

REPRODUCTION, WHEN FED TOXIC OR NON-TOXIC DIETS DURING CONTINUOUS COHABITATION, OF MICE SELECTED FOR RESPONSE TO FESCUE TOXICOSIS

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SUMMARY

In previous work, one mouse line was selected for resistance to fescue toxicosis (R) and a second line was selected for susceptibility (S). Post-weaning growth of R mice was less severely depressed by a toxic fescue-containing diet than was growth of S mice. The current experiment was conducted to determine whether long term reproduction of mice on a toxin-containing (+) versus non-toxic (-) diet was more severely depressed in S than in R mice. Twenty-eight mating pairs per line x diet combination were cohoused continuously for 36 weeks. Percentage changes in reproductive traits of mice on the toxin-containing diet, for R and S pairs respectively, were -11 and -28 for total number of offspring born, -7 and -24 for total number of offspring weaned, -11 and -13 for total number of litters produced per pair, -29 and -41 for grams of offspring weaned, and +1 and -1 for pup survival percentage to weaning. Selected lines differed in adaptation to the toxic diet as measured by its effect on several components of long term reproduction.

Keywords: selection, reproduction, fescue toxicosis, mice, continuous breeding

INTRODUCTION

Tall fescue (*Festuca arundinacea*) is a well adapted, hardy cool season grass used extensively as a forage in the southeastern United States. Concomitant with its agronomic benefits are several health challenges to cattle. These include fat necrosis, agalactia, fescue foot, and fescue toxicosis, which collectively result in heavy economic losses in the production system (Paterson *et al.* 1995). Mice are an excellent animal model for studying fescue toxicosis not only because they require little investment per unit but also because they exhibit measurable responses to *Acremonium coenophialum*, the endophyte responsible for toxin synthesis in affected plants (Zavos *et al.* 1987; Zavos *et al.* 1990; Godfrey *et al.* 1994).

Mouse lines in our laboratory have undergone seven generations of divergent selection for the impact of a toxin-containing diet on post-weaning gain. Growth depression caused by the toxic diet was greater in susceptible (S) than in the resistant (R) mice, and activities of two liver detoxification enzymes were higher in R than in S individuals (Hohenboken and Blodgett 1997). The current experiment was conducted to determine whether long term reproduction of R mice was less severely depressed by exposure to the toxic diet than reproduction of S contemporaries. Did selection create divergence in adaptability to the toxic diet, as measured by reproduction of continuously mated pairs?

MATERIALS AND METHODS

In the previous work, ICR mice (Harlan Sprague Dawley Inc., Indianapolis, IN) were divergently selected for seven generations for response to fescue toxicosis, resulting in susceptible (S) and resistant (R) lines (Hohenboken and Blodgett 1997). For the current experiment, offspring of generation 12 of both lines were weaned at three weeks of age and randomly assigned four like-sexed mice to a cage for a five week growing period. Within each line, half the cages were fed a finely ground and thoroughly mixed toxin-containing diet composed of one half rodent food and one half endophyte-infected KY-31 fescue seed (+) and half the cages were fed a ground and mixed non-toxic diet of one half rodent food and one half certified endophyte-free Forager fescue seed (-). This divided the population into four treatments: resistant mice on a non-toxic diet (R-), resistant mice on a toxic diet (R+), susceptible mice on a non-toxic diet (S-), and susceptible mice on a toxic diet (S+). At 8 weeks of age, 28 males and 28 females were sampled from each treatment and randomly mated (except that brother/sister matings were prohibited), for a total of 112 pairs. The four treatments were then assigned at random to adjacent cages in each of 32 blocks in two standard rodent cage racks. For laboratory conditions and management procedures see Hohenboken and Blodgett (1997).

Pairs were maintained in continuous cohabitation for 36 weeks. Mice were checked daily for new litters and the number of pups born, including dead pups, was recorded. Litters were weaned and pups weighed individually and killed on any day between 17 and 21 days postpartum. Pairs that failed to produce pups within a 56 day time limit were eliminated from the experiment.

The total numbers of pups born (tborn), of pups weaned (twean), and of litters produced (tnum) by each pair was recorded. In addition, weaning weights of all the pups from all litters produced by each pair were totaled (twght). The fifth variable, survival percentage, was computed from (twean) and (tborn). Each variable was analyzed by the GLM procedure in SAS (1985) with a model including sources of variation for line, diet, line x diet, and block.

RESULTS AND DISCUSSION

As shown in Table 1, averaged across diets, the R line was superior to the S line for all reproductive traits. Also, averaged across lines, the + diet caused significant and substantial reductions in all traits except pup survival percentage. Diets containing endophyte-infected fescue are known to influence both male and female reproduction (Zavos *et al.* 1987; Zavos *et al.* 1990; Godfrey *et al.* 1994), though it was not possible to tell in this study the extent to which males versus females were affected.

Line x diet interactions did not achieve statistical significance at $P < 0.05$, but this may be misleading. As shown in Figures 1-4, the reductions in a trait caused by the + diet, for R and S mice, respectively, were 11% and 28% for total number of pups born, 7% and 24% for total number of pups weaned, 11% and 13% for total number of litters produced, and 29% and 41% for total weight of pups weaned. This suggests better adaptability of R than S mice to the + diet. For pup survival percentage, there was no line x diet interaction.

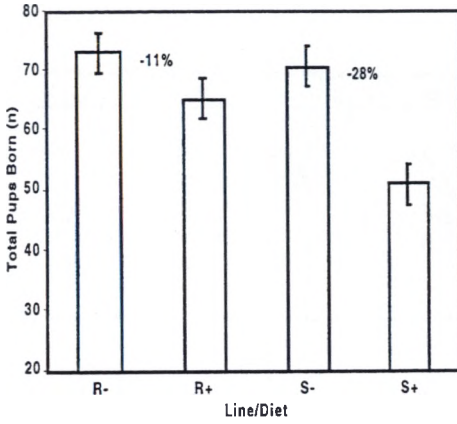


Figure 1. Total pups born per pair in 36 weeks cohabitation by resistant (R) and susceptible (S) mice on non-toxic (-) and toxic (+) diets.

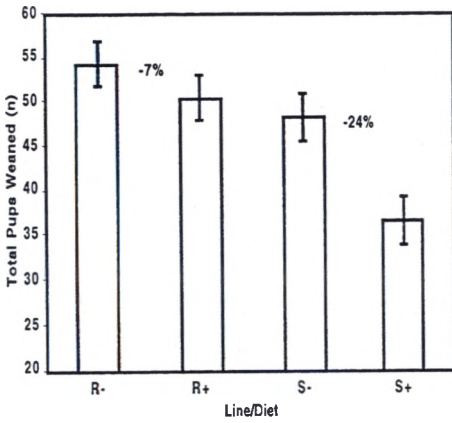


Figure 2. Total pups weaned per pair in 36 weeks cohabitation by resistant (R) and susceptible (S) mice on non-toxic (-) and toxic (+) diets.

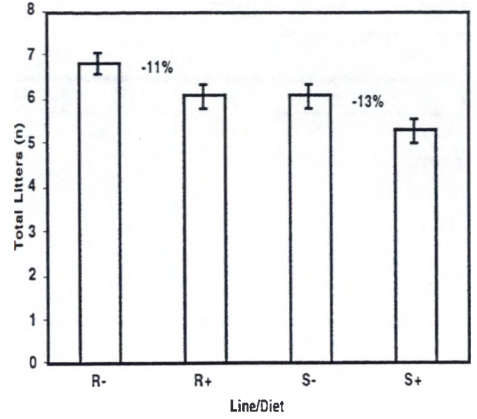


Figure 3. Total number of litters produced per pair in 36 weeks cohabitation by resistant (R) and susceptible (S) mice on non-toxic (-) and toxic (+) diets.

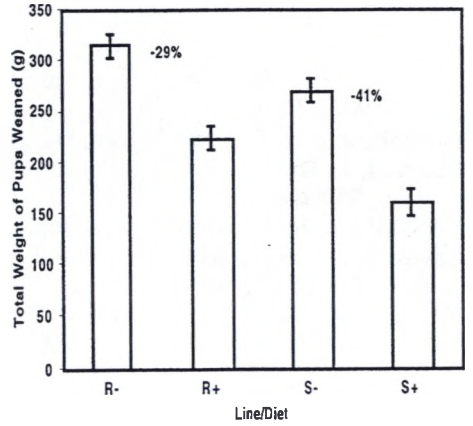


Figure 4. Total weight of pups produced per pair in 36 weeks cohabitation by resistant (R) and susceptible (S) mice on non-toxic (-) and toxic (+) diets.

Table 1. Least-squares means and P-values for line, diet, and interaction effects on reproductive traits

Trait	R	S	P _L ^A	(-)diet	(+)diet	P _D ^B	P _{LxD} ^C
tborn, n	69.2	61.0	0.02	71.9	58.2	<0.01	0.09
twean, n	52.4	42.4	<0.01	51.3	43.6	<0.01	0.14
tnum, n	6.4	5.7	<0.01	6.4	5.7	<0.01	0.98
twght, g	269.8	215.5	<0.01	293.0	192.3	<0.01	0.47
surviv, %	78	72	0.06	75	75	0.99	0.79

^AP-values for line effects.

^BP-values for diet effects.

^CP-values for line x diet interaction.

Earlier research established that the lines differed in the extent to which their post-weaning growth rate was depressed by the + diet and in activities of two liver detoxification enzymes (Hohenboken and Blodgett 1997). The results of this study indicate that these differences or possibly other coping mechanisms prevent reproduction in R mice from suffering as much as reproduction in S mice when challenged with the toxic diet.

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