
The Growth in Weight and Tail Length of Inbred and Hybrid Mice Reared at Two Different Temperatures. I. Growth in Weight. II. Tail Length

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THE GROWTH IN WEIGHT AND TAIL LENGTH OF INBRED AND HYBRID MICE REARED AT TWO DIFFERENT TEMPERATURES

I. GROWTH IN WEIGHT II. TAIL LENGTH

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PART I

Four inbred strains of mice and the F_1 hybrids between them have been reared from 3 to 16 weeks of age at 70 °F (d.b.), 61 °F (w.b.) (control-reared) and 90 °F (d.b.), 85 °F (w.b.) (heat-reared), using a split-litter experimental design. It is shown that growth in body weight is in part determined by environmental temperature. The weight of young heat-reared mice usually increases more rapidly than that of their control-reared litter-mates but at later ages, particularly during the maturation period, the latter typically grow more rapidly. The magnitude and direction of the environmentally determined responses is dependent upon the genotype of the animals. The growth of the F_1 hybrids in the two environments is more similar than the growth of the inbreds from which they were derived, and the differences in the responses of the various hybrids are smaller than the corresponding inbred differences. To some extent, however, the response of a hybrid can be predicted from the responses of its inbred parents. The variability in weight of heat-reared animals is usually smaller than that of control-reared ones. The variabilities of the two environmental forms show the greatest difference soon after the animals are separated, but they become more similar with increasing age; in some genotypes the variation between the heat-reared animals may ultimately exceed that of the control-reared ones. There is a correspondence between the growth rate and the variance and it is concluded that both reflect the optimality of the environ-

ment: a rapid growth rate and a low variation indicating a favourable temperature. Heterozygotes in any one environment usually have a smaller variability than homozygotes and this is indicative of their greater homeostasis, but the similarity of one of the inbreds to the hybrids in weight variance behaviour and weight responses shows that a marked reduction in somatic fitness is not an inevitable consequence of inbreeding.

PART II

Four inbred strains of mice and the F_1 hybrids between them have been reared from 3 to 16 weeks of age at 70 °F (d.b.), 61 °F (w.b.) (control-reared) and 90 °F (d.b.), 85 °F (w.b.) (heat-reared) using a split-litter experimental design. It is shown that growth in tail length is in part determined by environmental temperature: the higher the temperature, the faster the growth rate and the longer the adult tail. The magnitude of the tail response depends as well upon the animal's genotype and its maternal environment. These factors operate principally in determining the size of the tail in one of the environments: the shorter the control tail length, the greater the response to the hot environment. This phenomenon accounts for the smaller within-genotype variability and the greater phenotypic similarity of the various genotypes of the heat-reared animals. When allowance is made, however, for differences in control tail length the hybrid response is greater than that of the inbreds. Since the hybrids typically also have a smaller variability in both environments, the evidence supports the hypothesis that heterozygotes have a greater developmental flexibility than homozygotes.

PART I. GROWTH IN WEIGHT

INTRODUCTION

Although the physiological processes of acclimatization to high temperatures have been extensively studied in a wide variety of adult homeotherms (Robinson 1952) the effects of different thermal conditions on growth have received little attention. Yet the few studies that have been made indicate that the growth in body weight of homeotherms is profoundly influenced, among other things, by the external temperature; over a wide range of temperatures, there exists an inverse relationship between temperature and both growth rate and adult size (Sumner 1909; Sundstroem 1922, 1930; Ogle 1934; Allee & Lutherman 1940; Sakharov 1949). The aims of the present investigation were to confirm the results of rearing mice at a high environmental temperature, using genetically homogeneous material and to study the effects of genetic and maternal differences on the nature and extent of the responses.

It has been repeatedly shown in recent years that inbred strains are generally not as well buffered against disturbances in their external environment as first-generation hybrids between any two such lines (Emmens 1939; Robertson & Reeve 1952; Mather 1953; Biggers & Claringbold 1954; Grüneberg 1954; Lerner 1954; McLaren & Michie 1954; Claringbold & Biggers 1955; Jinks & Mather 1955; Maynard-Smith, Clarke & Hollingsworth 1955; Chai 1956*a*; McLaren & Michie 1956). Both inbred and hybrid mice are, therefore, used for determining the comparative effects of homozygosity and heterozygosity on the variance in weight at different ages during growth, under different temperature conditions.

Although heterozygotes appear to have a greater phenotypic uniformity than homozygotes in any one environment, they might be expected to make a larger response than the homozygotes to a totally different environment if their greater homeostasis is indicative of a superior overall fitness and the response is adaptive. Such a hypothesis has already

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been suggested by Thoday (1953) and Maynard-Smith (1956), and in part confirmed in *Drosophila*. It is, therefore, proposed to compare the growth in weight responses of inbred and hybrid mice to two different temperatures with this hypothesis in mind.

MATERIALS AND METHODS

Four inbred strains of mice, *C57BL*, *CBA*, *RIII* and *A* and the six possible hybrids between them, including reciprocal crosses, were used. All the different genotypes were bred throughout the 4 years of experimentation, so that they were all exposed to any uncontrolled changes that might have occurred in the environments during this period. Experimental animals were weaned when they were 3 weeks old, and each litter divided into two groups; one kept in the room where they were bred, at 70 ± 2 °F dry-bulb temperature (d.b.), 61 ± 3 °F Assman wet-bulb temperature (w.b.), termed for convenience the control room, and the other transferred into an adjoining room maintained at 90 ± 1 °F (d.b.), 85 ± 2 °F (w.b.), termed the hot environment. The males and females in a litter were treated separately and their weights at the age of 3 weeks used as a basis for separating them into the two groups. The animals were ranked in order of decreasing weight and allocated alternately to the two environments. In the next litter to be weaned of the same genotype, or, in the case of reciprocal crosses, of the same type of mother, the heaviest male and female animals were placed in the opposite environment to the heaviest animals in the preceding litter. This split-litter design ensures that maternal and other pre-weaning environmental effects are more or less equally distributed among both groups of experimental animals and makes possible a within-litter comparison of subsequent environmentally induced responses.

The animals were kept in large, flat open-topped cages, the bases of which were refrigerator trays with a series of holes one-eighth of an inch in diameter bored through two of the sides to facilitate a free circulation of air. The temperature conditions inside these cages were identical to those outside. To counterbalance the effects of slight differences in temperature from one part of a room to another and, in particular, a vertical thermal stratification of about 1 °F in the hot room, the positions of the cages on the shelves were rotated daily. The animals were fed on a commercially prepared composition rat cake, analysis of which revealed the following ingredients: 20% wheat offals, 10% ground wheat, 20% oatmeal, 15% maize corn, 10% maize germ, 10% grass meal, 10% fish and 5% vitamins and minerals. Tap water was supplied *ad libitum*. Both rooms were lit for 9 h in every day (between 9 a.m. and 6 p.m.) with mercury vapour lamps controlled by the same time-switch.

After weighing, weaned animals were etherized, given a distinctive ear mark and put in a cage with animals born on the same day of the week. Each week, on this day, the animals were weighed to the nearest 0.1 g until they were 16 weeks old. It would, no doubt, have been desirable to keep each individual animal in its own cage after weaning, but this was impractical and a number of animals were kept together in the same cage. The unknown effects of this procedure were in part controlled by the split-litter design; this meant that the cage-mates in the two environments were very similar and since the numbers to a cage were always between six and twelve this environmental factor was kept as constant as was practicable throughout the experiment.

The total numbers of animals of each sex and genotype in the two environments used in the analysis at 3, 4, 8, 12 and 16 weeks of age are given in tables 1*a* and *b*. The number of animals decreases with increasing age; this is because animals were removed from the experiment for other purposes; there were very few natural deaths.

TABLE 1. NUMBERS OF ANIMALS IN CONTROL AND HOT ENVIRONMENTS

(a) INBREDS										
genotype	control age (weeks)					heat age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>males</i>										
<i>C57</i>	30	23	21	14	13	28	22	19	11	11
<i>CBA</i>	28	18	14	10	10	27	20	15	12	10
<i>RIII</i>	26	24	18	16	16	24	29	22	20	19
<i>A</i>	13	10	9	6	6	11	10	10	8	8
<i>females</i>										
<i>C57</i>	20	20	21	16	14	27	27	28	23	22
<i>CBA</i>	16	15	20	12	12	18	16	21	14	14
<i>RIII</i>	22	21	21	17	17	18	17	18	14	14
<i>A</i>	4	5	5	4	4	6	7	7	6	6
(b) HYBRIDS										
genotype, females × males	control age (weeks)					heat age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>males</i>										
<i>C57</i> × <i>CBA</i>	15	14	12	7	7	16	15	13	10	10
<i>CBA</i> × <i>C57</i>	9	9	9	4	4	9	9	9	4	4
<i>C57</i> × <i>RIII</i>	50	42	40	21	16	55	44	48	26	20
<i>RIII</i> × <i>C57</i>	19	19	18	13	13	19	19	17	12	12
<i>C57</i> × <i>A</i>	31	26	20	16	12	24	23	16	13	11
<i>A</i> × <i>C57</i>	16	15	10	8	8	14	14	8	6	6
<i>CBA</i> × <i>RIII</i>	7	7	4	4	4	5	5	3	3	3
<i>RIII</i> × <i>CBA</i>	4	4	4	4	4	6	6	6	6	6
<i>CBA</i> × <i>A</i>	18	16	17	14	14	18	16	18	15	15
<i>A</i> × <i>CBA</i>	7	7	7	4	5	7	6	6	5	5
<i>RIII</i> × <i>A</i>	24	23	18	14	9	23	22	19	14	8
<i>A</i> × <i>RIII</i>	7	6	3	—	—	7	5	2	—	—
<i>females</i>										
<i>C57</i> × <i>CBA</i>	15	15	12	11	11	16	16	13	11	11
<i>CBA</i> × <i>C57</i>	14	14	11	3	4	13	13	11	2	4
<i>C57</i> × <i>RIII</i>	44	32	42	24	25	48	35	49	26	31
<i>RIII</i> × <i>C57</i>	29	29	29	20	20	27	27	27	21	21
<i>C57</i> × <i>A</i>	27	27	26	18	16	27	26	24	18	17
<i>A</i> × <i>C57</i>	15	15	11	6	9	12	11	11	6	10
<i>CBA</i> × <i>RIII</i>	9	6	5	1	1	12	8	6	1	1
<i>RIII</i> × <i>CBA</i>	5	2	4	4	4	5	3	5	5	5
<i>CBA</i> × <i>A</i>	15	11	15	15	15	13	9	13	13	13
<i>A</i> × <i>CBA</i>	8	8	8	6	3	11	11	10	8	5
<i>RIII</i> × <i>A</i>	21	20	18	14	11	19	18	17	13	10
<i>A</i> × <i>RIII</i>	8	8	8	6	6	7	7	7	5	5

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TABLE 2. MEAN WEIGHTS IN CONTROL AND HOT ENVIRONMENTS

(Expressed in grams.)

(a) INBREDS

genotype	control males age (weeks)					heat males age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>C57</i>	7.8	8.9	18.2	23.1	24.8	7.8	11.4	17.9	21.9	24.2
<i>CBA</i>	6.1	8.7	17.0	22.0	24.7	6.3	9.4	16.1	18.5	21.4
<i>RIII</i>	8.0	10.3	19.2	22.9	24.9	8.1	11.8	18.0	20.8	22.0
<i>A</i>	7.4	9.1	15.8	18.0	21.5	7.2	10.6	17.3	20.3	23.0

genotype	control females age (weeks)					heat females age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>C57</i>	8.0	9.7	15.7	18.2	19.1	8.1	11.1	15.7	17.8	19.3
<i>CBA</i>	7.0	9.9	16.7	18.8	20.5	7.0	10.8	15.8	17.6	19.1
<i>RIII</i>	7.9	10.0	16.4	18.0	19.4	8.0	11.3	15.6	17.2	18.0
<i>A</i>	7.1	8.8	13.3	15.8	17.0	7.3	9.8	14.8	17.5	19.0

(b) HYBRIDS (*males*)

genotype females × males	control males age (weeks)					heat males age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>C57</i> × <i>CBA</i>	8.6	12.1	22.2	25.1	27.1	8.8	12.7	21.3	24.5	27.0
<i>CBA</i> × <i>C57</i>	10.0	14.3	23.8	27.4	29.5	10.2	15.1	22.8	25.4	27.1
<i>C57</i> × <i>RIII</i>	7.1	9.7	21.9	25.8	27.3	7.2	11.3	21.1	25.5	27.3
<i>RIII</i> × <i>C57</i>	7.6	13.5	23.5	25.7	27.5	7.8	14.6	22.7	26.2	27.7
<i>C57</i> × <i>A</i>	8.4	10.9	21.5	25.2	27.9	8.9	12.8	20.8	23.9	27.3
<i>A</i> × <i>C57</i>	7.9	11.2	21.7	22.8	26.0	8.3	11.2	20.2	23.6	27.1
<i>CBA</i> × <i>RIII</i>	9.2	14.0	23.3	27.5	29.4	9.3	13.1	21.4	22.9	27.0
<i>RIII</i> × <i>CBA</i>	10.6	15.2	24.0	27.0	28.3	10.7	14.9	22.5	25.4	28.0
<i>CBA</i> × <i>A</i>	7.2	10.4	20.6	24.5	26.9	7.3	11.6	19.4	23.6	26.7
<i>A</i> × <i>CBA</i>	7.7	11.2	21.2	24.8	26.4	8.0	12.0	20.7	24.7	26.3
<i>RIII</i> × <i>A</i>	8.0	11.4	20.5	23.6	25.5	8.2	12.2	21.1	24.1	24.8
<i>A</i> × <i>RIII</i>	10.2	13.6	25.6	—	—	10.2	14.2	21.4	—	—

(c) HYBRIDS (*females*)

genotype females × males	control females age (weeks)					heat females age (weeks)				
	3	4	8	12	16	3	4	8	12	16
<i>C57</i> × <i>CBA</i>	8.3	11.1	17.8	20.6	21.7	8.2	11.6	17.5	20.2	22.1
<i>CBA</i> × <i>C57</i>	10.1	13.8	19.7	21.6	25.1	10.3	13.2	19.3	20.7	24.4
<i>C57</i> × <i>RIII</i>	7.2	9.9	18.0	20.8	21.9	7.3	11.6	17.8	20.6	22.0
<i>RIII</i> × <i>C57</i>	8.3	11.5	18.4	20.3	21.6	8.4	12.6	18.4	20.6	22.1
<i>C57</i> × <i>A</i>	8.5	11.7	18.8	21.5	22.7	8.6	11.8	18.0	20.4	22.7
<i>A</i> × <i>C57</i>	8.8	11.0	18.1	19.6	21.5	9.1	11.9	17.7	19.3	21.8
<i>CBA</i> × <i>RIII</i>	9.1	13.5	20.4	20.0	22.6	8.9	13.1	18.9	16.2	20.3
<i>RIII</i> × <i>CBA</i>	10.5	13.0	18.8	20.8	21.8	10.8	13.0	18.7	22.0	22.5
<i>CBA</i> × <i>A</i>	7.2	9.7	17.1	20.4	21.8	7.3	10.0	17.2	20.6	21.7
<i>A</i> × <i>CBA</i>	7.2	10.1	17.6	19.5	21.6	7.2	10.0	16.7	19.5	21.8
<i>RIII</i> × <i>A</i>	8.6	11.7	17.8	19.5	20.9	8.8	12.5	19.0	21.9	21.8
<i>A</i> × <i>RIII</i>	10.2	13.0	20.5	23.8	24.6	9.8	13.6	20.9	24.4	24.8

RESULTS

The mean weights of the control and heat-reared animals in each litter were calculated at each week of age, and from these litter means an overall mean for each genotype was derived. These means are based only on the litters which have both control and heat representatives of the same sex. The values for the four inbred strains, when they are 3, 4, 8, 12 and 16 weeks old, are given in table 2*a* and the corresponding values for the six hybrids, including reciprocal crosses, in tables 2*b* and *c*. These clearly demonstrate the heterosis of the hybrids in both environments. (The data for intermediate ages are tabulated in Harrison 1958*b*.)

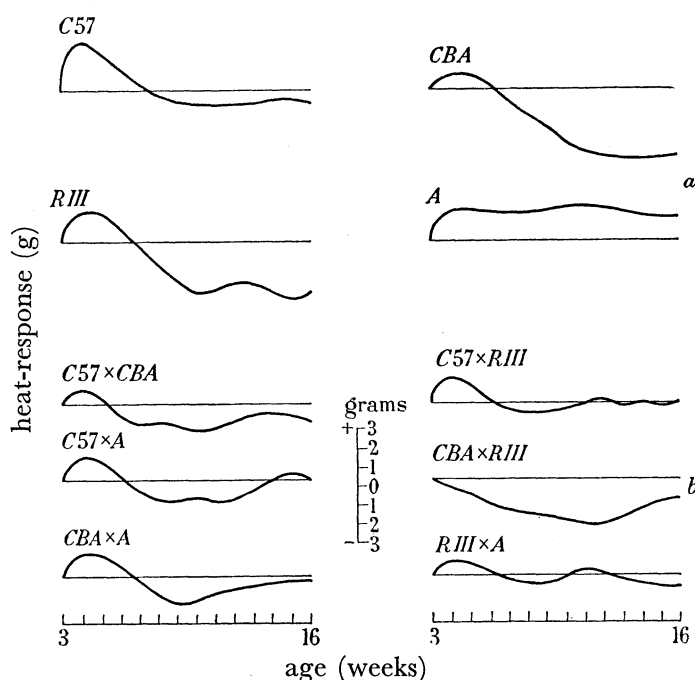


FIGURE 1. Body-weight heat-responses of (*a*) inbred and (*b*) F_1 hybrid male mice from 3 to 16 weeks of age.

Comparison of growth in the control and hot environments

(Throughout this paper 'significant' refers to the 5% level unless otherwise stated.)

The difference in growth of body weight produced by rearing animals in the two different environments may be termed the 'heat-response'; with the split-litter experimental design this is conveniently estimated as the mean of $(H-C)$ over all litters of a strain, i.e. the average difference between the mean weight (H) of litter-mates reared in the hot environment and the mean weight (C) of animals of the same litter reared in the control environment. The mean heat-responses of all the different genotypes at weekly ages are plotted in figures 1 and 2.

The statistical analysis is performed at 4, 8, 12 and 16 weeks of age; this samples the changes that occur when most of the growth in weight takes place and provides an analysis of the initial heat-responses when the animals are still small and of the responses during the maturation period. By 16 weeks, skeletal growth of the mouse is nearly complete and the transference of many animals at that age from one environment to the other considerably reduces the numbers available for a comparison of the simple heat-response.

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Table 3*a* gives the mean heat-responses, number of litters and standard deviations of the distribution for both the males and females of the four inbred strains. Before the corresponding figures for the hybrids are analyzed, it is necessary to know whether or not reciprocal crosses should be treated separately, i.e. whether or not the heat-response differs between the hybrids of the same genotype but with different type mothers. Analyses of variance reveal that there are no significant differences between the mean heat-responses of the female progeny of the reciprocal crosses at 4, 8, 12 and 16 weeks, nor between the male progeny at 4, 12 and 16 weeks; the significant difference found at 8 weeks can be attributed to the genotype $A \times RIII$; this is probably spurious since there are very few litters of the cross with the A mother at this age. It therefore appears that maternal effects are unimportant in determining the heat-response and, to facilitate the genetic analysis, the results for reciprocal crosses have been pooled in table 3*b* and figure 2.

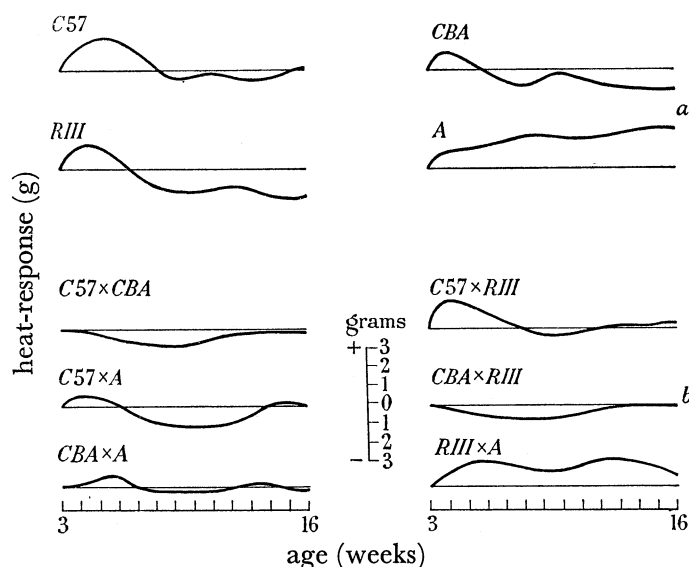


FIGURE 2. Body-weight heat-responses of (a) inbred and (b) F_1 hybrid female mice from 3 to 16 weeks of age.

Four weeks of age

From 3 to 4 weeks both the inbred and hybrid heat-reared animals grow more rapidly than their control-reared litter-mates. The overall estimates of the inbred heat-response at 4 weeks are 1.59 ± 0.254 g for the 58 male litters and 1.10 ± 0.208 g for the 47 female litters, with no significant differences between the strains. In both sexes, the $C57$ s make the greatest response, and in the case of the males this is significantly larger than the overall mean of the other inbreds.

The overall estimates of the hybrid heat-responses are 1.01 ± 0.173 g for the 114 male litters and 0.68 ± 0.139 g for the 119 female litters, but the 6 female genotypes are distinguishable by an analysis of variance, because of their smaller between-litter variance.

When the four inbred responses are compared individually with the overall hybrid responses by a t -test (the between-litter variances can be pooled since they do not differ significantly) it is found that the responses of the $C57$ males and $C57$ and $RIII$ females are significantly greater than the corresponding hybrid responses ($P < 0.01$, $P < 0.05$, $P < 0.05$ respectively).

The greater heat-response of the *C57*s is also reflected in those first-generation hybrids with a *C57* parent. This is clearly seen in table 4. Like *C57*, but to a lesser extent, the *A* contribution to the hybrids tends to produce a large positive response in the male progeny. On the other hand, the effect of a *CBA* parent is generally to reduce the response especially in the female offspring.

TABLE 3. MEANS AND STANDARD DEVIATIONS OF HEAT-RESPONSE

(Number of litters indicated in parentheses.)

genotype	age (weeks)							
	4		8		12		16	
	mean (g)	s.d.	mean (g)	s.d.	mean (g)	s.d.	mean (g)	s.d.
<i>(a) INBREDS</i>								
<i>males</i>								
<i>C57</i>	+2.47 (16)	1.656	-0.24 (14)	2.448	-1.17 (9)	2.284	-0.57 (9)	3.171
<i>CBA</i>	+0.68 (13)	2.068	-0.96 (10)	3.487	-3.47 (7)	1.580	-3.37 (7)	1.155
<i>RIII</i>	+1.52 (22)	2.067	-1.11 (17)	2.371	-2.19 (15)	2.163	-2.60 (15)	2.153
<i>A</i>	+1.52 (7)	1.012	+1.47 (7)	4.013	+2.30 (5)	2.589	+1.55 (5)	2.275
<i>females</i>								
<i>C57</i>	+1.39 (16)	1.528	+0.06 (17)	1.109	-0.35 (13)	1.801	+0.15 (13)	2.021
<i>CBA</i>	+0.89 (10)	1.660	-0.88 (13)	2.046	-1.14 (7)	1.569	-1.38 (7)	1.480
<i>RIII</i>	+1.24 (16)	1.175	-0.85 (17)	1.517	-0.87 (13)	1.543	-1.42 (13)	1.549
<i>A</i>	+0.96 (5)	1.674	+1.50 (5)	2.997	+1.69 (4)	1.217	+2.06 (4)	2.133
<i>(b) HYBRIDS</i>								
<i>males</i>								
<i>C57</i> × <i>CBA</i>	+0.74 (19)	2.180	-0.92 (18)	1.479	-1.14 (11)	1.620	-0.80 (11)	2.713
<i>C57</i> × <i>RIII</i>	+1.41 (36)	1.625	-0.65 (39)	2.523	+0.12 (20)	1.945	+0.11 (20)	1.203
<i>C57</i> × <i>A</i>	+1.21 (24)	2.337	-1.03 (18)	1.903	-0.47 (13)	2.407	+0.06 (13)	1.946
<i>CBA</i> × <i>RIII</i>	-0.60 (8)	1.384	-1.61 (6)	0.730	-2.60 (6)	1.885	-1.05 (6)	2.181
<i>CBA</i> × <i>A</i>	+1.12 (12)	0.649	-0.98 (13)	1.757	-0.75 (10)	1.507	-0.22 (10)	2.165
<i>RIII</i> × <i>A</i>	+0.78 (15)	1.590	-0.20 (12)	3.457	-0.08 (5)	1.489	-0.63 (5)	1.760
<i>females</i>								
<i>C57</i> × <i>CBA</i>	-0.09 (20)	1.671	-0.32 (16)	1.295	-0.52 (9)	1.313	+0.08 (10)	2.317
<i>C57</i> × <i>RIII</i>	+1.14 (39)	1.448	-0.13 (44)	1.313	+0.04 (26)	1.322	+0.23 (26)	1.695
<i>C57</i> × <i>A</i>	+0.64 (25)	1.437	-0.73 (24)	1.578	-0.91 (15)	1.263	+0.10 (16)	1.685
<i>CBA</i> × <i>RIII</i>	-0.31 (6)	0.992	-0.78 (6)	1.849	-0.04 (4)	2.798	-0.01 (4)	1.847
<i>CBA</i> × <i>A</i>	+0.16 (11)	1.689	-0.18 (13)	1.582	+0.14 (12)	1.820	+0.01 (11)	1.342
<i>RIII</i> × <i>A</i>	+0.70 (18)	0.946	+0.95 (17)	2.840	+1.83 (13)	2.649	+0.64 (11)	2.715

Eight weeks of age

At some time between the ages of 4 and 8 weeks, the growth rate of all the heat-reared hybrids and the inbreds, with the exception of the *As*, becomes slower than that of the control animals, and by 8 weeks the mean heat-responses are seen to be negative for all the hybrids apart from the female offspring of the mating *RIII* × *A*. The overall hybrid means are -0.80 ± 0.225 g for the 106 male litters and -0.16 ± 0.163 g for the 120 female litters, there being no significant differences between genotypes of the same sex.

Among the inbreds, the responses of the *C57*s, *CBA*s and *RIII*s do not differ significantly from one another or from the overall hybrid means. The *As*, however, are characterized at this age by their large positive heat-responses which are, both in the males and females,

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significantly greater than the corresponding overall means for the hybrids and the overall means for the other inbreds (-0.78 and -0.53 g for the males and females respectively). They are not, however, significantly greater in magnitude, i.e. the deviation from zero is not greater.

TABLE 4. INBRED EFFECTS ON HYBRID HEAT-RESPONSES AT 4 WEEKS

comparison	matings	males			females				
		mean of mean responses (g)	differ-ence (d)	s.e.	mean of mean responses (g)	differ-ence (d)	s.e.		
C57 with CBA	C57 × RIII	+1.31	+1.05	0.48	P < 0.05*	+1.03	+1.11	0.41	P < 0.01
	C57 × A								
	CBA × RIII	+0.26				-0.08			
	CBA × A								
C57 with RIII	C57 × CBA	+0.97	+0.88	0.49	P < 0.05	+0.28	+0.08	0.40	n.s.
	C57 × A								
	RIII × CBA	+0.09				+0.20			
	RIII × A								
C57 with A	C57 × CBA	+1.08	+0.13	0.44	n.s.	+0.66	+0.23	0.34	n.s.
	C57 × RIII								
	A × CBA	+0.95				+0.43			
	A × RIII								
CBA with RIII	CBA × C57	+0.93	-0.16	0.44	n.s.	+0.04	-1.02	0.34	P < 0.01
	CBA × A								
	RIII × C57	+1.09				+1.06			
	RIII × A								
CBA with A	CBA × C57	+0.07	-0.92	0.49	P < 0.05	-0.20	-0.87	0.40	P < 0.01
	CBA × RIII								
	A × C57	+0.99				+0.67			
	A × RIII								
RIII with A	RIII × C57	+0.41	-0.75	0.48	P < 0.1	+0.55	+0.15	0.41	n.s.
	RIII × CBA								
	A × C57	+1.16				+0.40			
	A × CBA								

* One-tailed *t*-test, using pooled between-litter variance for hybrids (table 5).

Because both the male and female *A* responses are distinguishable from those of the other inbreds at 8 weeks, an *A* effect has been looked for in the hybrid heat-responses by the same method as that used at 4 weeks (table 4). Although only one of the six possible comparisons involving hybrids with *A* parents attains significance, in four cases the heat-responses of the hybrids with an *A* component have smaller negative responses than the others, and in the other two cases the heat-response of the (*A* ×) hybrid is positive.

Twelve weeks of age

At this age, the inbreds have distinctive heat-responses, the *As* showing a positive response, the *C57s* a small negative response, and the *CBAs* and *RIII*s, especially in the males, a large negative response. The overall mean response for the male hybrids is -0.61 ± 0.247 g, which is similar to that for the *C57s*, but significantly different from the responses of the other inbreds. For the females, analysis of variance reveals significant

differences between the heat-responses of the six hybrid genotypes, but the overall mean of 0.10 g is similar in magnitude to that of the males.

The inbred effects on the heat-responses of the hybrids are analyzed as before. The heat-responses of the hybrids with a *CBA* parent are more negative in the males than the (*RIII* ×) hybrids, the (*C57* ×) hybrids ($P < 0.01$) and the (*A* ×) hybrids ($P < 0.05$), and in the females, than the (*A* ×) hybrids and the (*RIII* ×) hybrids ($P < 0.05$); it would seem then that some of the factors responsible for the large negative heat-responses of the inbred *CBA*s are transmitted to and function similarly in the hybrids with a *CBA* parent. It also appears that there is a direct *A* effect on the hybrid heat-responses which makes the response more positive since, in addition to the (*A* ×) hybrids having a less negative response than the (*CBA* ×) hybrids, the female hybrids with an *A* parent are more positive in their response than those with a *C57* parent ($P < 0.01$). A result which could not have been predicted from the inbred responses is the significantly more positive responses of the female (*RIII* ×) hybrids than the female (*C57* ×) hybrids ($P < 0.01$) and (*CBA* ×) hybrids ($P < 0.05$). The female responses of the (*RIII* ×) hybrids are also greater than those of hybrids with an *A* parent, and it would appear that, in the females, an *RIII* ancestry does not lower the heat-response as would have been expected if there were a direct inbred effect on the hybrids.

Sixteen weeks of age

An analysis of variance reveals no significant differences between the heat-responses of either the male or female hybrid genotypes, but the differences between the inbred strains are significant at the 1% level in both sexes. The overall means of the hybrid responses are -0.27 ± 0.238 g and 0.20 ± 0.212 g for the males and females respectively. The results of comparing each of the inbred responses with those of the overall hybrids show that the *C57*s are similar to the hybrids. On the other hand, the *RIII*s and *CBA*s are very different ($P < 0.001$ in both cases for the males, $P < 0.01$ and $P < 0.05$ respectively for the females) with the heat animals being very much smaller than the control ones. The relationship is reversed for the control and heat-reared *As*, although the heat-responses differ less from the hybrids ($0.1 > P > 0.05$), and the differences in magnitude of their responses are not significant.

Similar inbred effects on the hybrid heat-responses occur at 16 weeks as at 12 weeks, but probably because fewer animals have been reared to the later age, none of the comparisons is significant.

Summary of heat-response results

These results show that when the inbred and hybrid heat-responses are compared with each other, the males and females behave in very similar ways. The analysis reinforces the impression presented by the graphs that the effect of rearing both inbred and hybrid animals at high temperatures promotes early growth. This is evident in both the sexes and all genotypes except the *CBA* × *RIII* hybrids and females from the mating *CBA* × *C57*. It is particularly characteristic of *C57* males where its magnitude distinguishes this strain from all others. During the period when sexual maturity is developing, the growth rate of all the heat-reared inbreds and hybrids is slower than that of the control animals, and by 8 weeks of age their weights are nearly equal to, or smaller than, those of the control

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litter-mates in every case except for the *As*. The latter are distinguishable from this age onwards by their large heat-response in which the heat-reared animals are heavier than the controls. The weight responses of the other inbreds and hybrids are indistinguishable at 8 weeks of age. But, whereas the growth rate of all the heat-reared hybrids and *C57s* either becomes more rapid or equals that of the controls at or soon after this age, so that by 16 weeks there is no significant difference in the weight of animals reared in the two environments, the growth rate of *CBA* and *RIII* heat-reared animals continues to be slower than that of the controls, and by 16 weeks of age the responses of these animals are markedly different from those of the others.

It follows from what has been said that the responses of the hybrids are more uniform than those of the inbreds considered as a group. It is also obvious that the hybrids reared in the two environments are more similar to each other than are the inbreds and that they make in general a smaller heat-response than the inbreds. However, it has also been shown that apart from the large heat-response that the *C57s* make at 4 weeks, the responses of this strain after that age are indistinguishable from the hybrids and that this phenomenon of a small heat-response is not a unique hybrid character.

It may also be concluded that when the heat-response of an inbred is distinguishable from that of other inbreds, the distinguishing character is usually manifest in those first-generation hybrids which have the particular inbred concerned as a parent, despite the marked differences in absolute size of the inbreds and hybrids and the fact that the hybrid responses are more homogeneous and usually much smaller than those of the inbreds.

Causes of differences in heat-response

The question arises whether the particular heat-responses of the different genotypes are characteristic of the weight and pattern of growth of the strain. For example, do the smaller heat-responses of the hybrids follow inevitably from their greater control weight, and is the greater uniformity in this response associated with a greater similarity in their growth pattern?

Analyses of variance of the control weights of the male hybrids reveal that there are highly significant differences between the genotypes at 3 and 4 weeks of age, and the differences are approaching significance at 8 weeks yet, as has been shown, the heat-responses at 4 and 8 weeks do not differ. Also there are significant differences between the mean control weights of the reciprocal crosses in three of the six genotypes, which bear no close relationship to the magnitude of their heat-responses. It may, however, be argued that differences in weight are only of importance in determining the nature of the heat-response below a critical weight value, and the hybrids which all show 'vigour' exceed this value. One might expect that genetically small animals with a high surface area/volume ratio would find a high temperature environment suitable for rapid growth and, indeed, the rapid growth of the heat animals of most of the genotypes following weaning is probably attributable to this. It may be further pointed out that the heaviest hybrids at this age, *CBA* × *RIII* and *A* × *RIII*, make the smallest response and the inbred *A* which is unique at and after 8 weeks of age by having the heat-reared animals much heavier than the control ones, is significantly smaller than the other control inbreds at this time. It should be noted, however, that the male *CBAs*, which are the smallest of the inbreds

at 3 weeks, show the smallest heat-response at 4 weeks, whilst the mean weight of the *C57s*, which are unique at this age in their large heat-response, is intermediate among the inbreds.

The effect of weaning weight on the first week's heat-responses has been quantified by calculating the correlation of strain means of heat-response at 4 weeks ($H_4 - C_4$), with the control weight at 3 weeks, C_3 , and by determining the regression of litter means of ($H_4 - C_4$) on litter means of C_3 for all strains.

Both the male and female inbred means of ($H_4 - C_4$) are positively correlated with the corresponding C_3 means ($r = 0.62$, 2 d.f. and 0.95 , 2 d.f. respectively); the correlation coefficient is significant in the case of the females. On the other hand, the male and female ($H_4 - C_4$) means of the different types of hybrid are negatively correlated with the corresponding C_3 means ($r = -0.49$, 10 d.f. and -0.50 , 10 d.f. for males and females respectively), but neither of the correlation coefficients is significant.

The regression analysis was done separately for male and female hybrids and male and female inbreds. In each of the four groups a common regression line for all strains of heat-response on weaning weight was fitted; then a set of parallel lines for the different strains and finally independent lines for each strain. The residual variation about the estimated regression lines decreases as more constants are fitted to the data; the reductions produced at each stage of the analysis were tested for significance by comparison with the minimum residual mean square error (i.e. that about individual lines for each strain).

Although the split-litter technique was designed so that the average value of ($H_3 - C_3$) should be zero, there are inevitably a few litters for which $|H_3 - C_3|$ is large enough to have an appreciable effect on ($H_4 - C_4$). To simplify the analysis, all those litters for which $|H_3 - C_3|$ is greater than 0.5 g have been omitted, and the effect of ($H_3 - C_3$) subsequently neglected.

In the male inbreds, the regression coefficient for a common line is not significantly different from zero, i.e. there is no general trend of heat-response with weaning weight. There is, however, a significant reduction in residual mean square error for parallel lines, but the regression coefficient for parallel lines also is not significant. It may therefore be concluded that there are differences between the heat-responses of the four strains, due mainly to the large *C57* response which cannot be attributed to differences in weaning weight.

There is also no significant trend of heat-response with weaning weight for the female inbreds, so that no better estimates of heat-response can be obtained by making corrections for weaning weight.

The overall trend of heat-response with weaning weight is approaching significance in the male hybrids. However, there is a significant reduction in residual mean square error on fitting parallel lines and a further reduction by fitting different lines for each strain. The heat-responses of the hybrid lines do, therefore, differ significantly after accounting for the regression of heat-response on weaning weight within strains.

The female hybrid regressions of heat-response on weaning weight follow the same pattern as the male hybrids. The regression analysis again reveals differences which cannot be attributed to differences in weaning weight.

It may be generally concluded that although the rapid growth of young animals in the heat may result from the hot environment being more favourable for the growth of small

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animals than the control one, differences in the heat-responses of different genotypes cannot be attributed entirely to differences in their weaning weight.

The relationship between control weight and heat-response at 8, 12 and 16 weeks has been determined in a slightly different way: namely, by calculating the regression of litter means of $(H-C)$ on the control litter mean weights, C , at the same age (figure 3).

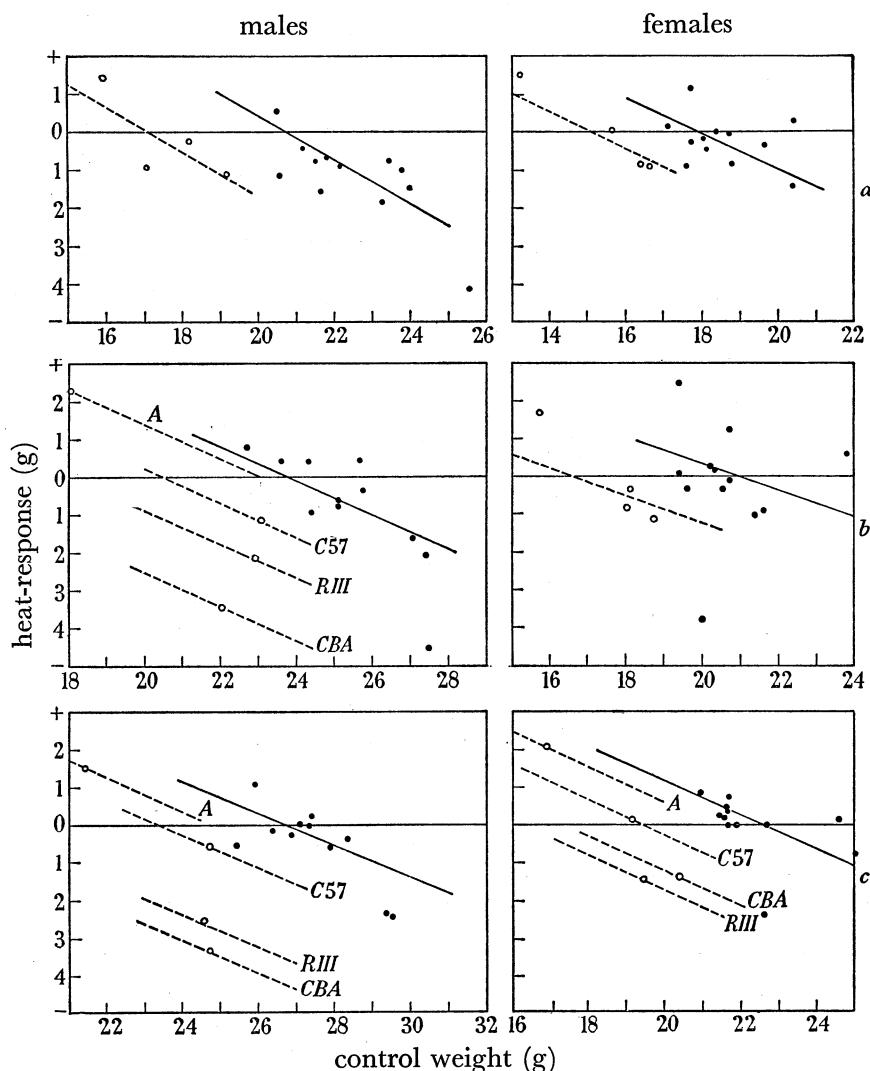


FIGURE 3. Male and female regression lines of heat-response on control weight at (a) 8, (b) 12 and (c) 16 weeks of age. (The points plotted represent the means for the different genotypes and their reciprocal crosses.) \circ , inbred; \bullet , F_1 hybrid; - - - - -, inbred regression lines; ———, hybrid regression lines.

This is based on the assumption that the average control weight of animals in a litter represents the expected weight of their heat-reared litter-mates, had they also been reared in the control environment; the method of allocating animals to the different environments at weaning allows such an assumption for those litters with several animals in both environments, but in those litters with only one animal in each environment, the heat-response will be over- or underestimated according to whether the weight of the control animal is below or above the theoretical average control weight for the litter. Since the

within-litter variation in weight is small compared with the between-litter variation, it is unlikely that the error introduced from this source can account for all the negative correlation of heat-response with control weight within strains; this is supported by the fact that the regression coefficients for the hybrids are in general greater than, or equal to, those of the inbreds, whilst the within-litter variance is smaller and there are more animals per litter in each environment. One effect of the error will be to increase the residual variation about the estimated regression lines and thus reduce the sensitivity of the analysis for detecting differences between strains.

At 8 weeks the regression lines for the four male inbred strains do not differ significantly and one common line can therefore be fitted to show the relationship between heat-response and control weight (regression coefficient, -0.64). This means that differences in heat-response between the four strains can be attributed to differences in control weight. A common line can also be fitted to the twelve types of male hybrid (regression coefficient -0.54). The regression coefficients of the inbreds and hybrids do not differ significantly but the residual mean square error about two parallel lines is significantly less than that about one line at the 0.1% level. The two lines are represented by the equations:

$$\begin{aligned}\text{inbreds } (H-C) &= 9.78 - 0.57C \pm 1.867, \\ \text{hybrids } (H-C) &= 11.79 - 0.57C \pm 1.867.\end{aligned}$$

The regression of the female inbred heat-response on the control weight at 8 weeks can also be represented by a single line (reg. coeff. -0.46) and the same is true for the twelve types of hybrid (reg. coeff. -0.49). There is no significant difference between the inbred and hybrid coefficients, and two parallel lines are sufficient to represent the relationship between heat-response and control weight:

$$\begin{aligned}\text{inbreds } (H-C) &= 7.31 - 0.48C \pm 1.459, \\ \text{hybrids } (H-C) &= 8.66 - 0.48C \pm 1.459.\end{aligned}$$

At 12 weeks four parallel lines are necessary to represent the male inbred regressions (reg. coeff. -0.41), which indicates that the differences in heat-response of the different strains cannot be attributed entirely to differences in control weight. The residual variation about twelve parallel lines for the male hybrids is just significantly less than that about one common line, but to facilitate a comparison with the inbreds one common line is fitted to the hybrids (reg. coeff. -0.48). Five parallel lines are sufficient to predict the heat-response from the control weight in a comparison of the inbreds and hybrids.

These lines have the general equation:

$$(H-C) = a + bC \pm e,$$

where b is estimated to be -0.45 ;

a is estimated to be 9.23 (*C57*), 8.16 (*CBA*), 6.46 (*RIII*), 10.43 (*A*), 10.77 (hybrids);
 $e = 1.627$.

The 12-week female inbred regression can still be represented by a single line (reg. coeff. -0.36) but, like the males, twelve parallel lines provide a better fit for the female hybrids. However, a single line is fitted to facilitate a comparison with the inbreds (reg. coeff. -0.38) in which two parallel lines are sufficient:

$$\begin{aligned}\text{inbreds } (H-C) &= 6.21 - 0.37C \pm 1.714, \\ \text{hybrids } (H-C) &= 7.76 - 0.37C \pm 1.714.\end{aligned}$$

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The same regression relationships hold for the males at 16 weeks as at 12 weeks, except that one line is sufficient for the hybrids (inbred reg. coeff. -0.35 , hybrid reg. coeff. -0.48). The five parallel lines are represented by the general equation given above where:

b is estimated to be -0.43 ;

a is estimated to be 10.08 (*C57*), 7.24 (*CBA*), 7.94 (*RIII*), 10.75 (*A*), 11.44 (hybrids);

$e = 1.885$.

Precisely the same situation occurs in the 16-week females (inbred reg. coeff. -0.44 ; hybrid reg. coeff. -0.53).

b is estimated to be -0.46 ;

a is estimated to be 9.02 (*C57*), 8.11 (*CBA*), 7.57 (*RIII*), 9.91 (*A*), 10.42 (hybrids);

$e = 1.576$.

It may be concluded from this analysis of the regression of heat-response on the control weight that the significant differences found previously in the female inbred heat-responses at 8 and 12 weeks can be attributed to differences in the control weight of the four strains. The causation of these differences is therefore through genetically determined differences in the body size of the strains. Although the heat-responses between the different strains of inbreds at 8 weeks and between the different types of male and female hybrids at 8 and 16 weeks do not differ significantly, such differences as do occur can also be attributed to differences in control weight. However, the significant differences in heat-response between the male inbreds at 12 and 16 weeks, between the female inbreds at 16 weeks and between the male and female hybrids at 12 weeks cannot be entirely attributed to differences in control weight, and there must be some other genetic causation for the heat-response other than that which determines size. The significant difference in the hybrids at 12 weeks originates from the comparatively large responses of the offspring of the mating $A \times RIII$ in the females and the large negative response of the offspring of the $CBA \times RIII$ s with *CBA* mothers; this, however, is only estimated from one litter. With the exception of this one case it does appear that the hybrids behave uniformly as a group with any differences resulting from differences in control weight. It follows from the fact that regression lines can be drawn at each of these ages, that there is a control weight (determined by the point where the line crosses the abscissa) at which the corresponding heat-response is zero. Thus for litters with control animals of this weight, the heat-reared litter-mates are expected to have the same weight: for convenience this weight is termed the 'weight of no response'. The 'weight of no response' naturally changes with age, is different for hybrids and inbreds, always being greater for the hybrids, and differs in the different inbreds when their regressions of heat-response on weight differ.

In figure 3 the mean heat-responses of the different inbreds and hybrids have been plotted against their mean control weight, with the regression lines based on litter-means; it will be noticed that whereas the control weights of *C57*s and the hybrids tend to be arranged around the 'weight of no response', the mean control weights of the other inbreds are far removed from their estimated 'weight of no response'.

It is also worthy of note that for heavy animals when the heat-response is negative, the heat-response of the hybrids is expected to be smaller in magnitude than that of the inbreds of the same control weight.

Variability in weight

The split-litter experimental design precludes a reliable estimate of the within-litter variation. Attention is therefore focused only on the between-litter variation, but it may be added that the relative magnitudes of crude estimates of the within-litter variability for each strain in the two environments are consistent with conclusions based on the between-litter variation (Harrison 1958*b*).

TABLE 5. INBRED AND HYBRID BETWEEN-LITTER VARIANCES OF WEIGHT
(Degrees of freedom in parentheses.)

genotype	control		heat	
	males	females	males	females
3 weeks				
hybrids (pooled)	3.993 (120)	2.875 (125)	3.558 (120)	3.056 (125)
<i>C57</i>	2.418 (21)	2.053 (15)	1.386 (21)	2.232 (15)
<i>CBA</i>	2.294 (16)	1.277 (10)	2.299 (16)	2.068 (10)
<i>RIII</i>	4.801 (17)	5.303 (16)	5.021 (17)	4.988 (16)
<i>A</i>	1.618 (7)	1.937 (3)	2.103 (7)	1.961 (3)
4 weeks				
hybrids (pooled)	6.635 (108)	5.582 (113)	5.740 (108)	4.095 (113)
<i>C57</i>	4.315 (15)	3.895 (15)	2.203 (15)	3.085 (15)
<i>CBA</i>	4.540 (12)	3.264 (9)	4.442 (12)	2.846 (9)
<i>RIII</i>	9.866 (20)	7.156 (15)	8.938 (20)	6.698 (15)
<i>A</i>	4.012 (6)	6.934 (4)	1.629 (6)	6.396 (4)
8 weeks				
hybrids (pooled)	6.427 (100)	4.421 (114)	5.071 (100)	2.773 (114)
<i>C57</i>	5.547 (13)	2.895 (16)	2.431 (13)	1.070 (16)
<i>CBA</i>	13.136 (9)	4.387 (12)	7.171 (9)	6.343 (12)
<i>RIII</i>	10.290 (16)	4.792 (16)	8.214 (16)	3.244 (16)
<i>A</i>	18.786 (6)	14.487 (4)	1.223 (6)	8.299 (4)
12 weeks				
hybrids (pooled)	7.020 (59)	3.506 (73)	3.865 (59)	3.912 (73)
<i>C57</i>	4.462 (8)	3.245 (12)	4.789 (8)	1.791 (12)
<i>CBA</i>	10.682 (6)	2.508 (6)	5.815 (6)	2.960 (6)
<i>RIII</i>	8.063 (14)	3.724 (12)	8.197 (14)	6.214 (12)
<i>A</i>	15.223 (4)	18.605 (3)	3.183 (4)	14.663 (3)
16 weeks				
hybrids (pooled)	5.431 (59)	4.075 (72)	4.241 (59)	3.786 (72)
<i>C57</i>	5.742 (8)	3.973 (11)	8.434 (8)	2.813 (11)
<i>CBA</i>	4.446 (6)	2.001 (6)	6.563 (6)	2.970 (6)
<i>RIII</i>	5.262 (14)	3.532 (12)	7.915 (14)	3.965 (12)
<i>A</i>	19.180 (4)	24.386 (3)	5.864 (4)	7.876 (3)

The between-litter variance (table 5) has been calculated as the variation between litter means for those litters with both control and heat representatives of the same sex. A runt *C57* control male and a runt *CBA* heat male have been removed from the analysis because they increase the variances out of all proportion to their significance. The variances for each of the hybrid genotypes are pooled at each age.

The use of coefficients of variation to express variability permits one to compare animals differing in size and therefore in sex, but the use of a 't' test to compare coefficients statistically is only justifiable if the number of degrees of freedom is large (Bader 1955). In the present experiment such an assumption is not valid for the inbreds and the statistical analysis has, therefore, been done on variances. Since the hybrids are heavier than the

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inbreds at most ages, this analysis is weighted against the expectation that the hybrids have a smaller variance. The coefficients (table 6) show, however, that this is a slight effect.

The comparison between the control and heat variances of the same strain has been made by finding the significance of the correlation between $(H+C)$ and $(H-C)$ over all the litters since the corresponding variances are not independent (Pitman 1939); the comparisons between different strains in the same environment are made by 'F' tests. The

TABLE 6. INBRED AND HYBRID COEFFICIENTS OF BETWEEN-LITTER VARIATION OF WEIGHT (Corrected for sample size (Haldane 1955).)

genotype	control			heat		
	males	females	pooled	males	females	pooled
3 weeks						
hybrids (pooled)	24.03	19.58	21.81	22.36	19.99	21.18
<i>C57</i>	20.27	18.22	19.24	15.36	18.69	17.03
<i>CBA</i>	25.18	16.39	20.79	24.57	21.02	22.79
<i>RIII</i>	27.62	29.62	28.62	28.00	28.19	28.09
<i>A</i>	17.73	20.79	19.27	20.63	20.40	20.52
4 weeks						
hybrids (pooled)	22.18	20.78	21.48	18.98	16.82	17.90
<i>C57</i>	23.74	20.50	22.12	13.22	16.30	14.76
<i>CBA</i>	24.88	18.79	21.84	22.79	16.08	19.44
<i>RIII</i>	30.83	27.12	28.98	25.57	23.35	24.46
<i>A</i>	22.82	31.27	27.05	12.63	27.13	19.88
8 weeks						
hybrids (pooled)	11.53	11.42	11.48	10.63	9.02	9.83
<i>C57</i>	13.21	11.00	12.11	8.86	6.64	7.75
<i>CBA</i>	21.79	12.82	17.31	17.09	16.27	16.68
<i>RIII</i>	16.93	13.54	15.24	16.11	11.74	13.93
<i>A</i>	28.33	30.17	29.25	6.65	20.49	13.57
12 weeks						
hybrids (pooled)	10.52	9.08	9.80	8.03	9.57	8.80
<i>C57</i>	9.40	10.08	9.74	10.28	7.65	8.97
<i>CBA</i>	15.37	8.75	12.06	13.46	10.12	11.79
<i>RIII</i>	12.59	10.90	11.75	14.02	14.81	14.42
<i>A</i>	22.71	28.93	25.82	9.19	23.23	16.23
16 weeks						
hybrids (pooled)	8.56	9.18	8.87	7.65	8.77	8.21
<i>C57</i>	9.96	10.61	10.29	12.31	8.87	10.60
<i>CBA</i>	8.82	7.15	7.99	12.42	9.33	10.88
<i>RIII</i>	9.49	9.86	9.68	13.01	11.27	12.14
<i>A</i>	21.44	30.95	26.20	11.05	15.69	13.37

great similarity (table 6) in the between-litter variances of animals destined for the high-temperature room and those kept in the control indicates that the method of splitting litters at 3 weeks of age introduces no bias in the later analysis.

The variance in weight of the control-reared animals is usually greater than that of the heat-reared ones at each of the ages, though it is only significantly so in the case of the male *As* at 8, 12 and 16 weeks ($P < 0.05$) and the female *As* at 16 weeks ($P < 0.001$). This larger variation in the control room animals is, no doubt, in part due to the less constant conditions in this room, but since it is also evident in a within-litter comparison of variance, it must also be a function of the particular temperature. Further, the situation is reversed at 16 weeks in the male *C57s*, *CBAs* and *RIIIs*, at 8 weeks in the female *CBAs*

and at 12 weeks in the female *RIII*s, though in no case does the heat variance become significantly greater.

In table 7, the pooled coefficients of heat variation (i.e. male and female) are expressed as percentages of the pooled coefficients of control variation. This clearly demonstrates the similarity between the two groups of animals allocated to the different environments at 3 weeks, and shows that the heat variance is subsequently smaller than the control. As age increases the heat variability increases relative to the control in all genotypes except the *As*, and by 12 weeks is greater for the *RIII*s, *CBA*s and *C57*s.

TABLE 7. COEFFICIENTS OF HEAT VARIABILITY OF WEIGHT EXPRESSED AS PERCENTAGES OF CONTROL VARIABILITY

genotype	age (weeks)				
	3	4	8	12	16
hybrids (pooled)	97.0	83.3	85.6	89.8	92.5
<i>C57</i>	88.5	66.7	64.0	92.0	103.0
<i>CBA</i>	109.6	89.0	96.4	97.7	136.2
<i>RIII</i>	98.1	84.4	91.4	122.7	125.4
<i>A</i>	106.5	73.5	46.4	62.8	51.0

When the animals are small, the control between-litter variances of the *CBA*s and *RIII*s are very similar in both sexes to the variance of the pooled hybrids with the *CBA* variance usually being slightly less and the *RIII* variance slightly greater. At 8 and 12 weeks, however, the male variation of these inbreds becomes greater than that of the hybrids, being significantly so in the case of the 8-week-old *CBA*s and nearly significantly greater in the 8-week-old *RIII*s. This tendency for the control inbreds to have a higher variance than the hybrids is particularly marked in the *As* which, although at 3 weeks are less variable, show the phenomenon at the 5% level at 8 weeks, and the 1% level at 12 and 16 weeks in the females. The fact that, whenever the variance of these inbreds is significantly different from that of the hybrids, it is the inbreds which have the greater variation, supports the thesis that inbreds are less well buffered against environmental fluctuations than hybrids. However, that this phenomenon is not an inevitable consequence of inbreeding is shown in the comparison of the *C57* and hybrid control variances in which the variation in this inbred is in all but one case less than that of the hybrid and is nearly significantly smaller in the males at 3 weeks.

Using the hybrid variance again as a point of reference, the between-litter variance of the heat-reared *RIII*s is high, always being greater than that of the hybrids and significantly greater at 12 and nearly so at 16 weeks of age in the males. The *CBA* variance is more similar to the hybrids but is significantly greater in the 8-week-old females, and although the males are less variable when young, they become considerably more variable by 8 weeks, though not significantly so. There is a little evidence then that in the heat these two inbreds are more variable relative to the hybrids, particularly at the later ages, than they are in the control. On the other hand, the variance of the heat-reared *As* is relatively smaller in comparison with the corresponding hybrids than the control-reared *As*, only being significantly larger than the hybrid variance at 8 and 12 weeks in the females and being significantly smaller in the males at 8 weeks. The evidence, however, still suggests that as in the control conditions these inbreds are less well buffered than the hybrids.

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Initially, however, the heat *C57s* show the same low variance relative to the hybrids as they did in the control environment and this is significantly smaller in the males at 3 and 4 weeks and in the females at 8 weeks, but the variance behaviour of the males at 12 and 16 weeks indicates that in the hot environment the *C57s* are becoming more like the other inbreds, for by these ages the variance of the males is greater than that of the hybrids and almost significantly so by 16 weeks.

No evidence has been obtained that the (*C57* ×) hybrids have a smaller between-litter variance than the hybrids without a *C57* parent. There is, however, some indication that a maternal effect is at least in part responsible for the low variance of the *C57s* since, both in the control and in the heat at all ages, the female hybrids with a *C57* mother have a lower variance than the hybrids from the other inbred females, and the same is true of the heat males. (Significant at the following ages: heat females, 8 weeks $P < 0.05$, 12 weeks $P < 0.05$; control females, 8 weeks $P < 0.001$; heat males, 12 weeks $P < 0.05$.) On the other hand, the variance of the control-male hybrids with a *C57* mother is significantly greater at 8, 12 and 16 weeks than the corresponding variance of the hybrids without a *C57* mother ($P < 0.001$, $P < 0.001$, $P < 0.05$ respectively) and the difference in variance is least when one would have expected it to be most, i.e. at the early ages. It cannot therefore be unequivocally concluded that the low variance of the *C57s* is entirely the result of a more constant maternal environment.

It may be concluded that there is some evidence for a lower variability in the weight of the hybrids than in the weight of the inbreds in both environments. This is most obvious when maternal effects have vanished or become small and during the puberty period. The variability of the *C57* inbred is, however, frequently as small and sometimes significantly smaller than the hybrid variances.

DISCUSSION

The results of this experiment confirm that the growth in weight of the mouse is influenced by the temperature of its environment. They do not, however, show that a high temperature always reduces the growth rate, although this has been claimed by all previous workers. In particular, the results are in contradiction with Ogle's (1934) findings, since the temperature environments she used were similar to those of this experiment, and the age of weaning was the same. Ogle reported a slower growth rate at all ages in the heat, whereas most of the genotypes used in the present investigation grow more rapidly in the heat when they are small. In our experiments even the heat-reared *CBAs* and *RIIs*, whose growth is most reduced, grow more rapidly relative to their control litter-mates than did Ogle's heat-reared mice. These conflicting results may be due to the less constant and slightly higher temperature conditions in Ogle's control room or to other environmental differences such as diet; but they may equally well be due to differences in the genotypes used. The analysis has certainly demonstrated that genetically different animals frequently have different heat-responses. Strain differences in weight are partly responsible for this, but there is evidence that other factors are also involved. Thus not all the differences in the various inbred responses, nor the differences between the inbreds and the hybrids can be explained completely by differences in control weight; particular inbred effects can be detected in the hybrid responses, despite the fact that the hybrid range of weight

variation is totally different from that of the inbreds. The nature of the factors, other than weight, which determine the heat-response have not been determined; if, as seems likely, they are metabolic in nature, it is interesting that some hybrid responses can be predicted from the behaviour of the inbreds from which they were derived, particularly as the effects of the genes which determine the differences in size of the inbreds seem to be lost in the heterosis of the hybrids. Hellman & Collins (1957) have investigated the thyroid activity of the mice whose growth has been described. They found that the ^{131}I uptake was much lower in the heat-reared animals, but their data is inadequate for demonstrating possible strain differences. A reduced metabolic rate as measured by ^{131}I uptake, however, may account for the general tendency for animals to grow more slowly in the heat, and it is known that inbred strains of mice differ in their endocrinology, including thyroid activity (Barry & Kennaway 1937; Loeb & Kirtz 1939; Grüneberg 1952; Lyon 1956).

The most generally accepted explanation for the greater phenotypic uniformity of F_1 hybrids than of inbreds, is that heterozygotes have a greater biochemical versatility than homozygotes (Haldane 1948; Robertson & Reeve 1952). Clarke & Maynard-Smith (1955) and McLaren & Michie (1956) point out also that one would expect a relationship between the amount of heterozygosity and the level of variability only in characters which are an index of an organism's vigour. There does, in fact, appear to be good evidence for a connexion between increased variance and reduced viability; but, whereas Lerner (1954) is of the opinion that they may be merely concomitant consequences of departures from the breeding system characteristic of the species, most workers see a causal connexion (Rasmussen 1949; Clarke & Maynard-Smith 1955; McLaren & Michie 1956). Harrison (1959) indeed has argued that both are merely facets of the same phenomenon, since maximum fitness is attained when the homeostatic mechanisms, which determine the variability of vigour characters, are most efficient (i.e. in optimal conditions). One can, therefore, make the following two propositions:

(a) Maximum fitness is attained in an environment in which the environmentally determined variance of 'vigour' characters is smallest and the larger the variance the less suitable the environment.

(b) In any one environment, the individuals of a strain with a small environmentally determined variance in 'vigour' characters, are more fit than individuals of a different strain with a high variance.

The first proposition is supported by the studies of King (1919), Hammond & Bird (1942), Went (1953), Searle (1954), Honeyman (1957), Ashoub, Biggers, McLaren & Michie (1958) who have found larger variances in characters reflecting overall fitness in organisms living in adverse conditions than those in more favourable environments.

Since weight is a function of the overall metabolic state of a homeotherm, it would appear to be a good index of vigour. It cannot, however, be automatically assumed that a reduced growth rate is always indicative of a reduction in fitness, particularly as a slower growth rate at high temperatures produces an adult accordance with Bergmann's climatic rule (1847). Applying the first of the above propositions to the present experiment one would conclude that the hot environment is more optimal than the control for all strains when the animals are small, and that somatic fitness is therefore greater in it. (It does not necessarily follow that evolutionary fitness is greater in the heat, since this is a

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function of reproductive as well as somatic fitness.) However, the weight variance of the heat animals increases relative to that of the controls as the animals become older in all strains except the *As*, and in some cases actually becomes greater. This indicates that during the later phases of growth the control environment is the more optimal for all the genotypes except the *As*. There appears to be a close correspondence between the variance behaviour and the heat-response since (a) most of the strains grow more rapidly in the heat when they are young but more slowly at later ages, (b) the heat variances of the two inbreds (viz. *RIII*s and *CBA*s) which have a markedly slower growth rate in the hot environment, ultimately become considerably greater than the control variances, and (c) the inbred *A*, on the other hand, which at all ages is much heavier in the heat, shows the maximum contrast between its weight control and heat variance, the latter being much smaller.

TABLE 8. CORRELATION COEFFICIENTS OF MEAN HEAT-RESPONSES ($H-C$) WITH RATIOS OF HEAT TO CONTROL BETWEEN-LITTER VARIANCES $\left(\frac{(\text{b.l.v.}H.)}{(\text{b.l.v.}C.)}\right)$

age (weeks)	inbreds (2 degrees of freedom)		hybrids (4 degrees of freedom)	
	males	females	males	females
4	-0.67	-0.53	+0.37	-0.28
8	-0.96	-0.54	-0.76	-0.65
12	-0.55	-0.51	-0.03	+0.01
16	-0.85	-0.94	+0.11	-0.29

The relationship between the growth in weight and the environmentally determined variance in the two environments is quantified in table 8 by correlating the genotype means of the heat-responses with the corresponding ratios of the heat between-litter variances to the control between-litter variances.

With the small number of degrees of freedom available, few of the coefficients are significant, but the inbred data indicates that the greater the heat-response the smaller the heat variance compared with the control variance, i.e. when the response is positive, the larger it is, the smaller is the variance ratio, whereas when it is negative, the more negative it is, the larger is the variance ratio. When the ratio is unity one would conclude that both environments are equally favourable and the response will be zero. A similar relationship is not revealed by the hybrid analysis except possibly at 8 weeks of age, but this is of no consequence since the responses and variances of the six hybrid genotypes are very similar. There is then evidence that not only the weight variance, but also the weight growth rate, reflects the optimality of the temperature conditions, with a rapid growth rate indicating a favourable environment for somatic fitness.

Although one of the experimental environments may be adverse for a strain, it is unlikely that they both are. The more similar growth pattern of the hybrids, at all ages in the two environments, in contrast with the inbreds therefore shows that not only do they find the favourability of the conditions more similar but also that they must be more fit in at least one of the environments than the inbreds. In fact, their better canalized development (Waddington 1953) or, in Lerner's (1954) terms, their greater developmental homeostasis, as shown by their generally lower variance, in both environments, indicates that in the control and in the heat they are more fit than the inbreds.

It has been shown, however, that one of the inbreds, *C57*, has a weight variance both in the control and in the heat which at most ages is very similar to that of the hybrids. Apart from finding the heat particularly favourable when it is small, this strain also has a similar relative growth pattern in the two environments. Chai (1956*b*) likewise records an instance in which the variance of a 'vigour' character (response to androgen) in inbred mice was no greater than in an F_1 hybrid. These results demonstrate that neither a reduction in vigour nor an increase in variance is an inevitable consequence of inbreeding a naturally outbreeding organism. They suggest that it is not heterozygosity as such which determines the buffering capacity and fitness of an organism, but the increased likelihood of obtaining an adaptable genotype in heterozygotes than in homozygotes.

PART II. TAIL LENGTH

INTRODUCTION

All those who have reared rats or mice at two widely different temperatures have noted that the environmental temperature, in part, determines the adult tail length: the higher the temperature, the longer the tail (Sumner 1909, 1915; Sundstroem 1922, 1930; Przibram 1925; Ogle 1934; Sakharov 1949). The tails of these animals, with their large surface area, absence of hair, rich vascular supply, and multiple arteriovenous anastomoses, function as important heat regulatory structures, as is evident from the lowered heat tolerance of animals whose tails have been removed (Harrison 1958*a*). The view that the increase in tail length of mice reared at a high environmental temperature is adaptive is further supported by the fact that the response to temperature is in accordance with Allen's climatic rule (1905). On the hypothesis that F_1 hybrids have a greater 'developmental flexibility' (Thoday 1953; Maynard-Smith 1956) than the inbreds from which they are derived, one might expect that (*a*) hybrids reared in two different climatic environments would differ more in their tail length than inbreds, i.e. make a greater adaptive response, but that (*b*) in both environments, the environmentally determined variance of inbred tail length will be greater than that of F_1 hybrids (Lerner 1954).

The aims of the present investigation were then:

- (1) To confirm, using genetically homogeneous material, that environmental temperature influences the tail length of the mouse.
- (2) To evaluate the extent to which differences in genotype determine the magnitude of the environmentally induced responses, and how far the hybrid responses can be attributed to those of their inbred parents.

In particular,

- (3) To compare the capacity of inbreds and hybrids to make environmentally determined adaptive responses as demonstrated by changes in tail length.
- (4) To test the hypothesis that in each of the two environments the variance of inbred mice is greater than that of F_1 animals.

MATERIALS AND METHODS

Four inbred strains of mouse, *C57BL*, *CBA*, *RIII* and *A* and the six possible first-generation hybrids between them, were used in this investigation. In view of the findings of Russell & Green (1943) and Russell (1948) on the maternal influence on the number of

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vertebrae in the mouse, the F_1 hybrids were bred from reciprocal crosses. Animals were weaned when 3 weeks old and then reared for the following 13 weeks either at 70 °F dry-bulb temperature (± 2 °F), 61 °F Assman wet-bulb temperature (± 3 °F), termed for convenience the control environment, or at 90 ± 1 °F (d.b.), 85 ± 2 °F (w.b.), termed the hot environment. A split-litter design, using body weight as the criterion for allocating animals to one environment or the other, was employed. A detailed description of the

TABLE 9. NUMBERS OF ANIMALS IN CONTROL AND HOT ENVIRONMENTS

(a) INBREDS								
genotype	control age (weeks)				heat age (weeks)			
	3	4	8	12	3	4	8	12
<i>males</i>								
<i>RIII</i>	22	25	16	12	24	28	20	15
<i>C57</i>	23	21	20	13	23	20	20	12
<i>CBA</i>	26	18	14	10	26	19	16	12
<i>A</i>	11	8	8	7	12	9	9	8
<i>females</i>								
<i>RIII</i>	23	22	23	15	21	20	21	14
<i>C57</i>	27	25	20	14	36	34	30	24
<i>CBA</i>	23	21	21	12	24	22	22	14
<i>A</i>	7	5	5	4	9	8	8	7
(b) HYBRIDS (<i>males</i>)								
genotype females \times males	control age (weeks)				heat age (weeks)			
	3	4	8	12	3	4	8	12
<i>RIII</i> \times <i>CBA</i>	4	4	4	4	6	6	6	5
<i>CBA</i> \times <i>RIII</i>	7	7	4	4	5	6	3	3
<i>CBA</i> \times <i>C57</i>	9	9	9	4	9	9	9	4
<i>C57</i> \times <i>CBA</i>	15	14	12	9	15	16	13	10
<i>A</i> \times <i>RIII</i>	6	6	4	1	5	5	3	1
<i>RIII</i> \times <i>A</i>	25	23	16	15	25	22	17	16
<i>RIII</i> \times <i>C57</i>	17	19	18	13	17	19	18	13
<i>C57</i> \times <i>RIII</i>	51	42	44	22	53	46	47	24
<i>C57</i> \times <i>A</i>	28	25	24	16	24	20	19	13
<i>A</i> \times <i>C57</i>	14	12	10	8	12	10	9	6
<i>A</i> \times <i>CBA</i>	7	7	7	5	7	6	6	5
<i>CBA</i> \times <i>A</i>	16	16	17	14	16	16	18	15
(c) HYBRIDS (<i>females</i>)								
<i>RIII</i> \times <i>CBA</i>	3	2	4	4	5	3	5	5
<i>CBA</i> \times <i>RIII</i>	9	5	5	1	12	10	6	1
<i>CBA</i> \times <i>C57</i>	14	13	13	6	13	12	11	7
<i>C57</i> \times <i>CBA</i>	15	15	14	11	16	16	14	11
<i>A</i> \times <i>RIII</i>	8	8	8	6	7	7	7	5
<i>RIII</i> \times <i>A</i>	21	20	18	14	19	18	17	12
<i>RIII</i> \times <i>C57</i>	26	23	26	20	24	24	23	20
<i>C57</i> \times <i>RIII</i>	47	35	39	27	51	38	41	32
<i>C57</i> \times <i>A</i>	28	26	23	19	29	27	23	21
<i>A</i> \times <i>C57</i>	13	13	10	8	11	11	10	9
<i>A</i> \times <i>CBA</i>	7	7	7	5	7	6	6	5
<i>CBA</i> \times <i>A</i>	16	14	15	15	14	10	13	13

experimental design, and environmental conditions under which the animals were kept during the 4 years of experimentation, is given in Harrison (1958*b*) and in Part I.

At weaning animals were put in a large open-topped cage with others born on the same day of the week. Each week, on this day, the tails of the animals were measured in centimetres, using a tail measuring box. This consisted of an oblong box into which the mouse was placed and gently held still by a spring attached to the lid. The box had a V-shaped incision at one of its ends through which the tail could be drawn and running horizontally from the apex of the 'V' was a firm centimetre rule. In measuring the tail a finger was placed on its base as it projected through the incision, while the tail was stretched along the rule with the other hand. A finger was then run over the tail from the base to the tip and a measurement taken. Three such readings to the nearest 0.1 cm were made on every occasion. The first two readings had low within-observer repeatabilities but the third had a very high within-observer repeatability and was accurate to within 0.2 cm with different observers. This reading has been used throughout the analysis. The tail, thus measured is not the structure defined by anatomists (i.e. neither post-anal nor post-sacral) but most of the extremity lies outside the box and very nearly corresponding parts are measured in different animals. The same tail box, of course, was used throughout the investigation. Although this method is probably not quite so accurate as that devised by Sumner (1927) for measuring dead animals, it is essentially the same and certainly the best for measuring live animals.

The total numbers of animals of each sex and genotype in the two environments used in the analysis at 3, 4, 8 and 12 weeks of age are given in tables 9*a*, *b* and *c*. The number of animals available decreases with increasing age since some animals were removed from the experiment for other purposes; there were very few natural deaths.

RESULTS

The mean tail length of the control and heat animals from each litter was calculated for each week; from these litter means an overall mean for each strain was derived. The values at ages 3, 4, 8 and 12 weeks are given in table 10*a* (four inbred lines) and tables 10*b* and *c* (six hybrid lines and their reciprocal crosses) in which the genotypes are tabulated in order of decreasing mature tail length in the control environment. These means are based only on those litters which have both control and heat representatives of the same sex. (The data at the other ages are tabulated in Harrison, 1958*b*.)

On examination of the data, the more rapid growth in tail length and the greater mature tail length of the heat-reared animals of all genotypes is immediately noticeable when compared with their control-reared litter-mates.

Tail growth of inbreds in the control and hot environments

(Throughout this paper, 'significant' refers to the 5% level unless otherwise stated.)

At weaning, the four inbred strains, both male and female, are characterized by different tail lengths (table 10*a*). At this time, as well as at 4 and 8 weeks of age in the control environment, the differences between strains can be shown by analysis of variance to be statistically significant. The *RIII*s have the longest tails, *C57*s the next, followed by the *As* and *CBA*s; the latter two reverse their positions at 8 weeks in the females, and at 12 weeks

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in the males. At 12 weeks and over, while the mean values persist in the order $RIII > C57 > CBA > A$, the groups overlap too greatly for the differences to remain significant. At all ages, the overall mean for inbred females is slightly but not significantly greater than that for the males.

One striking effect of exposure to heat is the reduction of the variation between strains, illustrated in figure 4 by the convergence of the inbreds towards a single 12-week tail length of approximately 8.5 cm in the males and 8.25 cm in the females.

TABLE 10. MEAN TAIL LENGTHS IN CONTROL AND HOT ENVIRONMENTS

(Expressed in centimetres.)

(a) INBREDS

genotype	control males age (weeks)				heat males age (weeks)			
	3*	4	8	12	3*	4	8	12
<i>RIII</i>	5.20 (18)	5.36	6.51	6.67	4.99 (18)	6.19	8.31	8.57
<i>C57</i>	4.78 (16)	5.13	5.91	6.41	4.88 (16)	5.99	7.90	8.40
<i>CBA</i>	3.77 (16)	4.38	5.58	6.08	3.78 (16)	5.21	7.95	8.42
<i>A</i>	4.28 (8)	4.78	5.64	6.05	4.24 (8)	5.69	7.80	8.55

genotype	control females age (weeks)				heat females age (weeks)			
	3	4	8	12	3	4	8	12
<i>RIII</i>	4.99 (19)	5.41	6.59	6.89	5.12 (19)	6.34	8.08	8.39
<i>C57</i>	4.94 (21)	5.21	5.97	6.40	4.95 (21)	5.97	7.66	7.93
<i>CBA</i>	4.07 (14)	4.63	5.97	6.18	3.97 (14)	5.43	7.86	8.30
<i>A</i>	4.32 (6)	4.66	5.54	6.00	4.43 (6)	5.58	7.56	8.08

* Number of litters at weaning indicated in parentheses. For number of litters at subsequent ages see table 12.

(b) HYBRIDS (males)

genotype females × males	control males age (weeks)				heat males age (weeks)			
	3	4	8	12	3	4	8	12
<i>RIII</i> × <i>CBA</i>	6.00 (4)	6.35	7.70	8.20	5.99 (4)	7.28	9.19	9.62
<i>CBA</i> × <i>RIII</i>	5.08 (4)	5.76	6.65	7.25	5.10 (4)	6.55	8.78	9.15
mean*	5.54	6.06	7.18	7.72	5.54	6.92	8.98	9.39
<i>CBA</i> × <i>C57</i>	5.28 (9)	5.67	6.88	7.42	5.30 (9)	6.36	8.56	9.02
<i>C57</i> × <i>CBA</i>	5.08 (10)	5.50	6.61	7.40	5.14 (10)	6.35	8.65	9.13
mean	5.18	5.58	6.74	7.41	5.22	6.36	8.60	9.08
<i>A</i> × <i>RIII</i>	5.40 (4)	5.81	6.90	7.40	5.44 (4)	6.64	8.67	8.90
<i>RIII</i> × <i>A</i>	4.89 (13)	5.20	6.54	6.89	4.92 (13)	6.13	8.64	8.88
mean	5.14	5.51	6.72	7.14	5.18	6.38	8.66	8.89
<i>RIII</i> × <i>C57</i>	4.98 (10)	5.49	6.70	7.06	5.04 (10)	6.53	8.68	9.12
<i>C57</i> × <i>RIII</i>	4.67 (30)	4.94	6.44	6.99	4.64 (30)	5.98	8.73	9.20
mean	4.82	5.22	6.58	7.02	4.84	6.26	8.70	9.16
<i>C57</i> × <i>A</i>	5.03 (15)	5.36	6.53	7.08	5.15 (15)	6.50	8.55	8.96
<i>A</i> × <i>C57</i>	4.32 (8)	4.84	6.47	6.81	4.34 (8)	5.75	8.43	8.98
mean	4.68	5.10	6.50	6.94	4.75	6.12	8.49	8.98
<i>A</i> × <i>CBA</i>	4.68 (3)	5.38	6.64	7.30	4.73 (3)	6.32	8.78	9.02
<i>CBA</i> × <i>A</i>	4.19 (9)	4.59	5.62	6.41	4.19 (9)	5.32	7.98	8.73
mean	4.44	4.98	6.13	6.86	4.46	5.82	8.38	8.88
overall mean	4.97	5.41	6.64	7.18	5.00	6.31	8.64	9.06

* Mean of the mean for the two reciprocal crosses.

TABLE 10 (cont.)

(c) HYBRIDS (females)

genotype females × males	control females age (weeks)				heat females age (weeks)			
	3	4	8	12	3	4	8	12
<i>RIII</i> × <i>CBA</i>	6.18 (3)	6.70	7.78	8.15	6.27 (3)	7.32	8.70	8.90
<i>CBA</i> × <i>RIII</i>	5.06 (6)	5.65	6.92	7.10	5.00 (6)	6.41	8.62	8.40
mean	5.62	6.18	7.35	7.62	5.64	6.87	8.66	8.65
<i>CBA</i> × <i>C57</i>	5.34 (10)	5.67	6.93	7.47	5.29 (10)	6.31	8.34	8.69
<i>C57</i> × <i>CBA</i>	4.99 (10)	5.36	6.55	7.23	4.98 (10)	6.21	8.09	8.52
mean	5.16	5.52	6.74	7.35	5.14	6.26	8.22	8.60
<i>A</i> × <i>RIII</i>	5.43 (5)	5.91	7.02	7.44	5.36 (5)	6.83	8.53	8.66
<i>RIII</i> × <i>A</i>	5.04 (14)	5.50	6.51	6.72	5.10 (14)	6.42	8.35	8.53
mean	5.24	5.70	6.77	7.08	5.23	6.63	8.44	8.60
<i>RIII</i> × <i>C57</i>	4.73 (16)	5.24	6.55	6.89	4.80 (16)	6.27	8.25	8.49
<i>C57</i> × <i>RIII</i>	4.72 (29)	5.27	6.42	6.86	4.75 (29)	6.28	8.44	8.80
mean	4.72	5.26	6.48	6.88	4.78	6.28	8.34	8.64
<i>C57</i> × <i>A</i>	5.05 (18)	5.58	6.72	7.16	5.10 (18)	6.39	8.20	8.56
<i>A</i> × <i>C57</i>	4.16 (7)	4.68	5.84	6.16	4.27 (7)	5.76	7.95	8.23
mean	4.60	5.13	6.28	6.66	4.68	6.08	8.08	8.40
<i>A</i> × <i>CBA</i>	4.93 (4)	5.37	6.54	7.16	4.86 (4)	6.03	8.14	8.43
<i>CBA</i> × <i>A</i>	3.95 (10)	4.57	5.51	6.12	4.01 (10)	5.42	8.00	8.42
mean	4.44	4.97	6.03	6.64	4.44	5.73	8.08	8.42
overall mean	4.96	5.46	6.61	7.04	4.98	6.31	8.30	8.55

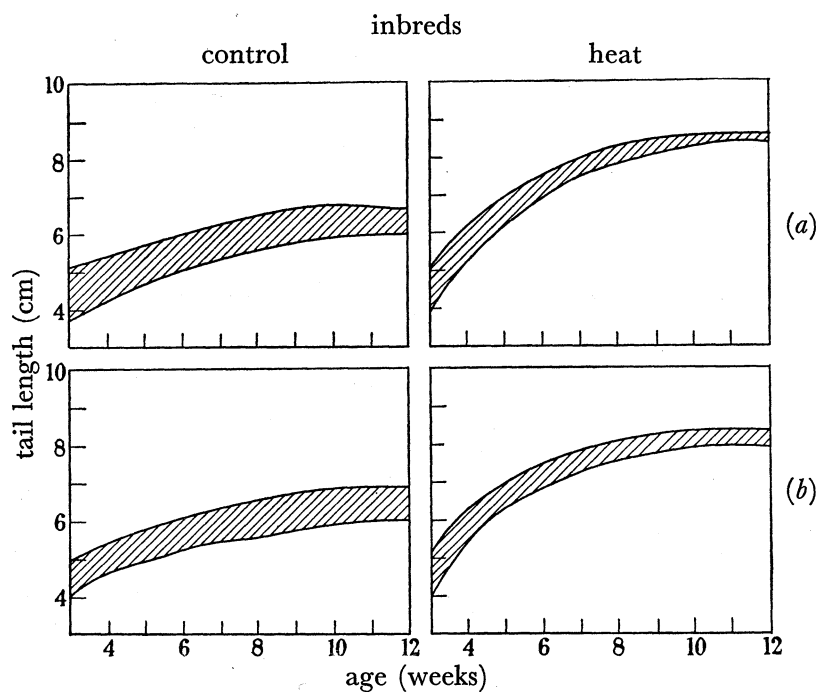


FIGURE 4. The growth in tail length of control- and heat-reared male (a) and female (b) inbred mice from 3 to 12 weeks of age. (The growth curves for the four genotypes fall within the shaded area.)

During the first week in the heat, there is considerable acceleration in the rate of tail growth, although, at 4 weeks of age, the strains still retain their original order of tail length. As in the control environment at this age, there are significant differences between

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the four inbred strains, both males and females. Thereafter, the effect of heat is not only to increase the rate of tail growth, but also to alter the serial order of the strains; this arises from the fact that the relative increase in growth rate is greater for those strains with a smaller tail length. At 12 weeks, *RIII*s still have the longest tail, but the other three strains have interchanged, the order becoming $RIII > A > CBA > C57$. There are now no significant differences between the inbred strains for the males at 8 and 12 weeks; for the females, however, the convergence is not so marked and there are still significant differences between the strains.

Whereas the tail length of the control males differs little from that of the control females, in the heat, the males have longer tails than the females ($P < 0.05$ at 12 weeks of age).

Tail growth of hybrids in the control and hot environments

In the control environment, the six types of hybrids, male and female, vary in tail length at 3, 4, 8 and 12 weeks ($P < 0.05$, 0.01 , 0.01 , 0.05 respectively for the males, $P < 0.01$, 0.05 , 0.01 , 0.01 for the females). The female offspring of reciprocal crosses also differ significantly; this is not so evident in the males because of their larger between-litter variances.

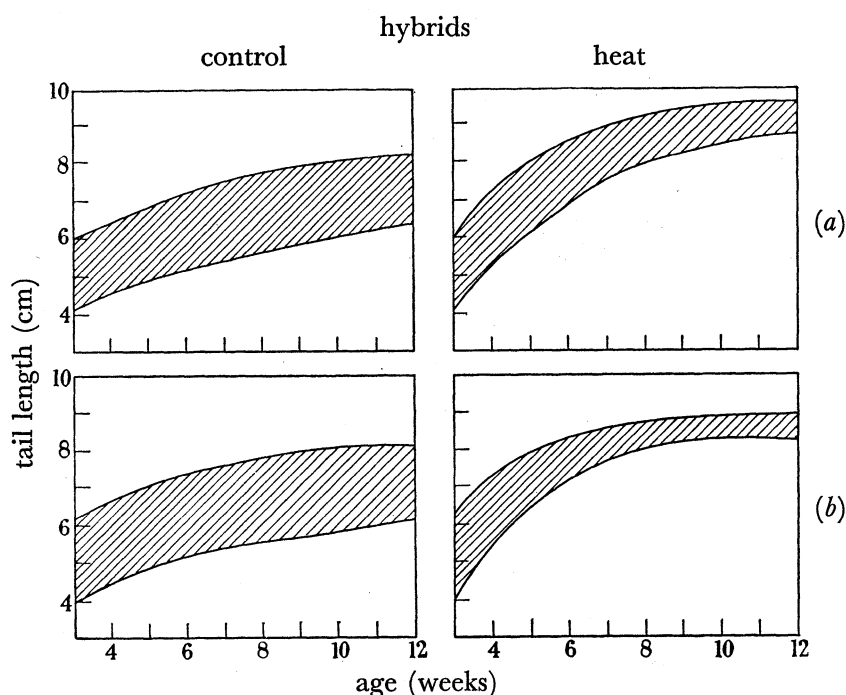


FIGURE 5. The growth in tail length of control- and heat-reared male (a) and female (b) F_1 hybrid mice from 3 to 12 weeks of age. (The growth curves for the six genotypes and offspring of reciprocal cross matings fall within the shaded area.)

The hybrid results are presented in tables 10*b* and *c* in order of decreasing mean control tail length (average of the two reciprocal crosses) for the six genotypes at 12 weeks of age. Despite the great difference in tail length of inbreds and hybrids, the tail order of the hybrids is obviously a function of the tail order of the inbred parents, the only exception to expectation being the *RIII* and *C57* animals.

Part of the dependence of hybrid tail length on inbred tail length may be due to a

maternal effect, since the longer tailed inbred mother has the longer tailed offspring in reciprocal crosses of the matings $C57 \times A$, $C57 \times RIII$ and $RIII \times CBA$ ($P < 0.05$ for the female progeny of $C57 \times A$). However, this does not appear to be a sufficient explanation for the order of hybrid tail length, since some of the maternal effects are contrary to expectation. In particular, the progeny of A mothers have longer tails compared with the progeny of CBA and $RIII$ mothers in the matings $CBA \times A$, and $RIII \times A$ ($P < 0.05$ for female progeny of $CBA \times A$).

In the heat, there are again differences between the six genotypes, significant at each of the ages in the males and at 4 and 8 weeks in the females. Their order of decreasing mature tail length is similar to that of the control hybrids and is not an apparent function of the responses of their inbred parents in the heat. An analysis of variance reveals no significant differences between tail lengths of reciprocal crosses (except in the males at 4 weeks of age). It is evident from the diagrams in figure 5 that in the heat the tail length converges to about 9 cm for the males and about 8.5 cm for the females.

Overall hybrid means (calculated as the mean of the twelve mean tail lengths) at each age are also tabulated in tables 10*b* and *c*. Whereas the tail lengths of the male and female hybrids are very similar in the control, in the heat as for inbreds, the females have much shorter tails than the males. (Overall means differ significantly at the 0.1% level at 8 and 12 weeks.)

Comparison of inbreds and hybrids

It is apparent by inspection that at 3 weeks the range of the hybrid means covers the four inbred values, but by 8 weeks both in the control and hot environments, all the inbred means (except $RIII$ controls) fall at the lower extreme of the hybrid range. At 12 weeks, in both environments, the means of the four inbred mean tail lengths are compared with

TABLE 11. COMPARISON OF TAIL LENGTHS OF INBREDS AND HYBRIDS AT 12 WEEKS OF AGE

	overall mean of hybrids (cm)	overall mean of inbreds (cm)	difference (<i>d</i>)	s.e. (d.f.)	
control males	7.18	6.30	0.88	0.194 (91)	$P < 0.001$
control females	7.04	6.37	0.67	0.171 (105)	$P < 0.001$
heat males	9.06	8.48	0.58	0.097 (91)	$P < 0.001$
heat females	8.55	8.17	0.38	0.076 (105)	$P < 0.001$

the corresponding overall mean for the hybrids in table 11. (This is done using a simple *t*-test and a pooled standard deviation since for both sexes and both environments, the pooled between-litter variance for inbreds is not significantly different from that for hybrids.) In each comparison, the mean hybrid tail length is greater than that of the similarly treated inbreds of the same sex ($P < 0.001$).

Heat-response in tail length of inbreds and hybrids

The differences in tail growth produced by rearing animals in the two environments may be termed the 'heat-response'; this is estimated as the mean of ($H - C$) over all litters of a strain, i.e. the average difference between the mean tail length (H) of litter-mates reared in the hot environment and the mean (C) of those of the same litter reared in the control environment. The mean heat-responses of the inbred strains and the hybrids at

Analyses of variance of the heat-responses of the inbreds at these ages reveal no significant differences between the strains for males and females. The order of magnitude of the heat-responses indicates, however, that the shorter tailed strains make the larger heat-response; this is the same phenomenon as the convergence of the heat growth curves. For the male inbred animals the order is $RIII < C57 < A < CBA$ and for the females

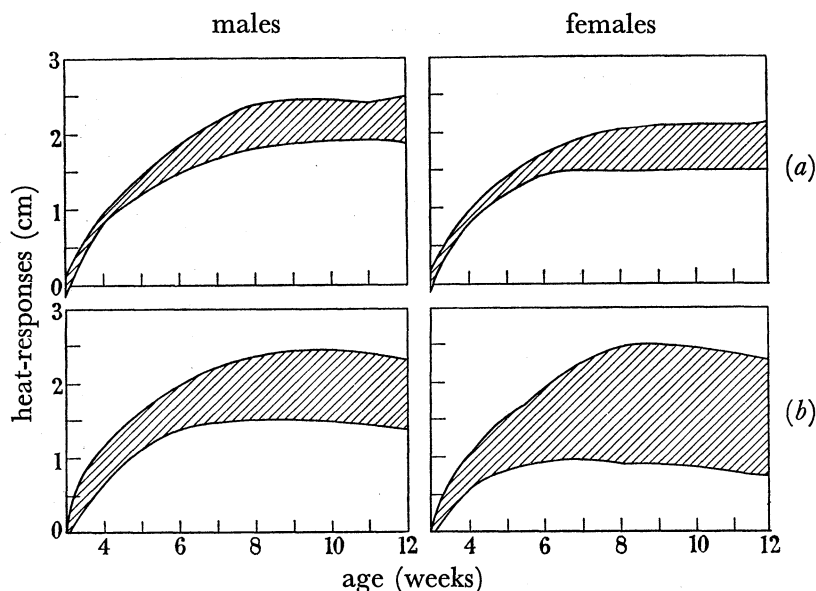


FIGURE 6. The tail length heat-responses of male and female inbred (a) and F_1 hybrid (b) mice from 3 to 12 weeks of age. (The response curves for the different genotypes and offspring of reciprocal cross matings fall within the shaded area.)

TABLE 13. COMPARISON OF THE HEAT-RESPONSES OF MALES AND FEMALES

(a) INBREDS					
Mean of heat-responses (cm). (Mean of four inbred means.)					
age (weeks)	males	females	difference	s.e. (d.f.)	
4	0.861	0.855	0.006	0.112 (100)	n.s.
8	2.083	1.771	0.312	0.131 (89)	$P < 0.05$
12	2.182	1.808	0.374	0.169 (60)	$P < 0.05$
(b) HYBRIDS					
Mean of heat-responses (cm). (Mean of twelve hybrid means.)					
age (weeks)	males	females	difference	s.e. (d.f.)	
4	0.901	0.846	0.055	0.070 (207)	n.s.
8	1.993	1.694	0.299	0.104 (202)	$P < 0.01$
12	1.877	1.514	0.363	0.124 (136)	$P < 0.01$

$RIII < C57 < CBA < A$. In other words, the sequence of increasing heat-response follows almost exactly the sequence of decreasing tail length in the control conditions. The mean heat-responses for the male inbreds are greater than those of the females at 8 and 12 weeks ($P < 0.05$) (table 13).

For the hybrids, the females, unlike the males, show significant differences in heat-responses between the six genotypes and between reciprocal crosses at 8 and 12 weeks. The magnitude of the heat-response in both sexes is inversely related to the control tail lengths, as it is for the inbreds. Also, within each genotype, the offspring of the reciprocal

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cross with the smaller tail make the greater heat-response; of these the differences between the progeny of the reciprocal crosses of $CBA \times A$ and of $C57 \times A$ are significant and it has previously been shown that it is in these two matings only that control tail lengths of reciprocal crosses differ significantly.

Overall hybrid means, again calculated as the mean of the twelve means, are used in table 13*b* to compare the heat-responses of males and females. As with the inbreds, heat has a greater effect on the males than on the females in lengthening the tail ($P < 0.001$ at 8 and 12 weeks).

TABLE 14. COMPARISON OF THE HEAT-RESPONSES OF INBREDS AND HYBRIDS

age (weeks)	inbred heat- response (cm) (mean of four inbred means)	hybrid heat- response (cm) (mean of twelve hybrid means)	difference (<i>d</i>)	s.e.	
MALES					
4	0.861	0.901	-0.040	0.092 (149)	n.s.
8	2.083	1.993	0.090	0.123 (138)	n.s.
12	2.182	1.877	0.305	0.155 (91)	0.1 > <i>P</i> > 0.05
FEMALES					
4	0.855	0.846	0.009	0.085 (158)	n.s.
8	1.771	1.694	0.077	0.113 (153)	n.s.
12	1.808	1.514	0.294	0.135 (105)	<i>P</i> < 0.05

A comparison of the overall means for hybrids and inbreds in table 14, using a pooled standard deviation, shows that the inbred heat-response is greater than that for the hybrids in the males and females at 8 and 12 weeks (at 12 weeks, $P < 0.05$ for the females, $0.1 > P > 0.05$ for the males). Furthermore, it is seen that, whereas the heat-response of the inbreds increases from 8 to 12 weeks, it decreases for the hybrids.

Effect of control tail length on heat-response

It has already been pointed out that (*a*) the inbreds in the control environment have on the average shorter tails than the hybrids, and (*b*) the shorter the control tail length, the larger the heat-response. The larger response of the inbreds may then be due entirely to the fact that they have shorter tails in the control environment. It is cogent, therefore, to make an estimate of the response that would be made by the inbreds and hybrids if they had the same control tail length. To do this, the regression of heat-responses on control tail length has been calculated at 8 and 12 weeks for male and female inbreds and hybrids, using the individual litter means for each genotype. These regression lines are drawn in figure 7, but only the mean of the litter means for each strain is plotted.

The regression lines for the four male inbred strains at 8 weeks do not differ significantly. Any difference between the strains can, therefore, be attributed to differences in their control tail length and a single line can be fitted to estimate the change of heat-response with control tail length. In the same way, a single line will serve for the twelve different hybrids. The regression coefficients for the inbreds and hybrids do not differ significantly but the residual variance about the two parallel lines is significantly smaller than that about a common line. The inbred line is estimated by

$$(H-C) = 5.56 - 0.59C \pm 0.364 \text{ (151 d.f.)},$$

and the hybrid line by

$$(H-C) = 5.91 - 0.59C \pm 0.364.$$

The same situation holds for the males at 12 weeks, and it is again necessary to fit two parallel lines to show the relationship between the heat-response and control tail length. The parallel lines are estimated to be:

$$\text{inbreds } (H-C) = 6.46 - 0.68C \pm 0.323 \quad (104 \text{ d.f.}),$$

$$\text{hybrids } (H-C) = 6.80 - 0.68C \pm 0.323.$$

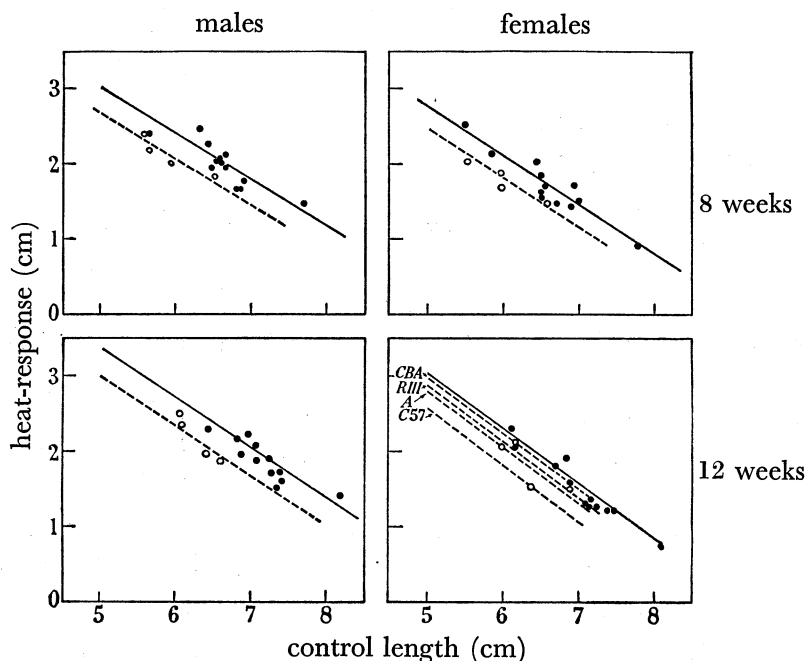


FIGURE 7. Male and female regression lines of heat-response on control tail length at 8 and 12 weeks of age. (The points plotted represent the means for the different genotypes and their reciprocal crosses.) \circ , inbred; \bullet , F_1 hybrid; - - - - -, inbred regression lines; ———, hybrid regression lines.

For the females at 8 weeks there are no significant differences between the regression lines of the four inbreds, but unlike the males there are significant differences between the regression lines for the twelve hybrids, which indicates that not all the differences in the female hybrid responses can be attributed to differences in control tail length. However, for purposes of comparison with the inbreds, a common line is fitted. Comparison of the common lines fitted to inbreds and hybrids reveals no significant difference between the regression coefficients, although two parallel lines give a better estimate of the relationship between heat-response and control tail length than one line:

$$\text{inbreds } (H-C) = 5.77 - 0.66C \pm 0.304 \quad (166 \text{ d.f.})$$

$$\text{hybrids } (H-C) = 6.08 - 0.66C \pm 0.304.$$

At 12 weeks, the relationship between heat-response and control tail length for the four female inbred lines is best estimated by four parallel lines. The differences between the female hybrids are also significant, but only just so, therefore a single line is fitted. The regression coefficients do not differ and the relationship is of the general form:

$$(H-C) = a + bC \pm e,$$

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where b is estimated as -0.73 ; estimates of a are 6.22 (*C57*), 6.65 (*CBA*), 6.55 (*RIII*), 6.47 (*A*) and 6.72 (hybrids). $e = 0.261$ estimated on 115 degrees of freedom.

These regressions for both sexes at the two ages demonstrate that the heat-response of the hybrids is in every case greater than that for the inbreds of the same control tail length. At 8 weeks, the mean tail length of the male hybrids in the heat exceeds that of the heat inbreds by 0.31 cm, if both hybrid and inbred heat-responses are scaled to the same tail length. At 12 weeks, the heat-response for the male hybrids would be 0.35 cm greater than that for the male inbreds of the same control tail length; although a single value cannot be allocated to the difference between the female hybrid and inbred heat-responses at 12 weeks, it is evident from the position of the regression lines that the hybrids make a greater response than any of the inbreds for a particular control tail length.

Variability in tail length

The split-litter experimental design precludes a reliable estimate of the within-litter variances, particularly for the inbreds in which litters are small, but the data are adequate for the determination of between-litter variances. These have been calculated as the

TABLE 15. INBRED AND HYBRID BETWEEN-LITTER VARIANCES OF TAIL LENGTH
(Degrees of freedom in parentheses.)

genotype	control		heat	
	males	females	males	females
3 weeks				
hybrids (pooled)	0.800 (107)	0.529 (120)	0.857 (107)	0.574 (120)
<i>C57</i>	0.188 (15)	0.182 (20)	0.203 (15)	0.187 (20)
<i>CBA</i>	0.511 (15)	0.533 (13)	0.458 (15)	0.637 (13)
<i>RIII</i>	0.684 (17)	1.021 (18)	0.753 (17)	0.657 (18)
<i>A</i>	0.401 (7)	0.870 (5)	0.507 (7)	0.438 (5)
4 weeks				
hybrids (pooled)	0.584 (100)	0.488 (107)	0.644 (100)	0.521 (107)
<i>C57</i>	0.191 (13)	0.212 (19)	0.273 (13)	0.211 (19)
<i>CBA</i>	0.524 (11)	0.572 (12)	0.643 (11)	0.715 (12)
<i>RIII</i>	0.906 (20)	1.151 (16)	0.968 (20)	0.768 (16)
<i>A</i>	0.398 (5)	1.083 (4)	0.419 (5)	0.287 (4)
8 weeks				
hybrids (pooled)	0.714 (97)	0.567 (105)	0.223 (97)	0.132 (105)
<i>C57</i>	0.200 (13)	0.232 (15)	0.065 (13)	0.053 (15)
<i>CBA</i>	0.743 (9)	0.748 (12)	0.326 (9)	0.292 (12)
<i>RIII</i>	0.836 (14)	0.824 (17)	0.318 (14)	0.206 (17)
<i>A</i>	0.522 (5)	0.743 (4)	0.346 (5)	0.259 (4)
12 weeks				
hybrids (pooled)	0.625 (62)	0.506 (74)	0.143 (62)	0.100 (74)
<i>C57</i>	0.262 (9)	0.291 (11)	0.161 (9)	0.077 (11)
<i>CBA</i>	0.714 (6)	0.917 (6)	0.272 (6)	0.150 (6)
<i>RIII</i>	1.094 (10)	0.599 (11)	0.278 (10)	0.075 (11)
<i>A</i>	0.905 (4)	0.973 (3)	0.108 (4)	0.308 (3)

variation between litter means for those litters with both heat and control representatives of the same sex (table 15). (Bartlett's test for homogeneity of variance reveals no significant differences between the hybrid lines; therefore, for them, a pooled between-litter variance is given (Brownlee 1949).) The heat and control variances of each strain have been compared by finding the significance of the correlation between $(H+C)$ and $(H-C)$ (Pitman

1939) and the comparison between different strains in the same environment made by 'F' tests.

The most obvious phenomenon, which occurs in every genotype, is the smaller variance of the heat-reared animals at 8 weeks and older compared with that of the control-reared animals. This results from the shorter tailed animals of a strain increasing their tail length more, when reared at a high temperature, than the initially longer tailed animals of the same strain. It therefore follows that the same factors which produce the convergence of the tail growth of different strains in the heat also apply within each strain.

TABLE 16. INBRED AND HYBRID COEFFICIENTS OF BETWEEN-LITTER VARIATION OF TAIL LENGTH

(Corrected for sample size (Haldane 1955).)

genotype	control		heat	
	males	females	males	females
<i>3 weeks</i>				
hybrids (pooled)	18.41	14.98	18.97	15.25
<i>C57</i>	9.21	8.73	9.37	8.84
<i>CBA</i>	19.27	18.26	18.19	20.46
<i>RIII</i>	16.11	20.51	17.63	16.03
<i>A</i>	15.25	22.47	17.31	15.56
<i>4 weeks</i>				
hybrids (pooled)	14.48	13.09	12.91	11.55
<i>C57</i>	8.68	8.95	8.87	7.79
<i>CBA</i>	16.89	16.69	15.72	15.87
<i>RIII</i>	17.98	20.10	16.08	14.03
<i>A</i>	13.74	23.44	11.84	10.08
<i>8 weeks</i>				
hybrids (pooled)	12.95	11.63	5.46	4.37
<i>C57</i>	7.69	8.20	3.29	3.06
<i>CBA</i>	15.85	14.77	7.36	7.01
<i>RIII</i>	14.28	13.97	6.90	5.70
<i>A</i>	13.34	16.34	8.05	7.07
<i>12 weeks</i>				
hybrids (pooled)	11.27	10.33	4.15	3.70
<i>C57</i>	8.19	8.61	4.90	3.57
<i>CBA</i>	14.40	16.05	6.41	4.84
<i>RIII</i>	16.04	11.46	6.30	3.33
<i>A</i>	16.51	17.47	4.03	7.30

The between-litter variances of the hybrids and the different inbreds (excluding *C57*s) are not significantly different at 3 weeks. The *C57*s are distinguished by a very low variance, which is significantly smaller than that of all other strains. (Comparisons involving the *A* strain cannot be very sensitive because of the few degrees of freedom available.) Both in the heat and control conditions the *C57*s retain their small between-litter variance, but by 12 weeks this is only significantly less than that for the control-reared male *RIII*s, control-reared female *CBA*s and heat-reared female *As*; it is matched by that for the heat-reared female *RIII*s, heat-reared male *As*, and male and female heat-reared hybrids. A small between-litter variance in the body weight of *C57*s also distinguished this strain from the other (see Part I, p. 496).

Among the control inbreds, the *RIII*s show the greatest variance in tail length, but this

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is never significantly greater than that of the other inbreds except *C57s*. In the heat, no one inbred has typically the largest variance.

Although at 3 weeks the male hybrids have the largest variance in tail length, this decreases relative to that of the inbreds with increasing age in both environments. The female hybrid variation at 3 weeks is relatively small and remains so. At no age is the hybrid variance significantly greater than that of the inbreds (with the exception of *C57s*) and it is, in fact, less than the corresponding inbred variances in 11 cases out of 16 in the control environment, and in 10 cases out of 16 in the hot environment, at 8 and 12 weeks. Moreover, the variance for hybrids is significantly less than that for female *RIII*s at 3 and 4 weeks in the control, female *CBA*s at 8 weeks in the heat, and male *RIII*s and female *A*s at 12 weeks in the heat.

Variances have generally been compared by other authors in terms of coefficients of variation (Bader 1956; Lerner 1954; Haldane 1955). The coefficient of variation, by making allowance for the effect of differences in absolute tail length on the variation, clearly demonstrates the smaller variability of the hybrids compared with the inbreds with the exception of the *C57* strain (table 16).

The hybrid coefficients are in fact smaller than the inbred coefficients in 7 out of 16 cases at 3 weeks, 9 out of 16 at 4 weeks, 12 at 8 weeks, and 11 at 12 weeks. Thus as the animals get older, the hybrid variation generally becomes smaller than that of three of the inbred lines; the *C57s* remain the least variable in the control conditions but in the heat the hybrids are comparable.

Coefficients of variation also show that the variability per unit length decreases much more with increasing age in the hot than in the control environment.

DISCUSSION

The dependence on environmental temperature of the tail growth rate and adult tail length of the mouse, irrespective of genotype, is amply confirmed by these experiments. The various studies that have now been made indicate that a temperature difference at high temperatures has a more marked effect than the same difference at low temperatures. A precise relationship between the magnitude of the response per unit temperature and the temperature range cannot, however, as yet be established, since the strains of mouse and experimental designs used in the different investigations were not the same.

How increases in temperature bring about an increase in tail growth remains undecided, but it seems unlikely that an environmentally determined long tail is produced by an increase in the amount of growth hormone secreted, since it is not necessarily associated with an increase in body weight (Part I). More probably it is a local phenomenon and due to an increased vascularization of the tail or a direct temperature effect on cell division. It does not follow that the response is a passive one, since it must also depend upon the sensitivity of the tissue, which is a function of the genotype of the animal.

The smaller variance of the tail length of the heat-reared animals, compared with the control-reared ones, has probably a different meaning than their smaller weight variance (Part I). Harrison (1959) has argued that although weight has a biological significance in itself, it is also an index of the overall vigour of an organism; he has concluded that, whereas genetically determined differences in size are no doubt adaptive, environmentally

induced modifications probably indicate that one of the environments is less favourable than the other. Tail length, however, seems to be a different type of character, since it does not reflect the overall physiological state of an organism but is rather a character which performs a particular biological function.

At any one temperature and within a single strain there is a close positive correlation between body weight and tail length (Falconer 1954). The functional reason for this correlation is, no doubt, that a larger animal requires both a longer balancing organ and a longer heat radiator than a small one. The difference in the dependence of tail length on body size at different temperatures could well be due to a difference in the relative importance of these two functions of the tail. Herrington (1940) finds that the mouse is thermally neutral between 86 and 91 °F, and Giaja (1938) has pointed out that, at temperatures below thermal neutrality, heat regulation is effected principally by chemical means. Certainly then, in control conditions differences in tail size will be of little consequence in thermoregulation, particularly if vascular changes can make tails of different length functionally equivalent. On the other hand, under conditions of thermal stress, differences in tail length may well have profound effects on thermal fitness (Harrison 1958*a*). Some of the smaller variability in tail length in the heat may be attributed to the smaller weight variance in this environment, but even when the weight variation is greatest in the heat the tail variability is still smaller (Part I). It seems, therefore, that the small heat variability is due to the fact that the hot environment demands a greater phenotypic uniformity of tail length than the control one. If this is so a small variability in a character such as the tail does not necessarily indicate optimal conditions but rather that, in the environment which produces low variability, the character concerned has great physiological importance.

It has been demonstrated that the absolute response of hybrid tail length to the hot environment is smaller than that of the inbreds. This could either be because the hybrids have a lower capacity to make the requisite response, or because with an already long control tail the further increment required for their thermoregulation is smaller. The fact that, when the responses of the hybrids and inbreds are scaled to the same tail length, the hybrids make the greater response indicates that it is not their capacity which is limited. In fact, it suggests that it is the response of the inbreds which is the inadequate one. This, however, cannot be categorically stated, since it cannot be assumed that the adaptiveness of the tail response necessarily increases with increasing magnitude of the response. Before the adequacy of a response is established, the metabolic state and amount of heat lost across the rest of the surface of the body must be determined. The evidence indeed suggests that the *C57s*, which have the shortest tails in the heat, have still fulfilled the requirements for their adaptation, since Harrison (1958*b*) has shown that not only has this strain the lowest body temperature in the heat, but also the difference between its control and heat temperature is the smallest. Nevertheless, it is worth pointing out that an analysis of growth in weight (Part I) shows that the hybrids find the hot environment more favourable than at least two of the inbreds, and if the tail plays the important role suggested, it seems likely that some of the superior heat fitness of the hybrids can be ascribed to their greater tail heat-response for a given control length. If, however, one uses the growth in weight, the body temperature, and the tail variance criteria as a measure of

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the adequacy of the tail response, it must be concluded that the *C57s* meet the environmental demand quite as well as the hybrids. (It seems, however, that too much importance should not be attached to the small variance of either *C57* or hybrid tail length since it may be an inevitable consequence of the low weight variance and have no independent meaning.) It may be concluded then that, although evidence has been found for the generally greater phenotypic flexibility of heterozygotes than homozygotes, in terms of effective adaptation to high temperatures, one homozygote is probably at least as successful.

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