal discharges, pneumonia) while some others included some other symptoms related to pasteurellosis (abscesses, wryneck, eye infections).

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