Gerontology *28*: 23–31 (1982)

Relationship of Sex, Exercise, and Growth Rate to Life Span in the Wistar Rat: a Multivariate Correlational Approach

Donald K. Ingram, Mark A. Reynolds, Charles L. Goodrick

Gerontology Research Center, Baltimore City Hospitals, Baltimore, Md., USA

Key Words. Body weight · Exercise · Growth · Life span · Rat · Sex

Abstract. Measures of body weight change were calculated and examined in relation to the life span of 68 male and 71 female Wistar rats that were maintained either in wheel-cage units or cages without wheels. The analysis revealed the following: (a) sex and wheel exercise accounted for nearly one third of the obtained variation in life span; (b) growth rate, defined as the ratio of peak body weight to growth duration, accounted for over 15% of the variance in life span unattributable to sex and exercise; (c) measures of body weight gain early in the developmental span were virtually unrelated to life span; (d) beyond 9 months of age, measures of body weight gain showed a significant positive relationship with life span. Thus, there was no evidence of a negative relationship between life span and body weight gain during early life.

A classic and fundamental question in gerontology has been the relationship between growth rate and life span [*Bidder*, 1932; *Brody*, 1924; *Comfort*, 1979; *Lansing*, 1947; *Minot*, 1908; *Pearl*, 1928; *Rubner*, 1908; *Sherman and Campbell*, 1935]. The general observation that the longer the growth period for a species, the longer the comparative life span of that species, has sparked numerous empirical studies. One of the major objectives in these studies has been to effect longevity by manipulating growth rate, typically within a species. Experimental manipulations have included caloric intake [*Berg and Simms*, 1960; *Comfort*, 1979; *Ingle* et al., 1937; *Nolen*, 1972; *McCay*, 1935; *McCay* et al., 1939, 1943; *Osborne and Mendel*, 1915; *Reisen* et al., 1947]; dietary protein intake [*Goodrick*, 1978; *Leto* et al., 1976; *Miller and Payne*, 1968; *Nakagawa and Masana*, 1971; *Ross*, 1959; *Stoltzner*, 1977]; feeding schedule [*Carlson and Hoelzel*, 1946; *Gerbase-DeLima* et al., 1975]; and exercise [*Drori and Folman*, 1976; *Goodrick*, 1978; *McCay* et al., 1941; *Retzlaff* et al., 1966]. In addition, the relationship of genetic variables, such as sex and strain, to growth rate and longevity has also been of interest [cf. *Comfort*, 1979].

In a recent study, *Goodrick* [1980] examined the effects of voluntary wheel exercise on life span, body weight, growth rate, and metabolic rate in male and female Wistar rats. Group differences were marked. Irrespective of sex, rats allowed wheel exercise lived significantly longer than nonexercised rats. Moreover, exercised animals tended to have lower body weights, higher metabolic rates, slower growth rates, and longer growth durations than did nonexercised animals. In addition to intergroup differences, significant intragroup relationships between parameters of growth and longevity emerged. Specifically, in each group, growth rate was negatively related to longevity, while growth duration was positively related.

In *Goodrick's* [1980] study, growth rate and growth duration were each defined in terms of body weight gain. The growth rate measure was defined quantitatively as follows:

$$\text{Growth rate (GR)} = \frac{\text{Peak body weight (PKWT)}}{\text{Growth duration (GD)}},$$

where PKWT is equal to the maximum body weight obtained by an animal, and GD is the corresponding age (in months) at which PKWT occurs. Thus, GR defines body weight increment as a linear function over time. However, body weight increment in rats is a nonlinear function over time, with the greatest body weight gain occurring early in the life span [*Brody*, 1945]. Moreover, because the upper limit of the time interval for which GR provides an estimate of growth rate is variable, since it is dependent on when PKWT is obtained, GR does not yield estimates of growth rate for equal chronological intervals.

Accordingly, there was a twofold objective to be achieved by further analysis of the data from *Goodrick's* [1980] study. Although the previous analysis detailed the separate contributions of sex and exercise to the obtained variation in life span, no attempt was made to assess the collective contributions of these two variables, nor the additional contribution of individual differences in GR to longevity. Therefore, through the use of multivariate techniques, our first objective was to quantify the collective contribution of sex, exercise, and GR to the obtained variation in life span for these animals.

As previously noted, GR is a developmentally determined parameter, in that it is dependent on when PKWT is obtained. Therefore, our second objective was to examine the relationship of other, more conventionally defined parameters of growth rate to longevity for these animals. Specifically, we were interested in identifying the relationship between longevity and estimates of growth rate early in the life span, as measured across equivalent chronological intervals. Consistent with past efforts using multivariate correlational analyses [*Ross* et al., 1976], the search for early life span growth correlates of longevity in the rat has both theoretical and practical significance. As such, our effort paralleled *Everitt and Webb's* [1957] study of this strain, but the additional analysis of longevity in females and exercised animals broadened the scope of the present research.

Method

Body weight data were analyzed for 139 Wistar rats, 68 males and 71 females. At 1.5 months of age, approximately half of each group were housed 2 per cage in either standard laboratory cages or in exercise wheel cages, where they remained until death. Measures of body weight were obtained monthly. *Goodrick* [1980] should be consulted for further procedural details.

Results

Using a hierarchical multiple regression analysis, we first quantified the separate and collective contributions of sex, caging condition, and the interaction term to the obtained variation in life span. Dummy-coded vectors were used in the analysis to denote the categorical independent variables, sex and caging condition [*Kerlinger and Pedhazur,* 1973]. Since our primary interest was in determining the unique variation in life span attributable to caging condition, i.e., exercise versus no exercise, we entered sex into the regression equation first, then caging condition, followed by the interaction term. Because our interest was also in assessing whether the growth rate parameter GR could contribute to the explainable variance in life span once the contribution of the design variables had been partialed out, we entered GR into the regression equation last. The results of this analysis are summarized in table I.

As expected, sex alone accounted for a substantial proportion of the obtained variation in life span, $R^2 = 0.20$. Nevertheless, exercise contributed a significant increment to the multiple R^2, accounting for an additional 10% of the explainable variance. As observed in *Goodrick's* [1980] previous analysis, the interaction term failed to account for any variation in life span beyond that already explained by sex and caging condition. Finally, the addition of GR into the regression equation resulted in a significant increment in the multiple R^2, accounting for an additional 16% of the variance in life span.

Collectively, then, sex and caging condition accounted for nearly one third of the obtained variance in life span. In turn, GR accounted for over one sixth of the variance in life span unattributalble to the design vari-

Table I. Summary of the hierarchical regression of sex, caging condition, sex by caging condition interaction, and GR on life span

Step	Variable entered	R	R^2	Adjusted[a] R^2	d.f.	F to enter[b]	F[c]
1	sex (A)	0.45	0.20	0.19	1/137	34.10*	
					1/137		34.10*
2	caging condition (B)	0.55	0.30	0.29	1/136	20.00*	
					2/136		29.39*
3	A × B	0.55	0.30	0.29	1/135	< 1	
					3/135		19.53*
4	GR	0.68	0.46	0.44	1/134	40.00*	
					4/134		28.43*

[a] The 'Adjusted R^2' statistic is based on unbiased estimates of the error variance and total population variance, providing a more conservative estimate than R^2 of the explainable variance in the criterion.

[b] The 'F to enter' is a test of the significance of the increment in the proportion of variance accounted for by a given variable when entered next in the regression equation.

[c] The F ratio for the overall R at each step.

* $p < 0.001$.

ables. This relationship was clearly negative, indicating that a slow rate of growth was associated with greater longevity irrespective of sex or caging condition.

Given the predictive power of GR, we proceeded next to assess whether other estimates of growth rate at more defined chronological intervals earlier in the life span would also show a similar association with longevity. To this end, four frequently applied measures of growth rate in the rat were selected and computed for the control and exercise groups. The computational formulas and references from which they were derived are listed below:

$$GR1 = (WTY - WTX)/(T_2 - T_1)$$ [*Brody*, 1945]

$$GR2 = (WTY - WTX)/1/2\,(WTY + WTX)$$ [*Brody*, 1945]

$$GR3 = (LGWTY - LGWTX)/(T_2 - T_1)$$ [*Brody*, 1945]

$$GR4 = (LGWTY - LGWTX)/(1/T_1 - 1/T_2)$$ [*Zucker* et al., 1941]

where T_1 and T_2 equal either 1.5 and 3.0, 3.0 and 6.0, 6.0 and 9.0, 9.0 and 12.0, 12.0 and 15.0, or 15.0 and 18.0 months, respectively; WTX = body weight at T_1; WTY = body weight at T_2; $LGWTX$ = natural log of body weight at T_1, and $LGWTY$ = natural log of body weight at T_2.

As noted above, the analysis examined body weight gain in terms of linear (GR1, GR2) and exponential (GR3, GR4) functions. The zero-order partial correlations of these growth rate estimates with life span are presented in table II. Sex was used as a covariate to control for growth rate differences between male and female rats.

No significant relationships emerged between estimates of growth rate and life span at intervals of 1.5–3.0, 3.0–6.0, and 6.0–9.0 months, in either the control or exercise group. Noteworthy, however, was the consistent negative trend of the correlations at these time intervals, but over 80% of the correlations were between –0.10 and 0. In the control group, all four estimates of growth rate showed significant positive relationships with life span at 9.0–12.0 months, while no such relationships emerged in the exercise group during this time interval. In the exercise group, significant positive relationships between all the growth rate estimates and life span emerged at both 12.0–15.0 and 15.0–18.0 months.

In summary, no significant *negative* relationships emerged between these measures of growth rate and life span at any of the time intervals examined, in either the control or exercise group, when sex was controlled. This finding is in contrast with the inverse relationship observed between GR and life span. Moreover, in this analysis significant *positive*

Table II. Zero-order partial correlations of growth rate measures with life span, with sex as a covariate

Life period months	Growth rate measures			
	GR1	GR2	GR3	GR4
Control group				
9.0–12.0	0.27*	0.25*	0.25*	0.25*
12.0–15.0	0.16	0.14	0.16	0.16
15.0–18.0	0.26	0.25*	0.22*	0.22*
Exercise group				
9.0–12.0	–0.04	0.02	0.02	0.02
12.0–15.0	0.46***	0.46***	0.47***	0.47***
15.0–18.0	0.29**	0.29**	0.29**	0.29**

Note that no significant relationship emerged between estimates of growth rate and life span at 1.5–3.0, 3.0–6.0, and 6.0–9.0 months, in either group.

* $p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

relationships emerged between the additional measures of growth rate and longevity late in the life span, in both the control and exercise groups. This relationship suggests that animals which gained weight at the highest rates at these ages lived the longest.

A closer examination of GR seemed appropriate. Thus, to assess the extent to which GR validly measured growth rate, i.e., the construct validity of GR [*Nunnally*, 1978], five additional growth rate measures were selected and computed for each group as shown below:

$$GRA = (WTY - WTX)/WTX \text{ [Brody, 1945]}$$
$$GRB = (WTY - WTX)/1/2\,(WTY + WTX) \text{ [Brody, 1945]}$$
$$GRC = (WTY - WTX)/(T_2 - T_1) \text{ [Brody, 1945]}$$
$$GRD = (LGWTY - LGWTX)/(T_2 - T_1) \text{ [Brody, 1945]}$$
$$GRE = (LGWTY - LGWTX)/(1/T_1 - 1/T_2) \text{ [Zucker et al., 1941]}$$

where WTX = weight at 1.5 months; WTY = weight at 18.0 months; $LGWTX$ = natural log of weight at 1.5 months; $LGWTY$ = natural log of weight at 18.0 months; T_1 = 1.5 months, and T_2 = 18.0 months.

Each comparative measure provided an estimate of growth rate during the period of maximum weight gain for these rats, ending at approximately 18 months of age [*Brody*, 1945]. Linear (GRA, GRB, GRC) and exponential (GRD, GRE) functions were again examined.

The intercorrelations of all the growth rate measures and the correlation of each with life span are presented in table III. This intercorrelation matrix was submitted to a factor analysis based on a principle-component solution with iteration of communalities, using orthogonal rotation to arrive at the terminal factors [*Nie* et al., 1975]. The analysis yielded two terminal factors, and the rotated factor loadings for the component variables are presented in table IV. The factor loadings clearly indicate that GR and life span are highly associated (factor 2) but unrelated to the five comparative growth rate measures. The comparative measures, in turn, defined a unique growth rate factor (factor 1). A high degree of association emerged between all of the comparative measures. The eigenvalue for factor 1 was 4.63, with the solution accounting for 74.5% of the common variance. The com-

Table III. Intercorrelation matrix of six growth rate measures and life span (LS)

Variable	Correlation coefficients						
	LS	GR	GRA	GRB	GRC	GRD	GRE
LS	1.00						
GR	−0.66*	1.00					
GRA	0.09	0.20	1.00				
GRB	0.30	−0.06	0.89*	1.00			
GRC	0.00	0.34	0.96*	0.85*	1.00		
GRD	0.33	−0.11	0.85*	0.99*	0.82*	1.00	
GRE	0.33	−0.11	0.85*	0.99*	0.82*	0.99*	1.00

* $p < 0.01$.

Table IV. Rotated orthogonal-factor matrix[1]

Variable	Factor loadings	
	factor 1	factor 2
LS	0.18	0.71
GR	0.11	−0.94
GRA	0.94	−0.12
GRB	0.96	0.24
GRC	0.93	−0.26
GRD	0.98	0.19
GRE	0.96	0.24

[1] The solution is based on the principle-component method with iteration of communalities.

parable figures for factor 2 were 1.58 and 25.5, respectively. Thus, the results of the factor analysis provided no support for the construct validity of GR, i.e., the validity of GR as a measure of growth rate.

Finally, since GR was defined as the ratio of PKWT to GD, it is likely that GR is functionally equivalent to either one or both of these other measures. The correlation of GR and PKWT in each group was as follows: (a) for the male control group, $r = -0.19$, NS; (b) for the female control group, $r = 0.54$, $p < 0.001$; (c) for the male exercise group, $r = 0.60$, $p < 0.001$; and (d) for the female exercise group, $r = 0.29$, NS. When the contribution of PKWT to life span was held constant, the relationship between GR and life span remained virtually unaffected, $r = 0.49$, $p < 0.001$, collapsing across groups. Thus, the separate contributions of GR and PKWT to life span appear to be independent of one another.

The correlation of GR and GD was much higher and consistent as follows: (a) for the male control group, $r = -0.89$, $p < 0.001$; (b) for the female control group, $r = -0.84$, $p < 0.001$; (c) for the male exercise group, $r = -0.90$, $p < 0.001$; and (d) for the female exercise group, $r = -0.78$, $p < 0.001$. Moreover, when the contribution of GD to the obtained variation in life span was held constant, the relationship between GR and life span virtually disappeared, $r = 0.03$, NS, collapsing across groups. Clearly, GR and GD represent 'redundant' variables [*Gordon*, 1968]. In effect, GR more accurately measured how long an animal continued to gain body weight rather than the rate at which body weight was actually gained early in life, i.e., the index lacked construct validity [*Nunnally*, 1978].

The end of growth duration was defined by a loss of body weight or the absence of body weight gain preceding death. Among male rats, body weight loss prior to death was recorded for 93% of the controls and 93% of the exercised animals. Among female rats, 64% of the controls and only 41% of the exercised animals lost weight. Thus, senescent body weight decline appeared virtually without exception among male rats but was less prevalent among females.

Discussion

Two objectives were sought in the current analysis of data from *Goodrick* [1980]. The first objective was to quantify the relationship of sex, exercise, and growth rate to the life span of the Wistar rat. A multiple regression analysis revealed that sex alone accounted for about 20% of the obtained variance in life span; that caging condition (exercise versus no exercise) contributed an additional 10% to the explainable variation in life span; and that GR, as applied by *Goodrick* [1980], accounted for 16% of the variance in life span unattributable to these design vari-

ables. Thus, our first objective was accomplished. Collectively, then, sex, exercise, and GR accounted for nearly 50% of the obtained variance in life span. We intend this analysis to provide a basis for comparison with data produced in future studies.

The predictive potential of GR also prompted our second objective, namely, to quantify the relationship between life span and measures of growth during early development. Whereas GR showed a clearly negative relationship with longevity, our further analysis, which applied several other conventional measures of body weight gain, yielded no significant correlations with life span during early development. In contrast, significant positive correlations between the various estimates of growth rate and longevity emerged at chronological intervals later than 9 months of age, when some animals had begun to lose weight. This finding paralleled those of earlier studies of the Wistar rat [*Everitt*, 1957; *Everitt and Webb*, 1957] and further documented the relationship in both exercised and nonexercised groups. The effect was somewhat delayed in the exercised animals, probably due to the later onset of senescent decline in body weight in this group.

Although our further analysis failed to reveal any early life span growth correlates of longevity, the analysis did permit insight into the nature of the relationship of GR to life span. Using a variety of growth rates computed over the interval spanning weaning to 18 months of age, we again found no significant relationship to life span. Moreover, we found no relationship between these measures of body weight gain and GR. Indeed, further analysis revealed that GR was a redundant measure of growth duration. Rather than being a valid index of the rate at which body weight was gained during specified intervals of the life span, this measure was found to more accurately reflect the age at which an animal either stopped gaining body weight, began losing it, or died.

With few exceptions, a period of body weight decline preceded death among our male Wistar rats, as observed previously [*Everitt*, 1957]. Consistent with reports for male rats of other strains [*Chesky and Rockstein*, 1976], this observation is not universal, as it did not apply to our female rats. Among females only 41% of the exercised group and 64% of the control groups lost weight. These data do not represent the final argument about this phenomenon because our measurements of body weight were spaced at relatively wide intervals, and because we did not adjust the measurements to account for the presence of tumors or other pathologies.

Whether the termination of body weight gain represented the presence of disease was also left to question, since no pathological examinations were conducted. Previous findings suggest that the termination of body weight gain is a frequent manifestation of chronic diseases [*Berg and Harmison*, 1957; *Berg and Simms*, 1962; *Everitt*, 1957; *Everitt and Webb* 1957; *Simms and Berg*, 1957]. These studies indicate that rats continue to gain weight across their life span provided they do not contract a chronic disease leading to a terminal decline in body weight and ultimately death due to the effects of the particular disease.

In summary, the present analysis produced no evidence of an association between the rate at which body weight is gained during early developmental intervals and subsequent life span in the Wistar rat. This finding supports those of past studies [*Everitt and Webb*, 1957; *Sherman and Campbell*, 1935] but conflicts with others [*McCay*, 1935;

McCay et al., 1939; *Ross* et al., 1976]. Only greater weight gain later in life was related to longevity. Manipulations of growth rate, such as exercise, effect longevity in the rat, but in the absence of a correlation between growth rate and longevity within groups of similarly treated animals, a causal link is not obvious. In search of a causal explanation, it is clear that more attention should be focused upon the relationship between life span and growth duration.

Several improvements in the nature of data collection will aid in the quality of future analyis. First, a more fine-grained analysis using weekly body weight data will allow for greater precision in determining actual rates of body weight gain. Moreover, the recording of weekly body weights will allow for other parameters of development, such as inflection points in growth, also to be identified. Second, quantitative determinations of the effect of fat deposition on body weight gain need to be made [*Lesser* at al., 1973]. Finally, the determination of morbidity will aid in identifying pathological factors affecting the variance in growth rate and longevity [*Ross and Bras*, 1965]. Until then, these issues will remain as current as they are classic.

References

Berg, B.N.; Harmison, C.: Growth, disease, and aging in the rat. J. Geront. *12:* 370–377 (1957).

Berg, B.N.; Simms, H.S.: Nutrition and longevity in the rat. II. Longevity and onset of disease with different levels of food intake. J. Nutr. *71:* 255–263 (1960).

Berg, B.N.; Simms, H.S.: Disease, rather than aging, as the cause of weight loss and muscle lesions in the rat. J. Geront. *17:* 452 (1962).

Bidder, G.P.: Senescence. Br. med. J. *ii:* 583–585 (1932).

Brody, S.: The kinetics of senescence. J. gen. Physiol. *6:* 245–257 (1924).

Brody, S.: Bioenergetics and growth (Reinhold, New York 1945).

Carlson, A.J.; Hoelzel, F.: Apparent prolongation of the life span of rats by intermittent fasting. J. Nutr. *31:* 363–375 (1946).

Chesky, J.A.; Rockstein, M.: Life span characteristics in the male Fischer rat. Exp. Aging Res. *2:* 399–407 (1976).

Comfort, A.: The biology of senescence (Elsevier, New York 1979).

Drori, D.; Folman, Y.: Environmental effects on longevity in the male rat: exercise, mating, castration and restricted feeding. Exp. Gerontol. *11:* 25–32 (1976).

Everitt, A.: The senescent loss of body weight in male rats. J. Geront. *12:* 382–387 (1957).

Everitt, A.; Webb, C.: The relation between body weight changes and life duration in male rats. J. Geront. *12:* 128–135 (1957).

Gerbase-DeLima, M.; Liu, R.K.; Cheney, K.E.; Mickey, R.; Walford, R.L.: Immune function and survival in a long-lived mouse strain subjected to undernutrition. Gerontologia *21:* 184–202 (1975).

Goodrick, C.L.: Body weight increment and length of life. II. The effect of genetic constitution and dietary protein. J. Geront. *33:* 184–190 (1978).

Goodrick, C.L.: Effects of long-term voluntary wheel exercise on male and female Wistar rats. Gerontology *26:* 22–33 (1980).

Gordon, R.: Issues in multiple regression. Am. J. Sociol. *73:* 592–616 (1968).

Ingle, L.; Wood, T.R.; Banta, A.M.: A study of the longevity, growth, reproduction and heart rate in *Daphnia longispina* as influenced by limitations in quantity of food. J. exp. Zool. *76:* 325–352 (1937).

Kerlinger, F.; Pedhazur, E.: Multiple regression in behavioural research (Holt, Rinehart & Winston, New York 1973).

Lansing, A.I.: Evidence for ageing as a consequence of growth cessation. Anat. Rec. *99:* 579–580 (1947).

Lesser, G.T.; Deutsch, S.; Markofsky, J.: Aging in the rat: longitudinal and cross-sectional studies of body composition. Am. J. Physiol. *225:* 1472–1478 (1973).

Leto, S.; Kokkonen, G.C.; Barrows, C.H.: Dietary protein, life span, and biochemical variables in female mice. J. Geront. *31:* 144–148 (1976).

McCay, C.M.: The effect of retarded growth upon the length of life span and upon the ultimate body size. J. Nutr. *10:* 63–79 (1935).

McCay, C.M.; Maynard, L.A.; Sperling, G.; Barnes, L.L.: Retarded growth, life span, ultimate body size and age changes in the albino rat after feeding diets restricted in calories. J. Nutr. *18:* 1–13 (1939).

McCay, C.M.; Maynard, L.A.; Sperling, G.; Osgood, H.: Nutritional requirements during the latter half of life. J. Nutr. *21:* 45–60 (1941).

McCay, C.M.; Sperling, G.; Barnes, L.L.: Growth, aging, chronic diseases, and life span in rats. Archs Biochem. *2:* 469–479 (1943).

Miller, D.S.; Payne, P.R.: Longevity and protein intake. Exp. Gerontol. *3:* 231–234 (1968).

Minot, C.S.: The problem of age, growth, and death; a study of cytomorphosis, based on lectures at the Lowell Institute, Moderne Probleme der Biologie (Jena, London 1908).

Nakagawa, I.; Masana, Y.: Effect of protein nutrition on growth and life span in the rat. J. Nutr. *101:* 613–620 (1971).

Nie, N.; Hall, C.; Jenkins, J.; Steinbrenner, K.; Bent, D.: Statistical package for the social sciences (McGraw-Hill, New York 1975).

Nolen, G.A.: Effect of various restricted dietary regimes on the growth, health and longevity of albino rats. J. Nutr. *102:* 1477–1494 (1972).

Nunnally, J.: Psychometric theory (McGraw-Hill, New York 1978).

Osborne, T.B.; Mendel, L.B.: The resumption of growth after long-continued failure to grow. J. biol. Chem. *23:* 439–454 (1915).

Pearl, R.: The rate of living (Knopf, New York 1928).

Ross, M.H.: Protein, calories, and life expectancy. Fed. Proc. *18:* 1190–1207 (1959).

Ross, M.; Bras, G.: Tumor incidence patterns and nutrition in the rat. J. Nutr. *87:* 245–260 (1965).

Ross, M.; Lustbader, E.; Bras, G.: Dietary practices and growth responses as predictors of longevity. Nature, Lond. *262:* 548–553 (1976).

Reisen, W.H.; Herbst, E.J.; Walliker, C.; Elvehjem, C.A.: The effect of restricted caloric intake on the longevity of rats. Am. J. Physiol. *148:* 614–617 (1947).

Retzlaff, E.; Fontaine, J.; Furuta, W.: Effect of daily exercise on life span of albino rats. Geriatrics *21:* 171–177 (1966).

Rubner, M.: Das Problem der Lebensdauer und seine Beziehungen zum Wachstum und Ernährung (Oldenburg, Munich 1908).

Sherman, H.C.; Campbell, H.L.: Rate of growth and length of life. Proc. natn. Acad. Sci. USA *21:* 235–239 (1935).

Simms, H.S.; Berg, B.N.: Longevity and the onset of lesions in male rats. J. Geront. *12:* 244–252 (1957).

Stoltzner, G.: Effects of life-long dietary protein restriction on mortality, growth, organ weights, blood counts, liver adolase and kidney catalase in BALB/C mice. Growth *41:* 337–348 (1977).

Zucker, T.F.; Hall, L.; Young, M.; Zucker, L.: The growth curve of the albino rat in relation to diet. J. Nutr. *22:* 123–138 (1941).

Received: February 24, 1981
Accepted: March 24, 1981

Donald Keith Ingram, PhD, Gerontology Research Center, National Institute on Aging, Baltimore City Hospitals, Baltimore, MD 21224 (USA)