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GENETIC AND SIDESTREAM SMOKE EFFECTS ON DIFFERENCES OF MURINE BIRTH WEIGHT

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Abstract: An inherent problem with any study involving the effects of an environmental factor on phenotypic expression is the separation of genetic from environmental impact. In this study, interstrain crosses of BALB/c and C57BL mice were examined in an attempt to separate genetic differences of birth weight from those produced by sidestream smoke. Birth weight means of progeny produced by parental generations of BALB/c (1.59 g) and C57BL (1.23 g) mice are significantly different ($P < 0.01$). Two sample T-tests of parental, F_1, F_2, and backcross generations show significant strain and treatment effects on birth weight variability and support an additive model of birth weight inheritance with no appreciable dominance. Two-way analysis of variance suggests that the influence of the genetic character of pups and dams is greater than that of the sires. Two-way analysis of variance also indicates that there is no interaction between genetic and sidestream smoke effects. A minimum number of two genes appears to be associated with murine birth weight.

INTRODUCTION

Numerous papers have discussed the effects of environmental factors on phenotypic expression. An environmental agent that has received attention in the past few years is sidestream smoke. Sidestream smoke is the smoke inhaled by nonsmokers by passive or involuntary smoking.

Recent research has shown that passive smoking may acutely aggravate angina pectoris (Aronow, 1978), increase the risk of fatal ischemic heart disease (Garland, *et al.,* 1985), induce small-airway dysfunction (Hulka, 1988; Tager, *et al.,* 1983; White and Froeb, 1980), enhance the effects of emphysema (Office of Smoking and Health, 1986), and increase the risk of lung cancer (Correa, *et al.,* 1983; Wigle, *et al.,* 1987). A reduction in the mean birth weight of infants of women passively-exposed to smoke has also been demonstrated (Campbell, *et al.,* 1988; Haddow, *et al.,* 1988; Martin and Bracken, 1986; Mochizuki, *et al.,* 1985).

In addition, a variety of animal studies have demonstrated the deleterious effects of sidestream smoke. These include reduced birth weight (Mays, 1986; Resnik and Marquard, 1980) and increased perinatal mortality (Essenberg, *et al.,* 1940; Mays, 1986; Mays, *et al.,* 1988).

An inherent problem with any study of the effects of an environmental factor on phenotypic expression is the separation of genetic impact from that of the environment (treatment). One of the major advantages of animal experimentation is that variables can be better controlled than they can in human studies. In this investigation, gene differences of birth weight of two inbred strains of mice were evaluated in an attempt to separate genetic from sidestream smoke (environmental) effects. Interstrain crosses between the two lines of mice were used to evaluate differences in birth weight. The following aspects of birth weight were assessed: the 1) degree of birth weight differences; the 2) influence of pup, dam, and sire genetic character; the 3) effect of sidestream smoke; the 4) type of genetic variance (e.g., additive or non-additive; dominance,

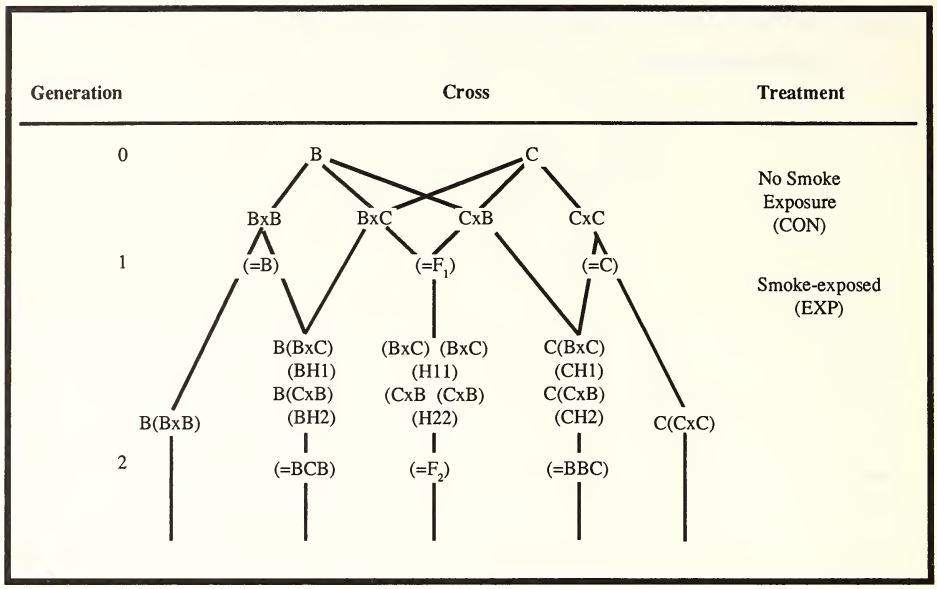

Figure 1. Schematic outline of genetic crosses performed between BALB/c (B) and C57BL (C) mice. Treatments for each generation are indicated. Parenthetical symbols are consistent with and identify the crosses as they are referred to in the analysis of results (e.g., BCB and BCC indicate backcrosses to the BALB/c and C57BL parents, respectively). The first letter of a cross represents the female.

incomplete dominance, or no dominance); and the 5) number of genes involved. Data were pooled by genetic character of pups, dams, and sires to illustrate strain (genetic) and treatment (environmental) effects.

MATERIALS AND METHODS

Crosses of adult BALB/cAnNHsd and C57BL/6NHsd mice were performed according to the scheme of Hayes (1987) as outlined in Figure 1. Symbol designates are: B = BALB/c, C = C57BL, H1 = hybrid produced by a BxC cross, H2 = hybrid produced by a CxB cross, BCB = backcross to BALB/c parent, and BCC = backcross to C57BL parent. The parental cross equals the 0 generation. The first letter of a cross represents the strain of the female.

Control and experimental female mice were mated overnight with appropriate males. The day a copulation plug was found was designated as gestation day 1. Pregnant mice were maintained in separate cages under environmental conditions controlled with respect to room temperature (20-25° C), humidity (55-60%), and photoperiod (12 hr light, 12 hr dark). They were fed Lab Blox pellets (Wayne Feed Division, Continental Grain Co.) and water *ad libitum* between trials.

Experimental mice were placed in a plexiglass smoking chamber (25.5 cm x 30.5 cm x 21.0 cm) containing 6 airholes 6.5 mm in diameter on two opposite sides and exposed each day of gestation (21 days) to sidestream smoke from one filter-tip cigarette. The duration of each smoking session was 40 minutes. At the end of each

Table 1. Genetic model for birth weight. Control cumulative (cum) mean birth weights of progeny obtained from parental, F1, F2, and backcrosses using the inbred strains of BALB/c and C57BL mice.

Cross	N[1]	Observed Birth Weight (g) (Mean ± SD)	Predicted Birth Weight (g)
BxB	21	1.593 ± 0.11	
CxC	25	1.231 ± 0.18 [2]	
P(cum)	**46**	**1.412 ± 0.21**	
BxC	19	1.500 ± 0.13	
CxB	24	1.380 ± 0.13	
F1(cum)	**43**	**1.440 ± 0.14**	**1.412 ns[3]**
H11	26	1.346 ± 0.11	
H22	10	1.294 ± 0.05	
F2(cum)	**36**	**1.320 ± 0.10**	**1.412***
BH1	15	1.480 ± 0.12	
BH2	22	1.468 ± 0.13	
H1B	8	1.422 ± 0.11	
H2B	12	1.412 ± 0.20	
BCB(cum)	**57**	**1.446 ± 0.15**	**1.513***
CH1	22	1.281 ± 0.11	
CH2	13	1.361 ± 0.04	
H1C	25	1.372 ± 0.13	
H2C	13	1.341 ± 0.08	
BCC(cum)	**73**	**1.339 ± 0.12**	**1.336 ns[3]**

[1] N = number of litters.
[2] The difference between BxB and CxC mean birth weights is significant ($P < 0.01$).
[3] ns = not significant.
* $P < 0.05$.

Table 2. Experimental cumulative (cum) mean birth weights of progeny obtained from parental, F1, F2, and backcrosses using the inbred strains of BALB/c and C57BL mice.

Cross	N[1]	Observed Birth Weight (g) (Mean ± SD)	Predicted Birth Weight (g)
BxB	38	1.526 ± 0.12	
CxC	35	1.219 ± 0.09[2]	
P(cum)	**73**	**1.373 ± 0.19**	
BxC	23	1.491 ± 0.12	
CxB	23	1.279 ± 0.13	
F1(cum)	**46**	**1.385 ± 0.16**	**1.373 ns[3]**
H11	74	1.371 ± 0.22	
H22	12	1.138 ± 0.08	
F2(cum)	**86**	**1.255 ± 0.22**	**1.373***
BH1	10	1.463 ± 0.06	
BH2	14	1.427 ± 0.20	
H1B	27	1.456 ± 0.19	
H2B	15	1.286 ± 0.14	
BCB(cum)	**66**	**1.408 ± 0.18**	**1.456 ns[3]**
CH1	15	1.280 ± 0.19	
CH2	8	1.252 ± 0.18	
H1C	8	1.263 ± 0.12	
H2C	14	1.249 ± 0.17	
BCC(cum)	**45**	**1.261 ± 0.16**	**1.302 ns[3]**

[1] Number of litters.
[2] The difference between BxB and CxC mean birth weights is significant ($P < 0.01$).
[3] ns = not significant.
* $P < 0.05$.

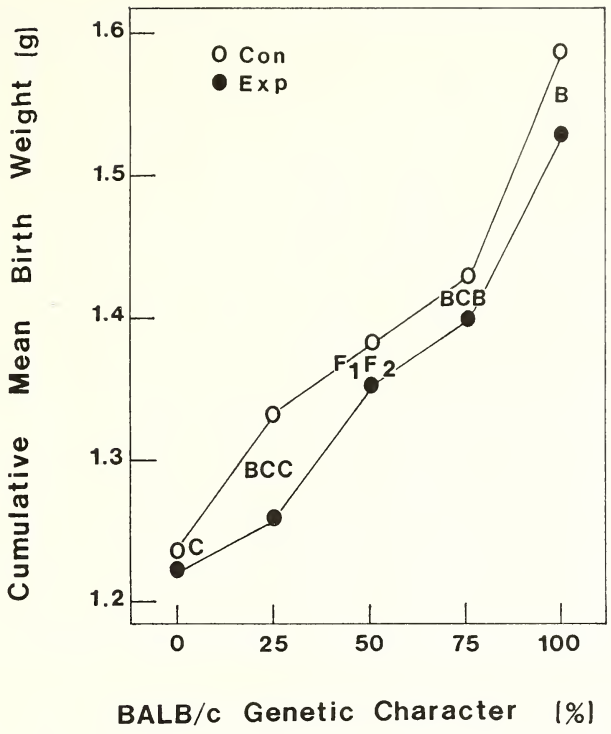

Figure 2. A comparison of cumulative mean birth weights of control and experimental progeny of crosses involving lines of BALB/c (B) and C57BL (C) mice. F1F2 represents the mean value of F1 and F2 progeny.

treatment period, dams were returned to their respective cages. Treatment was terminated at parturition. On postnatal day 1 (within 16 hr of birth), all litters were sexed and weighed. A total of four groups (F_1, F_2, BCB, BCC) were set up following the scheme in

$$E_F1 = (BW_B + BW_C)/2$$
$$E_F2 = (BW_B + BW_C)/2$$
$$E_BCB = (BW_C + BW_F1)/2$$
$$E_BCC = (BW_C + BW_F1)/2.$$

Statistical analyses were made using the Minitab program and VAX (Digital) mainframe computer. Two sample T-tests were used to compare observed and predicted cumulative mean birth weight values and to analyze differences between control mean birth weights (genetic effects), differences between experimental mean birth weights (treatment effects), and differences between control and experimental mean birth weights. Two-way analysis of variance (Rohlf and Sokal, 1969) was used to test for genetic (strain) effects, treatment (environmental effects), and interaction of strain and treatment as a function of pup, dam, and sire genetic character.

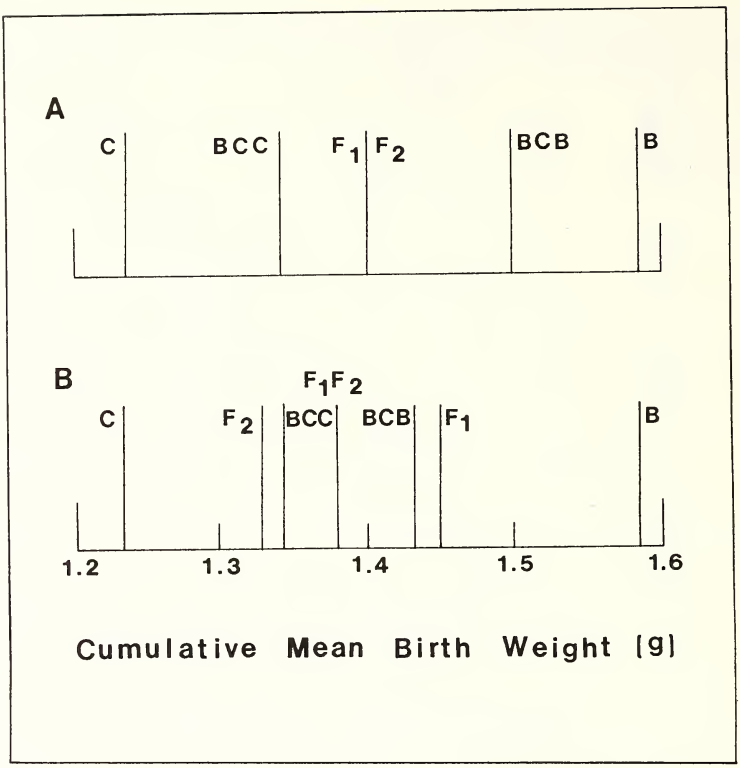

Figure 3. A comparison of observed cumulative mean birth weights among control progeny of crosses involving lines of BALB/c and C57BL mice with results predicted for an additive model with no dominance. Actual data for BALB/c (B), C57BL (C), and F1 were used to calculate expected values for F2 and the backcrosses to the BALB/c (BCB) and C57BL (BCC) lines. F1F2 represents the mean value of F1 and F2 progeny.

An estimate of the minimum number of genes contributing to character variation expressed by a quantitative trait (Angus, 1983; Lande, 1981) was used to define more precisely the genetic architecture underlying the differences in birth weight of the BALB/c and C57BL mouse populations.

RESULTS

Comparisons of cumulative mean birth weights of parental, F_1, F_2, and backcross generations are shown for control (Table 1) and experimental mice (Table 2). The progeny mean birth weight of BALB/c controls (1.593 g) differs significantly ($P < 0.01$) from the mean birth weight of C57BL control progeny (1.231 g), and the mean birth weight of BALB/c experimental progeny (1.526 g) differs significantly ($P < 0.01$) from the mean birth weight of C57BL experimental progeny (1.219 g).

Our results suggest that the genetic effect on birth weight is additive (Figure 2). The data were tested to see if they fit an additive model with no dominance according to an inheritance model described by Henrich and Denlinger (1983). If inheritance of birth weight is additive with no dominance, the F_1 progeny should show a cumulative mean

Table 3. A comparison of mean birth weights (BW) of control and smoke-exposed mice as a function of pup genetic character.

% BALB Genetic Char (Pups)	Con Cross	N[1]	BW	Group Pooled N	Group Pooled BW[2]	Exp Cross	N	BW	Group Pooled N	Group Pooled BW[2]
0	CxC	25	1.23	25	1.23 (0.18)	CxC	35	1.22	35	1.22 (0.09)
25	CH1	22	1.28	73	1.34	CH1	15	1.28	45	1.26
	CH2	13	1.36		(0.12)	CH2	8	1.25		(0.16)
	H1C	25	1.37			H1C	8	1.26		
	H2C	13	1.34			H2C	14	1.25		
50	BxC	19	1.50	36	1.38	BxC	23	1.49	132	1.32
	CxB	24	1.38		(0.12)	CxB	23	1.28		(0.19)
	H11	26	1.35			H11	74	1.37		
	H22	10	1.29			H22	12	1.14		
75	BH1	15	1.48	57	1.45	BH1	10	1.46	66	1.41
	BH2	22	1.47		(0.15)	BH2	14	1.43		(0.18)
	H1B	8	1.42			H1B	27	1.46		
	H2B	12	1.41			H2B	15	1.29		
100	BxB	21	1.59	21	1.59 (0.11)	BxB	38	1.53	38	1.53 (0.12)

F-Interaction = (MS INTER)/(MS ERROR); 4df/140df
= 0.00424/0.00302
= 1.04 ns[3]

F-Strain = (MS STRAIN)/(MS ERROR); 4df/140df
= 0.48865/0.00302
= 161.805**

F-Treatment = (MS TREAT)/(MS ERROR); 1df/140df
= 0.07990/0.00302
= 26.457**

[1] N = number of litters.
[2] Pooled mean birth weights (± SD) for the various genetic groupings.
[3] ns = not significant.
** $P < 0.01$.

Table 4. A comparison of mean birth weights (BW) of control and smoke-exposed mice as a function of dam genetic character. F- ratios are presented for two-way analysis of variance of observed (pooled) data.

% BALB Genetic Char (Pups)	Con Cross	N[1]	BW	Group Pooled N	Group Pooled BW[2]	Exp Cross	N	BW	Group Pooled N	Group Pooled BW[2]
0	CxB	24	1.38	84	1.31	CxB	23	1.28	81	1.26
	CH1	22	1.28		(0.12)	CH1	15	1.28		(0.15)
	CH2	13	1.36			CH2	8	1.25		
	CxC	25	1.23			CxC	35	1.22		
50	H1B	8	1.42	94	1.36	H1B	27	1.46	150	1.30
	H2B	12	1.41		(0.11)	H2B	15	1.29		(0.15)
	H11	26	1.35			H11	74	1.37		
	H22	10	1.29			H22	12	1.14		
	H1C	25	1.37			H1C	8	1.26		
	H2C	13	1.34			H2C	14	1.25		
100	BxB	21	1.59	77	1.51	BxB	38	1.53	85	1.48
	BH1	15	1.48		(0.13)	BH1	10	1.46		(0.13)
	BH2	22	1.47			BH2	14	1.43		
	BxC	19	1.50			BxC	23	1.49		

F-Interaction = (MS INTER)/(MS ERROR); 2df/84df
= 0.00098/0.00385
= 0.255 ns[3]

F-Strain = (MS STRAIN)/(MS ERROR); 2df/84df
= 0.4127/0.00385
= 107.057**

F-Treatment = (MS TREAT)/(MS ERROR); 1df/84df
= 0.04947/0.0038
= 12.849**

[1] N = Number of litters.
[2] Pooled mean birth weights (± SD) for the various genetic groupings.
[3] ns = not significant.
** $P < 0.01$.

Table 5. A comparison of mean birth weights (BW) of control and smoke-exposed mice as a function of sire genetic character. F-ratios are presented for two way analysis of variance of the observed (pooled) data.

% BALB Genetic Char (Pups)	Con Cross	N[1]	BW	Group Pooled N	Group Pooled BW[2]	Exp Cross	N	BW	Group Pooled N	Group Pooled BW[2]
0	BxC	19	1.50	82	1.36	BxC	23	1.49	80	1.31
	H1C	25	1.37		(0.13)	H1C	8	1.26		(0.13)
	H2C	13	1.34			H2C	14	1.25		
	CxC	25	1.23			CxC	35	1.22		
50	BH1	15	1.48	108	1.37	BH1	10	1.46	133	1.32
	BH2	22	1.47		(0.09)	BH2	14	1.43		(0.16)
	H11	26	1.35			H11	74	1.37		
	H22	10	1.29			H22	12	1.14		
	CH1	22	1.28			CH1	15	1.28		
	CH2	13	1.36			CH2	8	1.25		
100	BxB	21	1.59	65	1.45	BxB	38	1.53	103	1.39
	H1B	8	1.42		(0.14)	H1B	27	1.46		(0.15)
	H2B	12	1.41			H2B	15	1.29		
	CxB	24	1.38			CxB	23	1.28		

F-Interaction = (MS INTER)/(MS ERROR); 2df/84df
= 0.00026/0.00913
= 0.0285 ns[3]

F-Strain = (MS STRAIN)/(MS ERROR); 2df/84df
= 0.12402/0.00913
= 13.584**

F-Treatment = (MS TREAT)/(MS ERROR); 1df/84df
= 0.04733/0.00918
= 5.184*

[1] N = Number of litters.
[2] Pooled mean birth weights (± SD) for the various genetic groupings.
[3] ns = not significant.
* $P < 0.05$.
** $P < 0.01$.

Table 6. Comparison of the effects of genotype (controls) and environment (treatment) on birth weight (BW) as a function of pup genetic character determined by differences between controls (genetic effects) and differences between experimentals (treatment effects). The first letter of a cross represents the female.

Genetic Charac (Pups)	Differences Between Control Mean Birth Weights (Genetic Effects) Cross/(BW)	Differences Between Experimental Mean Birth Weights (Treatment Effects) Cross/(BW)	Control vs Experimental Differences Cross/(BW)
100% BALB/c	no diff	no diff	BxB * (1.59/1.53)
75% BALB/c 25% C57	no diff	BH1 vs H2B ** (1.46) (1.29) HIB vs H2B ** (1.46) (1.29)	no diff
50% BALB/c 50% C57	BxC vs CxB ** (1.50) (1.38) H11 ** (1.35) H22 ** (1.29) CxB vs H22 * (1.38) (1.29)	BxC vs CxB ** (1.49) (1.28) H11 ** (1.37) H22 ** (1.14) CxB vs H11 * (1.28) (1.37) H22 ** (1.14) H11 vs H22 ** (1.37) (1.14)	H22 ** (1.29/1.14) CxB * (1.38/1.28)
25% BALB/c 75% C57	CH1 vs H1C * (1.28) (1.37) CH2 * (1.36)	no diff	H1C * (1.37/1.26)
100% C57	no diff	no diff	no diff

* $P < 0.05$.
** $P < 0.01$.

Table 7. Comparison of the effects of genotype (controls) and environment (treatment) on birth weight (BW) as a function of dam genetic character determined by differences between controls (genetic effects) and differences between experimentals (treatment effects). The first letter of a cross represents the female.

Genetic Charac (Dams)	Differences Between Control Mean Birth Weights (Genetic Effects) Cross/(BW)	Differences Between Experimental Mean Birth Weights (Treatment Effects) Cross/(BW)	Control vs Experimental Differences Crosss/(BW)
100% BALB/c	BxB vs BH1 * (1.59) (1.48) BH2 * (1.47) BH1 ** (1.48) BxC * (1.50)	BxB vs BH1 * (1.53) (1.46)	BxB * (1.59/1.53)
50%BALB/c 50%C57	H1B vs H22 * (1.42) (1.29) H22 vs H1C * (1.29) (1.37)	H1B vs H2B ** (1.46) (1.29) H22 ** (1.14) H1C ** (1.26) H2C ** (1.25) H2B vs H22 ** (1.29) (1.14) H11 vs H22 ** (1.37) (1.14) H1C ** (1.26) H22 vs H1C * (1.14) (1.26)	H1C * (1.37/1.26) H22 * (1.29/1.14)
100% C57	CxB vs CH1 ** (1.38) (1.28) CxC * (1.23) CH1 vs CH2 * (1.28) (1.36) CxC ** (1.23) CH2 vs CxC * (1.38) (1.23)	CxB vs CxC * (1.28) (1.22)	CxB * (1.38/1.28)

* $P < 0.05$.
** $P < 0.01$.

Table 8. Comparison of the effects of genotype (controls) and environment (treatment) on birth weight (BW) as a function of sire genetic character determined by differences between controls (genetic effects) and differences between experimentals (treatment effects). The first letter of a cross represents the female.

Genetic Charac (Sires)	Differences Between Control Mean Birth Weights (Genetic Effects)	Differences Between Experimental Mean Birth Weights (Treatment Effects)	Control vs Experimental Differences
	Cross/(BW)	Cross/(BW)	Cross/(BW)
100% BALB/c	BxB vs H1B **	BxB vs H2B **	BxB *
	(1.59) (1.42)	(1.53) (1.29)	(1.59/1.53)
	H2B *	CxB **	CxB *
	(1.41)	(1.28)	(1.38/1.28)
	CxB **	H1B *	
	(1.38)	(1.46)	
50%BALB/c	BH1 vs H11 **	BH1 vs H11 **	H22 **
50%C57	(1.48) (1.35)	(1.46) (1.37)	(1.29/1.14)
	H22 **	H22 **	
	(1.29)	(1.14)	
	CH1 **	CH1 **	
	(1.28)	(1.28)	
	CH2 **	CH2 **	
	(1.36)	(1.25)	
	H11 vs CH1 *	H11 vs H22 **	
	(1.35) (1.28)	(1.37) (1.14)	
	CH1 vs CH2 *	H22 vs CH1 *	
	(1.28) (1.36)	(1.14 (1.28)	
100% C57	BxC vs H1C **	BxC vs H1C **	H1C *
	(1.50) (1.37)	(1.49) (1.26)	(1.37/1.26)
	H2C **	H2C **	
	(1.34)	(1.25)	
	CxC **	CxC **	
	(1.23)	(1.23)	

* $P < 0.05$.
** $P < 0.01$.

Table 9. Estimates (n ± SE) of the minimum number of genes contributing to the variation observed in progeny birth weights of BALB/c and C57BL lines revealed through crosses (made according to the scheme presented in Figure 1).

Population	N	μ	σ
PC57	25	1.231	0.01368900
BCC	68	1.333	0.02220100
F1	43	1.433	0.02073600
F2	36	1.332	0.00913936
BCB	40	1.437	0.01354890
PBALB	21	1.593	0.11363500

$n_1 = 1.3969491 \pm 0.6504702$ $n_3 = 2.8311284 \pm 5.2160255$

$n_2 = 1.6358308 \pm 0.8448572$ $n_4 = 1.1502128 \pm 0.5668104$

N = Litter size.
μ = Cumulative mean birth weight.
σ = Variance.

birth weight intermediate between the two parental lines. The actual F_1 cumulative mean birth weight (1.440 g) does not vary significantly from the predicted value of 1.412 g. Furthermore, statistical analysis produced no significant differences between the predicted (1.336 g) and observed (1.339 g) birth weights for the BCC cross (Table 1). Thus, an additive model with no dominance for birth weight is assumed. The observed values and those predicted by an additive model with no dominance are shown in Figure 3. The same general pattern of birth weight inheritance occurs for the smoke-exposed progeny (Table 2).

Comparative mean birth weight data for control and experimental crosses were analyzed as a function of pup, dam, and sire genetic character. Five genetic categories (100% BALB/c, 75% BALB/c:25% C57BL, 50% BALB/c:50% C57BL, 25% BALB/c:75% C57BL, and 100% C57BL) were used to analyze the effect of pup genetic character on birth weight (Table 3). Three genetic categories (100% BALB/c, 50% BALB/c:50% C57BL, and 100% C57BL) were used to examine the effect of dam genetic character (Table 4) and sire genetic character (Table 5) on birth weight. Control and experimental pooled data for pup, dam, and sire genetic character produce an additive pattern. Although the analysis of both dam and sire genetic character indicates a slight bias toward the C57BL line, no significant differences were noted between any of the predicted and observed pooled values. Two-way analysis of variance shows the

impact of genetic (strain) effects, treatment (environmental) effects, and interaction of strain and treatment as a function of pup (Table 3), dam (Table 4), and sire (Table 5) genetic character. Data from Tables 3 (pups), 4 (dams), and 5 (sires) were used to make a comparison of the effects of genetic character (strain) and environment (treatment) on birth weight. These effects were determined by differences between control mean birth weights (genetic effects), differences between experimental mean birth weights (treatment effects), and differences between control and experimental mean birth weights (genetic vs treatment effects) for pup (Table 6), dam (Table 7), and sire (Table 8) genetic character.

The minimum number of genes contributing to quantitative character variation between and within populations was estimated using the method proposed by Lande (1981). An estimate of two genes was obtained by comparing the phenotypic means (μ) and the variances (σ) of the cumulative mean birth weights of parental (n_1), F_1 (n_2), F_2 (n_3), and backcross (n_4) generations. The results are presented in Table 9.

DISCUSSION

A major difficulty associated with the analysis of the impact of environmental factors on a given phenotype is the separation of genetic effects. This investigation of the influence of sidestream smoke on the birth weight of mice is an attempt to make such a determination.

Employing modified Mendelian techniques, our control data from crosses between BALB/c and C57BL mice tend to fit an additive model of birth weight inheritance with no appreciable dominance. These results are in agreement with body weight inheritance for mammals in general (Roberts, 1981). Body weight tends to be highly heritable, where almost half of the natural variation may be genetic, and suggests that body weight is not a major component of fitness (Roberts, 1981). The results from smoke-exposed mice generally fit an additive model as well. However, for both control and experimental results, the fit to an additive model with no dominance is not perfect. The F_2 and BCB control crosses (Table 1) and the F_2 experimental cross (Table 2) differ from their respective predicted birth weights. In each of these cases, the observed cumulative birth weights are significantly lower than the birth weight predicted by the additive model. For example, the control F_2 cumulative mean birth weight is 1.320 g, which is significantly lower than the predicted weight of 1.412 g, but is close to the weight (1.380 g) of the lighter CxB parent. The fact that pooled mean birth weight data as a function of pup genetic character (Table 3), dam genetic character (Table 4), and sire genetic character (Table 5) demonstrate an additive pattern and that there are no significant differences between any of the predicted and observed pooled mean birth weights is supportive of an additive genetic model of birth weight inheritance with no dominance.

Two-way analysis of variance shows that there are significant strain (genetic) and treatment (environmental) effects on birth weight. F-ratios (Tables 3-5) suggest that genetic differences between pups and between dams have a larger effect on birth weight variability than do genetic differences between sires. The lack of significant interaction between genetic and sidestream smoke effects lends further support for an additive model of birth weight inheritance.

In some genetic categories, the genetic effects (differences between controls) and treatment effects (differences between experimentals) have an impact on birth weight variation. This is observed in the comparison of the crosses BxC and CxB in the

50%B:50%C category of pup genetic character (Table 6). In other cases, only the effects of genotype or treatment affect birth weight. A comparison of the control crosses CH1 (1.28 g) vs H1C (1.37 g) in the 25% B:75% C category of pup genetic character reveals significant genetic variation (Table 6). However, when exposed to sidestream smoke (experimental crosses), CH1 pup weight is unaffected (1.28 g vs 1.28 g), whereas H1C birth weight is reduced from 1.37 g to 1.26 g. Thus, the comparative birth weights upon smoke exposure (treatment effects) of 1.28 g (CH1) vs 1.26 g (H1C) are no longer significantly different. Similar examples are observed as a function of dam (Table 7) and sire (Table 8) genetic character.

There are four crosses that are significantly affected by sidestream smoke as shown by a comparison of differences between control and experimental mean birth weights. These crosses include BXB, CxB, H1C, and H22 with birth weight reductions of 0.07 g (4.4%), 0.10 g (7.3%), 0.11 g (8.0%), and 0.15 g (11.6%), respectively (Tables 6-8).

An important genetic factor controlling progeny birth weight is dam size. However, this does not completely explain the additive genetic effect noted. Dam size generally agrees with corresponding pup birth weight, but not absolutely. For instance, BALB/c dams are the largest (27.6 g) and have the largest pups (1.593 g), whereas C57BL dams are the smallest (21.4 g) and have the smallest pups (1.231 g). F_1 dams are intermediate in size (22.7 g) and have pups of intermediate size (1.440 g). But, although F_1 pup size falls in the predicted range based on an additive genetic model with no dominance, the dams are only slightly larger than C57BL dams. Therefore, additional genetic factors are indicated with regard to birth weight inheritance.

Following a mathematical model of Lande (1981), with modifications, four estimates were made of the minimum number of genes contributing to the variation in birth weight between and within BALB/c and C57BL lines. These estimates consistently indicate there are approximately two genes controlling birth weight of these two inbred murine lines. However, the estimate based on F_2 data was somewhat higher ($n_3 = 5.2$). The minimum number of genes estimated by this method can not exceed the number of chromosomal segments segregating independently in one generation (Lande, 1981). This is known at the **recombination index** (Darlington, 1937) and equals the haploid number of chromosomes plus the mean number of recombination events per gamete. In most higher plants and animals, the number of recombinations is limited to one or a few per chromosome per generation, so that the recombination index is usually on the order of a few times the haploid number of chromosomes. Since mice have a haploid number of 20, the actual number of genes associated with birth weight is probably greater than two with some linkage between them. The estimates reported here are in line with the average range of 5-10 genes reported for similar genotypic studies (Lande, 1981).

SUMMARY

The purposes of this investigation were to determine the model that best fits murine birth weight inheritance, to separate genetic from environmental (sidestream smoke) influences on birth weight, and to identify the minimum number of genes associated with birth weight heritability. The results showed: that 1) the general pattern of birth weight inheritance is additive with no appreciable dominance, and that the same pattern occurred in smoke exposed mice; that 2) both genetic factors and sidestream smoke have a significant effect on birth weight variance; that 3) there is no significant interaction be-

tween genetic effects and sidestream smoke (treatment) effects; that 4) some crosses (genetic groups) involving C57BL and BALB/c strains are affected by sidestream smoke more than others; and that 5) the minimum number of genes controlling birth weight was found to be about two.

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