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Growth of the Laboratory Mouse

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Summary. Body weights and tail lengths were observed every 3 days from birth to 60 days of age and every 6 days from 60 to 96 days in four lines of mice: C57BL/6J, an inbred; J, a synthetic outbred; GR, Goodale large body size line; and FR, Falconer large body size line. Mean 96-day body weights for lines C57BL, J, GR and FR were 25. 4, 29.7, 48.8 and 49.1 gm for males, and 19.9, 23.8, 38.5 and 38.2 gm for females, respectively. Lines GR and FR gave identical body weights at all ages studied. Both of these lines had previously plateaued in response to selection for large body size. The variability in body weight was smallest for lines C57BL and J, intermediate for FR and highest for GR. The pattern of variance over time was very similar in all lines and both sexes, showing a minimum at birth and a maximum at age of inflection. Growth in tail length of the four lines showed similar between line differences except that length in GR was greater than in FR. Age at vaginal opening in females coincided closely with age of inflection in body weight growth. Age at point of inflection did not differ between lines but appeared to occur somewhat earlier in females than in males.

Introduction

Over the years selection experiments (Goodale, 1938; Rahnefeld et al., 1963) and studies involving genotype-environment interactions (Falconer, 1955; Eisen and Legates, 1966) utilizing a body weight characteristic of the laboratory mouse have been very common. The mouse has also been utilized in other scientific areas in which the basic experimental criterion is also a body weight trait. In such studies it is important to know and understand the growth behavior of the experimental organism. This study demonstrates the growth patterns of four strains of mice each unique in genetic origin.

Source of Data

Four strains were employed each of which had undergone varying genetic changes through specific mating systems and selection methods. All strains were maintained by random mating prior to and during this study.

STRAIN J.: A synthetic stock made by and obtained from Jackson Laboratories, Bar Harbor, Maine. It was composed of (LP/J♀ × SJL/J♂)♀ × (BALB/cJ♀ × C57BL/6J♂)♂ and was randomly mated for three generations prior to data collection.

STRAIN C57BL/6J: An inbred stock obtained directly from Jackson Laboratories which had undergone 79 generations of brother-sister mating. It was maintained under random mating for one generation.

STRAIN GR: A stock selected for high 60-day body weight by Goodale (1938) for 80 generations and by us for an additional 15 generations. It was maintained by random mating for two generations. The stock had apparently plateaued in its response to selection.

STRAIN FR: A stock selected for high 42-day body weight (Nutrition Full diet) by Falconer and Latyszewski (1952) for 34 generations before transfer to the Mount Hope Farm where selection for high 60-day body weight was practiced. Selection for the latter trait was continued by use to a total of ten generations. The stock was then maintained by random mating for five generations. This stock had also apparently plateaued in its response to selection.

Data for body weight and tail length were collected on progeny from two consecutive generations referred to hereinafter as replicates I and II. The number of single pair matings and total number of progeny observed for each strain in each replicate are shown in Table 1. The data for replicates I and II_0 concern first litter progeny and that for replicate II_1 were for second litter progeny produced by the mating pairs observed in replicate II_0. Strain FR failed to produce second litters. As there were no significant differences between replicates I and II_0 for body weight or tail length, the data from the two replicates have been pooled. Data were obtained on age of vaginal opening by examining all female progeny in replicate II at three-day intervals beginning on the 15th day.

Table 1. *Number of single-pair matings by line and replicate with number of progeny in parenthesis*

Line	Replicate		
	I	II_0	II_1
J	13 (96)	16 (114)	13 (113)
C57	9 (41)	11 (48)	10 (55)
GR	13 (85)	16 (127)	5 (51)
FR	10 (80)	6 (44)	—

All litters studied were born within the 15-hour period from 5:00 P. M. to 8:00 A. M. and within a three-week period in each replicate. All mice in a litter were weighed as a group on day of birth (day 0) after insuring that all litters had suckled at least once. Subsequent weighings and measurements of tail length began at day 3; they were every three days thereafter up to and including the 60th day and every six days thereafter up to and including the 96th day. The mice were sexed and marked on day 3 and weaned on day 27. At weaning the sexes were separated and housed with either 3, 4 or 5 mice per cage.

Results

The growth curves for the two sexes and the four lines have the same general characteristics and are shown in Figures 1 and 2. On the basis of an approximate t-test, females were significantly smaller than males beyond 18, and 21 days in lines C57 and J, respectively, and beyond 24 days in lines GR and FR.

Both sexes of line C57 were the smallest and lines GR and FR the largest at all ages. Within both sexes, lines GR and FR demonstrated identical body weights at all ages well within the limits of the respective variances. Such a finding is of interest in light of the selection history of these lines. It should be noted however, that the major difference between

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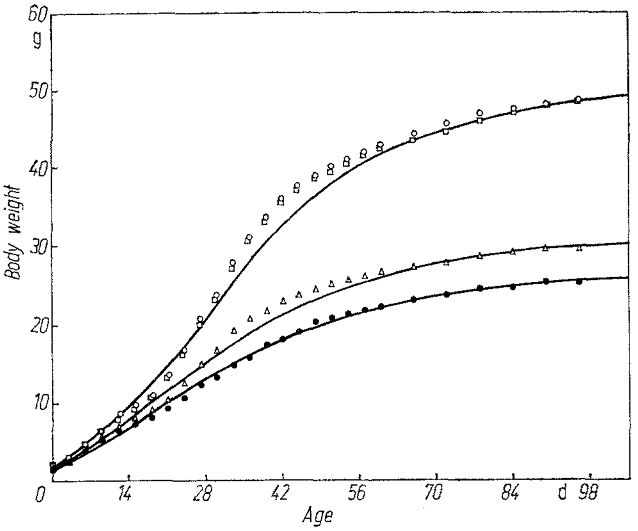

Fig. 1. Mean body weight of male mice; line C57BL/6J,–●–; line J, –△–; line GR, –□–; line FR, –○–. Smooth curve calculated using the method of FABENS (1965)

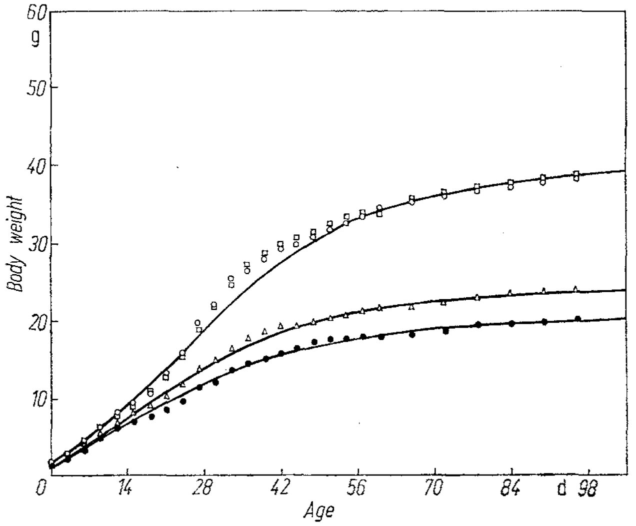

Fig. 2. Mean body weight of female mice. Legend as in Figure 1

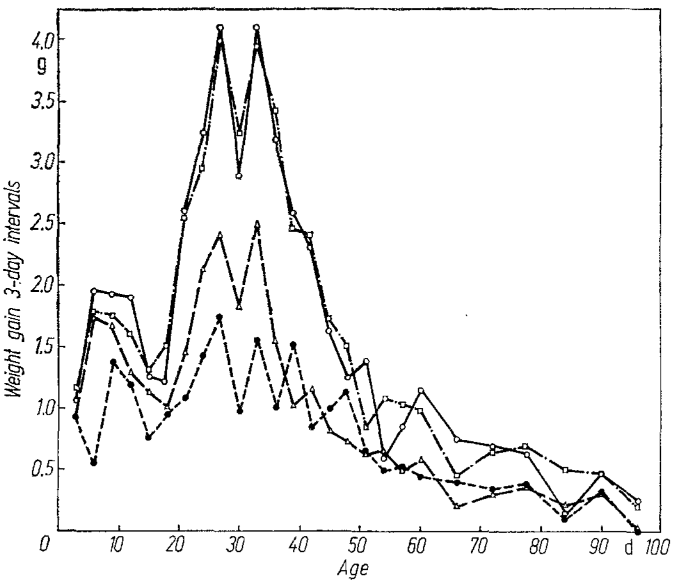

Fig. 3. Mean body weight gain in male mice calculated for 3-day intervals. Legend as in Figure 1

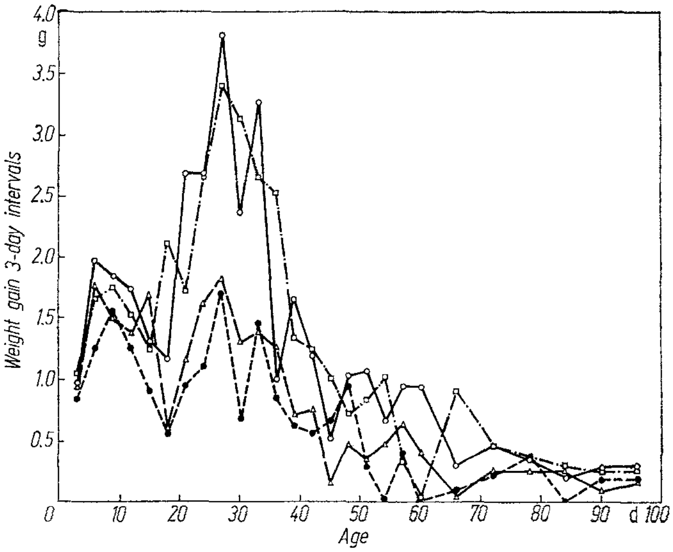

Fig. 4. Mean body weight gain in female mice calculated for 3-day intervals. Legend as in Figure 1

lines GR and FR and the other two lines occurs after 18 days and becomes more pronounced with age. The two selected lines are approximately twice as heavy at maturity as the inbred line. The growth curves for the four lines would suggest that lines C57 and J enter the decelerating growth phase earlier than lines GR and FR; the growth patterns also indicate a temporary deceleration in rate of gain between 9 and 18 days in all four lines.

Examination of weight gain in the four lines can shed some light on the latter observation since the inflection point coincides with the point of maximum gain. The data shown in Figures 3 and 4 are the simple weight gains of the mice over three-day intervals; beyond 60 days weight gain was calculated as one-half the gain over a six-day interval. Several pertinent observations can be made from these plots. There was a deceleration in growth rate by both sexes between 9 and 18 days. The only exception was line C57 which showed an increasing rate of gain at nine days. The drop in growth rate was followed by an abrupt and rapid acceleration. The pattern of early growth was extremely uniform for males of the four lines but was somewhat variable for females. Males and females of all four lines exhibited a maximum growth rate at 28 days with males showing a second maximum at 33 days; the growth rate of females at the latter age was lower than at 28 days. Males also exhibit a minimum between these ages, i. e., at 30 days. The weight gain at this point represents the gain during the three days immediately following weaning and the reduction was undoubtedly due to the stress of weaning. Females of lines C57 and FR, and line J to a lesser extent, also show a reduction in growth rate due to weaning. These data do not show the same effect for line GR; however, it is possible that these mice recovered from the stress more rapidly.

If we assume that the mice had fully recovered from the stress of weaning by 33 days and if we ignore the reduction in growth rate at 30 days we can postulate that the point of maximum growth rate for males is between 28 and 33 days (possibly 30 days) and that it is in the same range but somewhat earlier for females, especially those in line GR.

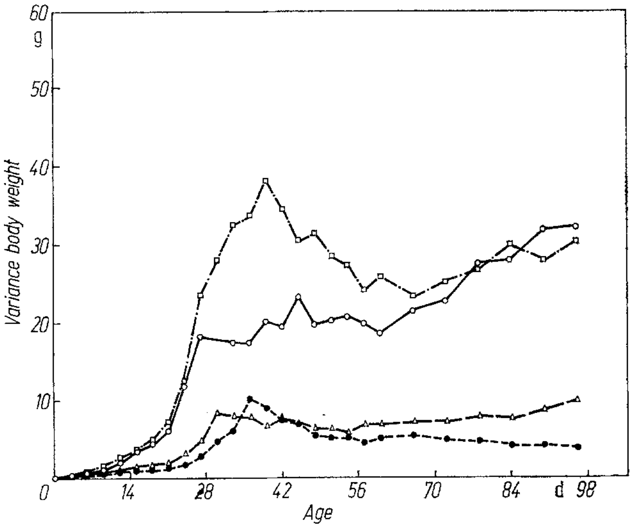

Fig. 5. Total variance in body weight of male mice. Legend as in Figure 1

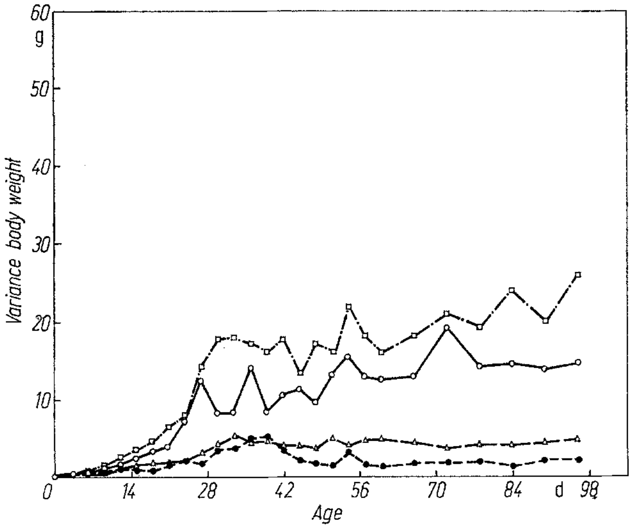

Fig. 6. Total variance in body weight of female mice. Legend as in Figure 1

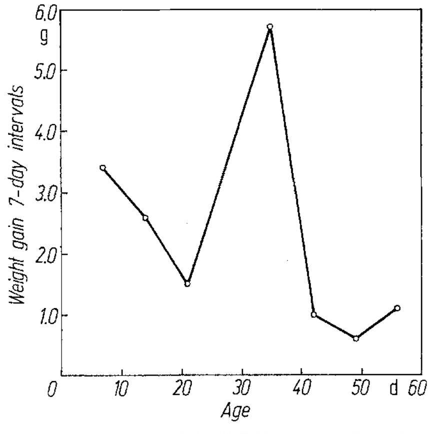

Fig. 7. Mean weight gain of BALB/C mice taken from Carmon (1965)

All four lines display a steady but variable deceleration in growth rate after 33 days and approach zero growth rate asymptotically. Lines GR and FR do not deviate greatly from the time pattern of the other two lines. The latter lines hold this pattern by dropping from the 33-day maximum much more rapidly than the other two lines. Line C57 gave the most variable growth rate pattern during the period of most rapid growth, 21 to 42 days. These findings suggest that the pattern of growth of the two selected lines, GR and FR, was very similar to the synthetic stock. The larger size of the selected lines was achieved through more rapid growth with little change in the chronological time pattern of the growth phases.

The total variance in body weight for the two sexes is shown in Figures 5 and 6. Lines GR and FR displayed a much greater variance than the other two lines to a degree roughly proportional to the difference in body weight and males of all lines showed a larger variance than females. Line GR males differ from the other lines and from females by displaying a very large variance over the period of rapid growth, approximately 27 to 42 days. The variance patterns do not reflect the deceleration in growth rate observed from 9—18 days.

An effort was made to determine if the observed deceleration in growth rate between nine and 18 days of age was due to husbandry practices unique to this study. Data on a sample of eight BALB/c mice from Carmon (1965) was examined for the effect (Figure 7). The mice studied by Carmon also showed a slow growth rate over the period in question. To further examine the phenomenon a group of 120 male mice from an 8-way cross stock maintained at the university of California, Davis was divided into a control group and a supplementary fed group. Supplemental feeding consisted of placing pelleted feed directly into the cage, beginning at nine days of age. The rational for the trial was that the young mice were not able to obtain solid food sufficient to supplement the dam's milk supply. The growth curves from three to 27 days for the two groups and for line J are shown in Figure 8 and their growth rates over three-day intervals in Figure 9. The decelerating growth rate phenomenon is evident from these data. Supplemental feeding appears to have partially alleviated the decline; however, even this group displayed a substantial reduction in rate of gain.

The curves for growth in tail length for males of the four lines are shown in Figure 10. The curves for females were similar, the only difference being that length at 96 days was approximately 3 mm less than for males. All four lines display the characteristic monotonically decreasing exponential pattern expected for growth in a linear dimension. The lines do not differ as widely for this characteristic as they do for body weight. Lines GR and FR have similar growth patterns for length of tail up to approximately 42 days after which growth slows to a steady state more rapidly in line FR than in line GR. This difference between the selected lines deviates from that found for body weight. Figure 11 demonstrates the allometric relationship between tail length and body weight by means of a log-log plot for line J and GR males. The relationship is not linear, thus the allometric equation $y = b\, x^a$ does not apply. It is interesting to note that the region of lowest slope on the log-log plot coincides with the age of most rapid acceleration in growth rate for body weight, approximately 18 to 30 days of age in both lines.

It suffices to say that the growth data observed for second litters (Replicate II_1) did not show any

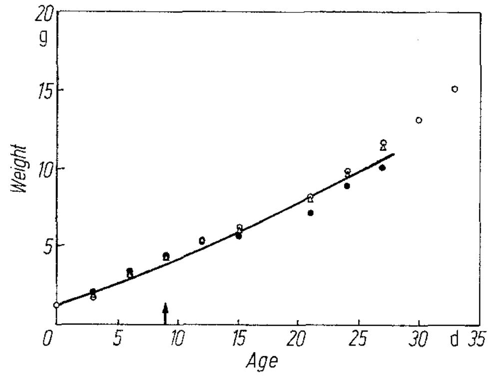

Fig. 8. Mean body weight of 8-way cross male mice given supplemental feed, –△–, no supplemental feed, –●–, and compared to line J, –○–. Line J data is the same as that given in Figure 1

real deviation from those of first litters for the three lines studied; however, there was a trend indicating that second litters were slightly smaller than first litter progeny.

The data for age at vaginal opening for the females in replicates II_0 and II_1 are summarized in Table 2.

Table 2. *Age at vaginal opening for females in Replicates II_0 and II_1 (observed at 3-day intervals)*

Line	Replicate II_0			II_1			Average
	No.	Mean	s. d.	No.	Mean	s. d.	
C57	25	33.6	2.83	29	31.4	4.92	32.5
J	60	28.0	4.30	51	23.8	6.17	25.9
GR	58	31.1	13.05	20	28.6	14.80	29.8
FR	18	23.0	6.15	—	—	—	23.0

There were no real differences between lines or first and second litter progeny but some trends were indicated. Line GR appears to be more variable than the other lines. The average age at vaginal opening coincides with the inflection point on the weight growth-curve as determined by the point of most rapid weight gain.

Discussion

The finding that two independent weight-selected lines of mice have identical growth patterns was unexpected. Such an observation would imply a near perfect genetic correlation between body weight at different ages. However, it must be noted that both of the lines studied have been extensively selected beyond the point of the apparent plateau; a similar study carried out at a time prior to the occurrence of the plateau may not have given the same results. If the lines were different in growth pattern at the point at which the plateau occurred, we could imply that the principle genetic component for body weight had responded to selection and that subsequent selection, the results of which may have been slow but cumulative, may have resulted in a response of associated and/or modifying genetic components such that a normal homeostatic pattern of growth was reestablished. A response to selection by modifying systems subsequent to selection for the principle component has been reported by Fraser (1967).

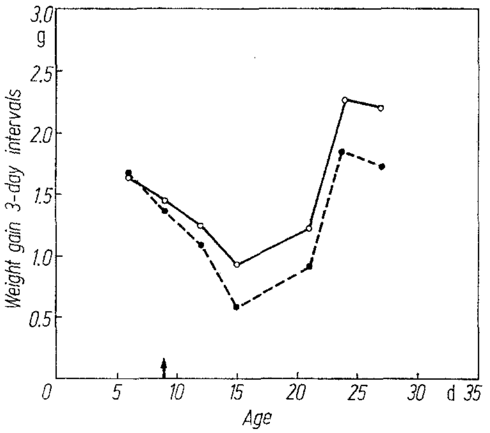

Fig. 9. Mean weight gain of 8-way cross male mice given supplemental feed –○– or no supplemental feed –●–

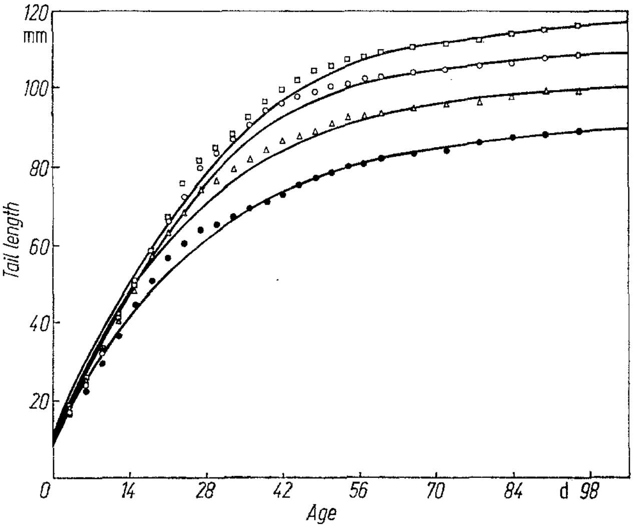

Fig. 10. Mean tail length of male mice. Legend as in Figure 1. Smooth curve calculated using the method of Fabens (1965)

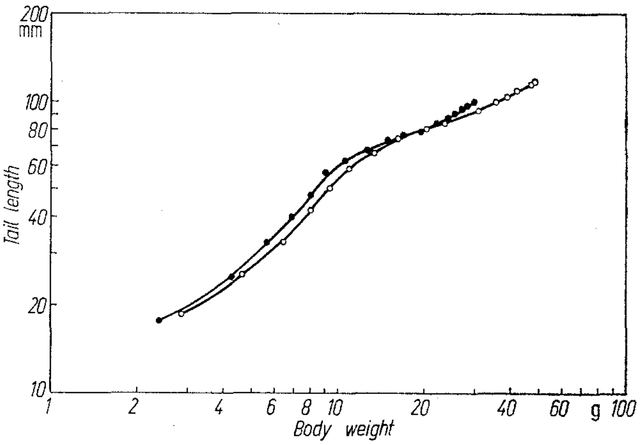

Fig. 11. A log-log allomeric plot of the relationship between mean body weight and mean tail length for male mice of line J, –●–, and line GR, –○– from 3 days to 96 days of age

Although the four lines studied differ widely in their genetic composition and have quite different body weights at a specific age, there are a number of similarities between the lines. The age of maximum rate of gain (inflection point) is consistent from line to line as is age at vaginal opening in females. All lines display an exponential increase in variance of body weight to a peak at similar ages. The break in exponential increase coincides with the age at inflection in the growth curve; the change in variance pattern at this time is similar to a metamorphic change in growth of an insect at the larval-pupal interface (see ENGLERT and BELL, 1963). The two selected lines did, however, show a difference in the magnitude of variance between 27—56 days of age, line GR being more variable at these ages. It is possible that selection for 42-day weight (line FR) affected a variance change different from that resulting from selection for 60-day weight (line GR).

Another state of similarity between the four lines was their consistent response to the environmental forces causing the drop in growth rate at nine days. Assuming that part of this complex pattern is due to a maternal interaction of the amount of milk the dam can supply and the demand for milk by the litter, the data suggests that the four lines were genetically similar in pattern of response and differed only in the magnitude of response. This interpretation is further substantiated by the growth response of the 8-way cross mice studies in the supplemental feeding experiment. All the above similarities suggest that chronological time is a good measure of gross physiological time in mice.

Zusammenfassung

Vier Linien von Laboratoriumsmäusen: der Inzuchtstamm C57BL/6J, der Kreuzungsstamm J, eine von GOODALE auf Körpergröße selektierte Linie GR und die von FALCONER auf Körpergröße ausgelesene Linie FR, wurden auf Körpergewicht und Schwanzlänge untersucht, und zwar von der Geburt bis zum 60. Lebenstage in 3 tägigem Abstand, von 60. bis 96. Lebenstage in 6tägigem Abstand. Am 96. Lebenstag betrugen die Durchschnittsgewichte für die 4 Linien 25,4; 29,7; 48,8 und 49,1 g für Männchen und 19,9; 23,8; 38,5 und 38,2 g für Weibchen. Die Linien GR und FR zeigten in allen untersuchten Altersstadien gleiche Gewichte. Beide waren durch vorangegangene Selektion auf Körpergröße weitgehend angeglichen. Die Variabilität des Gewichtes erwies sich bei den Linien C57BL und J als am geringsten, als intermediär bei FR und als am höchsten bei GR. Das Varianzmuster war bei allen Linien und für beide Geschlechter innerhalb des Untersuchungszeitraumes sehr ähnlich, mit einem Minimum bei der Geburt und einem Maximum am Ende der Wachstumsperiode (Inflexion). Das Schwanzwachstum zeigte die Linienunterschiede in gleicher Weise, lediglich der Stamm GR hatte eine größere Länge als FR. Das Öffnen der Vagina fällt zeitlich mit der Inflexion der weiblichen Tiere zusammen. Der Zeitpunkt der Inflexion differiert nicht zwischen den untersuchten Linien, scheint jedoch bei den weiblichen Tieren etwas früher als bei den männlichen zu liegen.

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