

Dwarf Mice and the Aging Process

Brown-Borg et al have reported that Ames dwarf mice (*df/df*) live longer than their normal siblings of the same strain given the same environmental conditions. The authors followed 28 normal and 34 Ames dwarf mice born during July and August 1992 from the same litters. Both types of mice were maintained in a conventional environment and fed the same unrestricted lab chow and tap water. The male dwarf mice lived 350 days longer than normal male mice and the female dwarf mice lived 470 days longer than the normal female mice. Mean age at death for normal males is 723 ± 54 days; for normal females 718 ± 45 days; for dwarf males $1,076 \pm 56$ days; and dwarf females $1,206 \pm 32$ days.

Ames dwarf mice are characteristically normal size at birth but severely growth retarded after birth and are approximately one-third normal size as adults. They have primary pituitary deficiency, including absence or extreme reduction in GH, prolactin, and thyroid-stimulating hormone. The GH/IGF-1 axis is markedly depressed, and the mice exhibit reduced immune function.

The mechanisms suggested for longevity in these geneti-

cally dwarf mice are related to low GH and IGF-1 levels; low thyroid-stimulating hormone and thyroid hormone levels and hypogonadism; reduced metabolic rate, possibly due to reduced body size and underlying endocrine defects; reduced caloric intake; and failure of sexual maturation.

Brown-Borg HM, et al. *Nature* 1996;384:33. Letter.

Editor's comment: Aging is a complex process influenced by genetic and environmental forces. Genes and hormones, especially GH, IGF-1, and sex hormones, appear to play a role in longevity. It is well known that individuals with elevated GH levels resulting in acromegaly and pituitary gigantism have a shorter life span. The observation that female dwarf mice lived longer than male mice also suggests that female hormones play some role in the aging process. These animal models are important for studying the effects of hormones on growth, aging, and the aging process, and almost surely will improve our understanding of the aging process in both rodents and humans.

Judith G. Hall, MD

Mechanisms and Treatment of Growth Retardation in Children With Liver Transplants

Sarna et al report on their experience with 18 months of rhGH treatment, beginning at least 18 months after liver transplant, in 8 children (5 boys, 3 girls). A total of 41 children have had liver transplants with a 70.2% graft survival after 1 year. The inclusion criteria for the study were: age > 2 years; liver transplant at least 18 months previously; height SD score (SDS) < -2.0 or growth velocity SDS < 0 for chronologic age and sex; bone age < 14 years in boys and ≤ 13 years in girls; and no serious complications due to transplantation. The patients were treated with 1.0 IU/kg/wk (approximately 0.3 mg) rhGH. They were measured at 2 weeks, 6 weeks, and 3 months, and at 3-month intervals thereafter using a Harpenden stadiometer. Height SDS was calculated.

These 8 children received their liver transplants for a variety of causes, including hepatoblastoma (3), biliary atresia (4), and α_1 -antitrypsin deficiency (1). The median growth rate increased from 3.2 to 6.0 cm/y ($P=0.012$) (Figure 1). The median height SDS increased from -3.9 to -3.0 ($P=0.036$) during treatment. The individual growth responses did not correlate with baseline age, time elapsed after transplant, nocturnal GH secretion, serum IGF-1, or IGFBP-3. No rejection episodes were documented during treatment.

Sarna S, et al. *Transplant Proc* 1997;29:447-448

Editor's comment: The patients in this study had a significantly accelerated linear velocity despite receiving low doses of glucocorticoids (amount not specified). The authors state that traditional predictors of response to rhGH such as low GH secretory status and young age were not shown to be predictors of a good response in the current study. The study itself included too few subjects to be able to characterize individuals who might benefit the most

from GH therapy. This editor hopes that a larger, multicenter, multinational study could be performed so that such variables can be clearly identified. Since GH has some effects on the immune system, it is important to continue to monitor liver function tests closely during its administration. Although the authors conclude that "growth response is variable and difficult to predict," it is not unreasonable to expect that such information might be forthcoming from future studies.

William L. Clarke, MD

