Age, Vol. 1, Pages 130-142, October, 1978

DIET AND LIFE EXTENSION IN ANIMAL MODEL SYSTEMS *

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Abstract

Recent studies have shown that beneficial effects can be brought about when underfeeding is initiated in adult as well as young growing animals. In addition, such dietary manipulations have been shown to delay the onset of a variety of diseases although its relationship to total incidence has not been established. It has been proposed that dietary restriction reduces protein synthesis and increases lifespan by retarding genetic informational transfer during early life and reducing the use of the genetic code and thereby minimizing genetic imperfections as they may occur during late life.

Introduction

Dietary restriction has been shown to increase the lifespan of laboratory animals. In general, dietary restriction has been brought about by: 1) reducing the daily intake of a nutritionally adequate diet (one which supports maximal growth); 2) intermittently feeding a nutritionally adequate diet (e.g., feeding every second, third, or fourth day); and 3) feeding *ad libitum* a diet containing insufficient amounts of protein to support maximal growth.

Any increase in lifespan associated with dietary manipulations is generally believed to be due to a restriction of dietary calories. However, most studies in an attempt to accomplish caloric restriction have restricted the intake of a nutritionally adequate diet so that not only has the caloric intake been reduced but also the protein and other dietary components as well. It must be recognized that it is experimentally difficult to hold all dietary components constant and reduce only calories. In order to achieve only caloric restriction under *ad libitum* conditions, there must be adjustments in the diets according to an animal's intake which changes markedly with growth and is dependent upon dietary composition. This has been accomplished (1) and the data indicated that restriction of calories indeed increased the life span of C_3 H mice.

* This is the first paper of the mini-symposium on nutrition and aging organized by Charles H. Barrows, Jr., and presented on Thursday, September 29, 1977 as part of the 7th Annual Meeting of the American Aging Association in New York City.

The *ad libitum* feeding of a diet containing insufficient amounts of protein to support maximal growth has been shown to increase the life span of both young growing and adult animals (2). However, it is not clear the degree to which caloric restriction occurs under these experimental conditions. For example, it has been reported that reducing dietary protein did not affect the caloric intake of adult rats (3). However, Ross (4) reported that the caloric intake of rats fed a synthetic diet containing 8% casein was reduced when compared to that of animals fed a commercial diet. Similar data has been reported by Barrows, et al. (5). In contrast, Stoltzner (6) has reported a marked increase in the caloric intake of BALB/c mice fed *ad libitum* diets containing low amounts of protein. Therefore, on the basis of data presently available, it is not possible to conclude that calories are the sole dietary component which influence life span.

It has been generally believed that nutritional manipulations which increase lifespan had to be imposed during early growth. This concept originated as a result of the early work of Minot (7,8) postulating that senescence follows the cessation of growth. In addition, McCay, et al. (9,10), showed that increased lifespan of rats was associated with growth retardation. Furthermore, Lansing (11) indicated that aging in the rotifer involves a cytoplasmic factor the appearance of which coincides with the cessation of growth. However, more recently, studies have indicated that dietary restriction imposed in adult life was effective in increasing lifespan. Therefore, the results of experiments reported here have been divided wherever possible into whether dietary restriction was imposed on young growing animals or on adult organisms.

Life Span

Young Growing Animals. Increased lifespan associated with underfeeding has been reported in the following animal model systems: *Tokophyra* (Figure 1) (MacKeen, P. C., and Mitchell, R. B.:

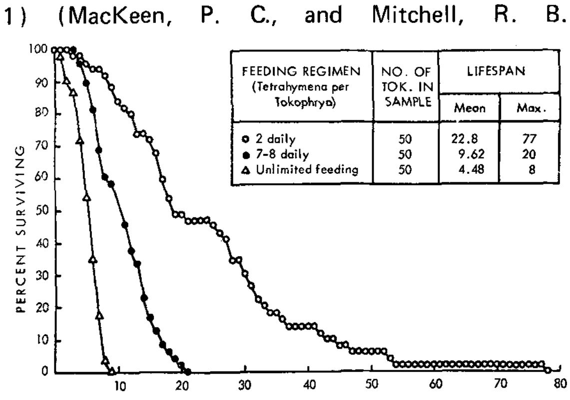

Figure 1. The Percent Survivorship of *Tokophrya lemnarum.*

Cytophotometric determination of cytoplasmic azure B RNA levels throughout the lifespan of *Tokophrya Lemnarum*. The Gerontologist, 15: No. 5, 27, 1975); *Campanularia flexuosa* (Figure 2) (Brock, M. A.: Gerontology Research Center, National Institute on Aging, Baltimore, Maryland; personal communication); *Daphnia* (Figure 3) (12); rotifers (Table 1) (13); *Drosophila* (14); and fish (Figure 4) (15). In addition, a number of laboratory experiments have been carried out on rodents.

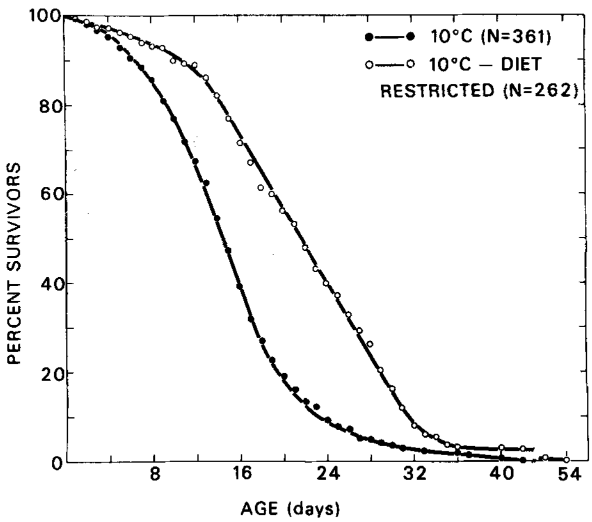

Figure 2. The Percent Survivorship of *Campanularia flexuosa* Fed Artemia Daily or Every Third Day.

Table 1. Effect of Nutrition on Life Span of Rotifers

		Mean life span (days)		
		Diet [a]		
		I	II	III
Exp. 1	Mn	35.7	43.8	58.6
	omn	±2.1	±3.0	±1.9
Exp. 2	Mn	36.0	45.6	56.5
	omn	±1.2	±2.5	±2.2
Exp. 3	Mn	29.0	46.2	49.1
		±2.8	±3.2	±2.2
Mean	Mn	34.0	45.3	54.7
		±1.1	±1.7	±1.3

[a] (I) Algae and fresh pond water daily;
(II) fresh pond water daily; and
(III) fresh pond water Mon., Wed., and Fri.

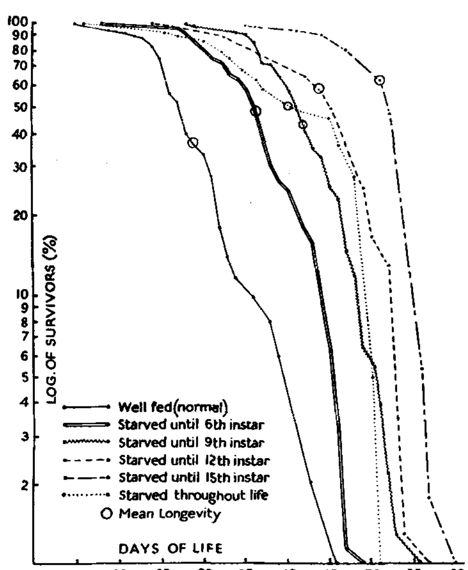

Figure 3. Effect of Restricted Food Upon the Survivorship of *Daphnia longispina.*

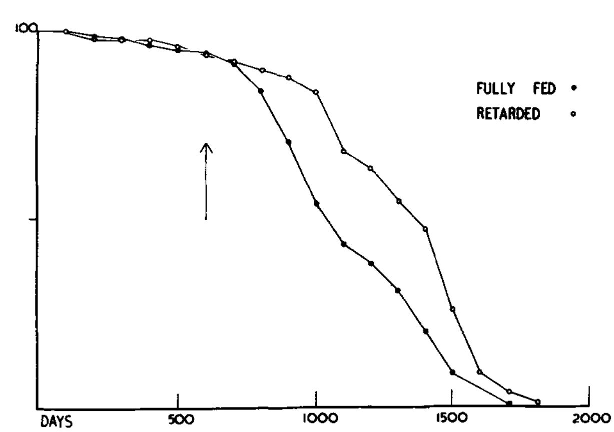

Figure 4. Survivorship Curve of Female *Lebistes reticulatus* Fed Live *Tubifex* Worms Weekly (•) or Biweekly (∘). Arrow indicates realimentation of the restricted fish. The animals were maintained at 23°C.