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Introduction of Retired Breeder F344/DuCrj Rats for Aging Research

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Abstract: Male retired breeder F344/DuCrj rats of 17 months of age were purchased in three lots and maintained for aging studies until 25 months of age. These rats were compared with male virgin rats of the same strain for survival percentage, body weight and food consumption. In the retired breeders, decrease in body weight and low food consumption were noted after delivery, and one or two months were required for these parameters to return to the delivery level. After recovery, the body weight and food consumption as well as survival percentage in the retired breeders were similar to those in virgins. From our results, we consider that it takes one to two months to acclimatize aged rats.

Key words: aged rat, F344 rat, transportation stress

Pharmacological studies of aged rats have received attention recently, and the age of the animals used has been approximately 24 months or more [1, 5, 6]. But the oldest rats supplied by commercial breeders are 17–18 months of age in the case of retired breeder Fisher 344 (F344) rats, which have a relatively long life span [7]. There are few reports on the survival percentage, body weight and food consumption of the retired breeder F344 rats. We purchased retired breeder F344 rats and maintained them for eight months. Data were then compared with those for virgin rats of the same strain which had been maintained to a comparable age to obtain in-house data.

The conditions of transportation and maintenance in

our facility were as follows; rats were transported from the commercial breeder to our facility in an air-conditioned truck, with a transit time of approximately 8 hrs. During transportation the rats were kept in transport-boxes (40 × 16 × 18 cm) made of corrugated cardboard, and ventilation in the box was through filters. The number of animals per box was 12–13 young rats and three aged rats. Food, water and hardwood bedding were also provided in the boxes. The animals were housed individually in steel-wire cages (210 × 230 × 170 cm) in a barrier-system animal room with a temperature of 23 ± 1°C and a relative humidity of 50–60%. They were fed commercial pellets (Oriental Yeast Co., CRF-1, sterilized by 15 kGy ⁶⁰Co-gamma irradiation)

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and given water *ad libitum*.

One-month-old specific-pathogen-free (SPF) F344/DuCrj virgin rats (N=50 males and 50 females) were purchased from Charles River Japan Inc. All the animals were weighed every 4 weeks, and food consumption was measured in 15 males and 15 females (No. 1–15) once a week.

Autopsy was performed, for the first time, on a female animal that became moribund at 19 months of age and thereafter on animals found dead or moribund. The survival percentage at 25 months of age was 82% for males and 66% for females. When only three males and two females reached 35 months of age, we terminated the observation. The 50% survival age was 28

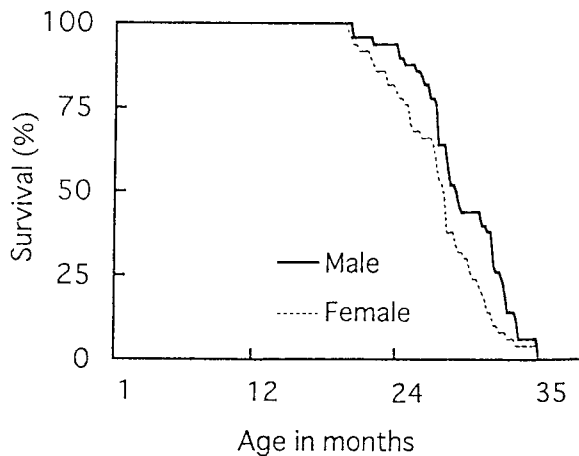


Fig. 1. Survival curves for virgin male and female F344/DuCrj rats.

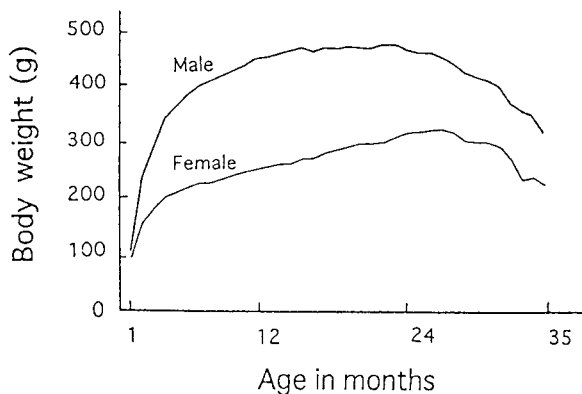


Fig. 2. Mean body weight of virgin male and female F344/DuCrj rats.

months for males and 27 months for females (Fig. 1). Male rats showed increases in body weight until 15 months of age, reaching 460 g. The weight was maintained until 25 months of age and then decreased. Female rats reached a maximal weight of 310 g at 26 months of age, after which weight decreased (Fig. 2). Food consumption per week was constant until 29 months of age in males and 24 months of age in females. It was approximately 130 g in males and approximately 90 g in females, but then fluctuations were noted (Fig. 3). On autopsy, enlargement of the spleen (male, 26%; female, 36%); nodule of the pituitary (male, 8%; female, 28%) and atrophy of the testes (64%) were commonly noted.

Referring to the above findings and the fact that male rats are generally used in pharmacological studies, male retired breeder SPF F344/DuCrj rats at 17 months of age were purchased in three lots from Charles River Japan Inc. (N=60 per lots). In the facility of the commercial breeder, the rats had been fed commercial pellets (Oriental Yeast Co., CRF-1, sterilized by autoclaving). The time lag from the first to the third lot was 9 months. At 25 months of age, the rats were delivered to the pharmacological department of our company for pharmacological studies of aged rats.

The animals were observed every day, and the number of animals found dead or moribund increased after 18 months of age. The mean survival percentage for the three lots was 98.9% at 18 months of age, and then decreased gradually to 77.2% at 25 months of age (Fig. 4).

All the animals were weighed once a week. The

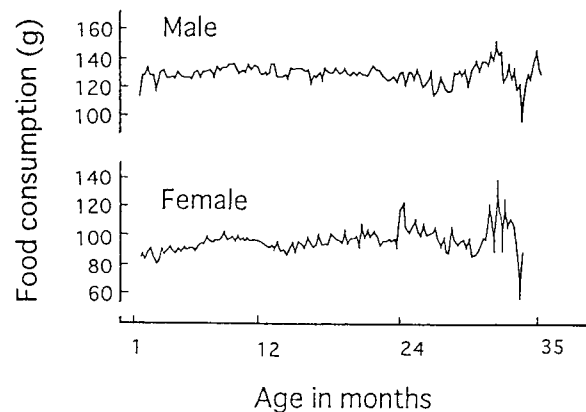


Fig. 3. Mean food consumption per week for virgin male and female F344/DuCrj rats.

mean weight of the three lots was 450 g at the time of delivery, decreased approximately 3% by 18 months of age, but then returned to the delivery level at approximately 19 months of age. Thereafter, a plateau of approximately 450 g was maintained (Fig. 5).

Food consumption was measured once a week in all animals. It was approximately 80 g at the time of delivery, but increased rapidly until 19 months of age. Food consumption per week thereafter reached a plateau of approximately 130 g (Fig. 6).

Animals found dead or moribund were subjected to microbiological examination, but we could detect neither infectious agents such as parasites and bacteria (*Pasteurella pneumotropica*, *Corynebacterium kutscheri*, *Bordetella bronchiseptica*, *Mycoplasma pulmonis*) nor antibody (Sendai virus, Sialodacryoadenitis virus, *Bacillus piliformis*).

To compare the survival percentages, body weight and food consumption were examined in the retired breeders and virgins, by using in-house data from the

virgin rats. Although the median life span of F344 rats was elsewhere reported to be longer in females than males [4], the reverse was observed in our study; the 50% survival age was 28 months for males and 27 months for females. This discrepancy may be associated with a higher incidence of the pituitary nodule and enlargement of the spleen in females in our study.

Three lots of retired breeders were observed in our study, and the lots were similar to each other in survival percentages, body weight and food consumption. The results may be attributable to the fact that the F344 rats, an inbred strain, are genetically identical and as a result show smaller inter-individual and inter-lot variation, and that the time lag from the first to the third lot was relatively short. These values for survival percentages, body weight and food consumption were also similar to those of virgin rats, and those reported in F344 rats maintained from a young age [8, 9, 12], except for the body weight and food consumption of retired breeder rats one to two months after delivery.

Transportation always causes considerable stress in rats and mice, results in loss of weight, and rats and mice need time to acclimate to their new surroundings [2, 3, 10, 11]. The recovery period for body weight after transportation in young rats was reported to be 4 days or less [10], but there are few reports of transport stress in aged rats. In our study on retired breeder rats, decrease in body weight and low food consumption were noted from the time of delivery, and recovery to the delivery level required one to two months. The difference between aged rats and young rats in recov-

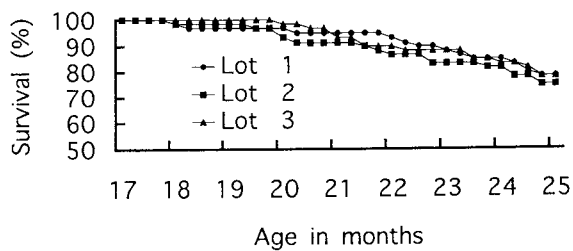


Fig. 4. Survival curves for male retired breeder F344/DuCrj rats.

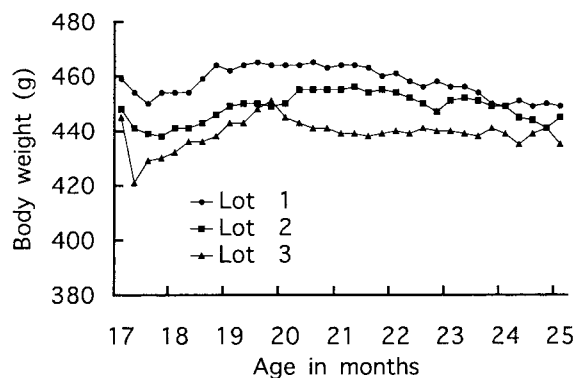


Fig. 5. Mean body weight of male retired breeder F344/DuCrj rats.

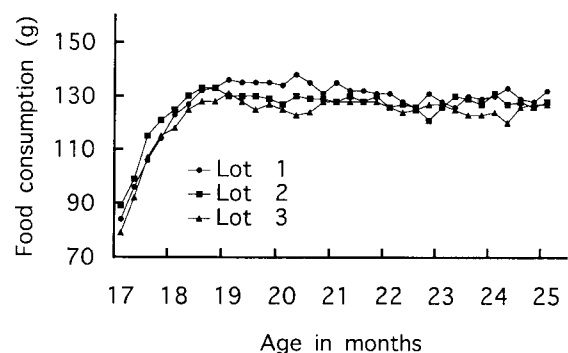


Fig. 6. Mean food consumption per week for male retired breeder F344/DuCrj rats.

ery periods may be attributable to the fact that the stress involved in transportation and the stress involved in new surroundings were more severe in aged rats than in young rats.

In conclusion, we consider that acclimation in aged rats requires one to two months, and that the survival percentage, body weight and food consumption of male retired breeder rats are similar to those of male virgin rats of the same age.

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