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Mechanisms of Aging in Pets

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Life expectancy has dramatically increased in industrialized countries since the 1900's due to advances in disease prevention and treatment, and improvements in nutrition and infant mortality. Thus, as a society we are living longer and experiencing more of the changes and declines associated with aging. Although the factors that cause our bodies to age are unknown, various medical interventions have been proposed and explored to prevent the process. Animal and human studies suggest potential benefits of dietary modification, exercise, antioxidants, hormones, and deprenyl. Many strategies



merit scientific inquiry, but they cannot be recommended for use. More extensive research is necessary to assess their safety, effectiveness, and socioeconomic impact, and to resolve ethical controversies before they can be considered applicable in humans.

The Normal Aging Process

Aging is the accumulation of progressive changes over time associated with or responsible for, disease, decreased physiologic function, and death. The phenomenon is universal among all living things. Life span and life expectancy differ among species and among individual members of a species, and this variability suggests that a genetic component is responsible for the manifestations of aging. Discounting genetic factors, the variations can be attributed to diseases and environmental stressors. The exact connections among aging, disease, and death challenge researchers. Aging is characteristically associated with gradual deterioration in the precise, delicate interrelationships among all the physiologic systems in an organism. This in turn predisposes the organism to disease. Some diseases cause an organism's death indirectly through their effects on cells, tissues, and organs (e.g., ischemic heart disease, diabetes mellitus). However, death is frequently assumed to be the result of aging. If one dies of natural causes at age 30 years, it is usually directly due to an underlying disease process.

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As death is a convenient and well-defined event with a strong correlation with age, it is a favorable end-point measure. Aging does not occur in a species or in all organisms of any species exactly the same way. Thus, a thorough evaluation of the differences among these species may clarify its specific and common biologic processes and mechanisms.

In humans, normal aging is associated with many physiologic changes, some of which occur in the neuroendocrine, immune, and central nervous systems. Abundant literature demonstrates that it is associated with loss of organ system function, which leads to accelerated cell death and the gradual decline of physiologic precision or homeostasis. Several classification systems have been developed to distinguish between aging due to disease and the normal process, but none has been universally accepted or applied.

When we try to decide what is normal or natural biologic aging, it may help to use three criteria: it occurs in everyone to different degrees; it causes irreversible changes in physiologic functioning from the cellular to the organ level; and it permanently increases the likelihood of gradual functional decline. Disease was described as “a condition in which functions are disturbed in comparison with some normal reference condition.” What reference condition can the scientific community agree on to assess the true impact of normal aging?

Life Span and Life Expectancy

It is important to define life span and life expectancy, as the terms are often erroneously used interchangeably. Life span refers to the maximum attainable survival time for a given species. The documented life span of human beings has ranged from 110-115 years. Anecdotal reports state as long as 120 years, but the accuracy of such claims is questionable. Life expectancy is the average observed years of expected life from birth or any other reference age. Based on data from the U.S. Bureau of the Census, the life expectancy at birth in 1990 in the United States was approximately 71.6 years in men and 79.2 years in women.

In 1900, the average composite life expectancy was 45 years and people over 65 constituted only 4.1% of the population. This percentage increased to 12.4% in 1990 and is projected to reach as high as 22% by the year 2040. Longevity gains continue upward for both men and women. The growth in number of those over age 65 can be attributed to gradual increases in life expectancy and gradual decreases in cardiovascular, cerebrovascular, and infant mortality. The largest gains occur in people over 85 years, and as a result, the oldest old population is rapidly expanding. In contrast, the life span has remained relatively constant.

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Theories of Biologic Aging

Many theories attempt to explain biologic aging. In a recent review of 24 different proposed theories of aging, the authors proposed a unified theory that essentially states that an organism's biologic progress is genetically determined and set in motion at conception, and lasts for the duration of life. It is accelerated or decelerated secondary to influences from many environmental forces, as well as stressors that occur within the body that are genetically programmed to a certain degree. The balance between these influences ultimately determines our biologic age. Increased understanding of the nature of aging reveals an extremely complex network of processes involving all levels of organism function. Evaluating and attributing the effects of various interventions in this complex system is equally difficult. Thus, a combination of individual strategies may be more appropriate. The rationale for the nonpharmacologic interventions includes pooled insurance company data from many different studies. These data suggest an indirect relationship between being underweight (below the average of the sample population) and longevity. According to one study, men and women have an increased risk of death if their body weight is 15% above or below the average weight of the sample population. Age-adjusted mortality ratios were lower within the 15 % range of deviation. This pattern was observed in the Heart Study. Beginning in 1948, a cohort of 5209 men and women participated in a biennial follow-up physical examination and ancillary testing. Metropolitan relative weight was used as the measure of underweight or overweight. This measure is the ratio of a person's body weight to the reference ideal body weight (lowest association with mortality) for height, expressed as a percentage. Men overweight by as little as 20% over the ideal reference had significantly high mortality. The mortality of underweight men was strongly associated with the prevalence of cigarette smoking (> 80%).

More recent literature critically evaluated the association of change in weight and longevity. A study of men from 1977 to 1988 revealed that both weight loss and weight gain (fluctuations > 5 kg) were associated with an increased relative risk (RR) of all-cause mortality (RR 1.57, $p<0.001$; 1.36, $p=0.003$) and coronary heart disease mortality (RR 1.75, $p=0.001$; 2.01, $p=0.0005$), but not cancer mortality. The lack of any relationship with cancer death may be attributed to disease-associated weight loss. Subjects with the lowest risk of mortality maintained their weight within 1 kg throughout the study period. However, data were not controlled for disease or diet, which precludes firm conclusions.

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The Framingham Heart Study also examined the fluctuation of body mass index (BMI, $\text{weight}/\text{height}^2 = \text{kg}/\text{m}^2$) over a 32-year period. After controlling for age, obesity, cigarette smoking, physical activity level, serum cholesterol level, systolic blood pressure, and glucose tolerance, fluctuations in BMI in both men and women were positively associated with all-cause mortality ($p=0.005$, $p=0.01$) and mortality from coronary heart disease ($p=0.009$, $p=0.009$). This association remained even after controlling for steady weight loss presumed due to chronic illness, but voluntary weight loss may confound the results. Losing excess fat (weight) and maintaining a healthy weight throughout life are prudent measures.

Geriatrics is that branch of medicine that treats problems peculiar to old age. The word “*geriatric*” is derived from a combination of the Greek words “*geras*” meaning old age and “*iatrike*” meaning medicine and surgery. Although the term “geriatric” has been commonly used in the veterinary profession, this word may sound overly “harsh” to some pet owners, especially when considering the fact that we are recommending routine thorough evaluations of patients as they reach and then advance beyond middle age. Use of the term “geriatric” may engender undue concern among some pet owners that may even lead to some avoiding the issue of more frequent evaluation of their older pets by their veterinarian. That is, they may be reluctant to face the fact that their pet is indeed getting older. Therefore, we prefer to use the words “**senior**” or “**mature**” instead to connote an age level beyond “middle age.” Our goal is to work closely with our clients in order to help their pets live as long and as comfortably as possible. We will help do this through promoting the best in medical surveillance and preventative care.

AGE PARAMETERS

There are no precise definitions or reference points established for age in animals as there are in humans. Middle age in humans is defined as 45 to 59 years old, “elderly” includes a range of 60 to 75 years, and “aged” is considered to be more than 75 years old. In animals, old age is generally referred to as the last 25% of their lifespan. In reality, old age is not just a chronological measurement of years lived, rather it is a measure of the functionality of the body systems subsequent to the effects of “aging” during those years. In addition to number of years lived, aging is affected by such important factors as *genetics*, *nutrition*, and *environment*.

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For practical purposes we consider dogs and cats that are eight years of age or older to be in their senior (geriatric years). It may be more technically correct to consider cats and small dogs (less than 20 pounds) to begin their senior years at nine years of age, medium size dogs (21-59 pounds) at eight years of age, large size dogs (51-90 pounds) at seven years of age and the giant breed dogs (more than 91 pounds) at six years of age.

MEDICAL IMPORTANCE OF A SENIOR QUALITY CARE PROGRAM

Senior (geriatric) pets undergo aging changes in organs and tissues the same as do elderly humans. It is well known that older animals have a higher incidence of such conditions as major organ failure, benign and malignant tumors, arthritis, and loss of special senses (especially hearing and vision). Older animals also develop more severe dental disease as they increase in age.

A comprehensive evaluation performed on a regular schedule is clearly the best way to detect subclinical diseases or to find increased risk factors of diseases in senior patients. It has repeatedly been documented that many of the chronic disorders and disease processes seen in older pets can be medically controlled, and in some cases resolved, if they are detected early enough. Earlier detection and prompt treatment of medical conditions improves the chances that older pets will live longer, happier, and better quality lives. The owners of senior pets have deep human/animal bonds with their pets and the medical and psychological benefits to the pet owners of this bond are well known. Anything that results in a longer lifespan while maintaining a high quality of life gives the pet owner more enjoyment time with their pet, and also allows them more time to prepare for the eventual loss of their pet. This Senior Pet Wellness Program is a preventive medicine program designed for early discovery and control of the risk factors of diseases and the early detection of subclinical diseases in aging pets.

Preventive care is the most important component of health care in all of the life stages for both humans and animals. No health care program is more important in maintaining and prolonging a high quality life for the pet, while meeting the most important needs of the owner, than a thorough senior pet wellness program that is carried out to its fullest.

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This program begins with the pet entering its senior years and is followed through the ensuing years, involving discussions and decisions regarding medical treatments, terminal illness, and eventually death or euthanasia. Ideally it would continue through disposition of the pet's remains, grief and bereavement counseling for the owner(s) if needed, resolution of the pet owner's loss, and culminating with the pet owner reestablishing the human/animal bond with another pet. This senior pet wellness program is good for our patients, it's good for our clients, and it's good for our hospitals because it promotes the best in high quality patient care.

BENEFITS OF A SENIOR PET WELLNESS PROGRAM

Pets today have an increased life expectancy primarily due to advances in veterinary medical care and nutrition, highly effective vaccination and heartworm prevention programs, a lower incidence of traumatic injuries, and better care provided by more informed pet owners. Today's pet owners want more thorough and better veterinary care for their pets and it is our responsibility to provide it for them.

Pets are very important to their owners, providing them not only with happiness and unselfish loyalty, but also with companionship, physical contact, a focus of attention, protection, and a stimulus for exercise.

Pet owners benefit both physically and emotionally when veterinary care prolongs a meaningful and better quality of life for their aging pets. This not only gives pet owners valuable time to spend with their pets, but also allows them time to prepare for the pet's eventual death.

Recent pet population surveys have revealed that 75% (41 million) of the pets in the United States are over six years of age. Further, companion animal hospital patient surveys reveal more than 25% of patients are pets in geriatric age groups.

Companion animal hospital income surveys reveal that more than 35% of gross income is derived from services to geriatric pets. As much as 60% of an animal hospital's gross income can be generated from a full service geriatric wellness program.

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THE ROLE OF GENETICS IN AGING AND LIFESPAN

Genetics plays its major role in the aging process by determining an animal's adult size. It has long been known that animals of small breeds live longer than those of the large breeds. One study of pet longevity revealed that only 13% of giant breeds of dogs lived past 10 years of age, and of those only 0.1% lived to be 15 years old. The same study revealed that more than 38% of the small breeds of dogs lived to be 10 years old while 7% went on to live to be 15 years or older. "Longevity genes" play a role in determining lifespan in ways other than adult size. Siamese cats and Standard Poodles have longer life expectancies than Persian cats, and Collies and Boxer dogs have shorter life expectancies, even when size is taken into consideration. This is presumably due to differences in longevity genes in those breeds.

SENIOR WELLNESS PROGRAMS

Many types of wellness programs are used by veterinarians. These are *baseline* programs offering varying levels of diagnostic testing. The Level 1 program is for pets in their senior years that are considered healthy by the owners and veterinarian. Level II is for senior pets experiencing newly appearing signs and or symptoms of a medical or surgical disorder. Level III is for senior pets with previously diagnosed disorders.

If abnormalities are identified on baseline testing then additional tests will be recommended based on what the clinician feels is indicated (e.g., more definitive testing for Cushing's disease or hypothyroidism, bile acids assay to evaluate liver function, pelvic or other orthopedic radiographic studies if physical examination identifies joint pain, ultrasound studies, etc.). All programs include a thorough consultation with the client after the testing is completed. Clients should see and receive an explanation of their pet's radiographs whenever possible. A written report summarizing our findings and recommendations should be sent to the client by 14 days after the patient evaluation is completed. Reminders will be sent to clients at appropriate times to remind them when follow-up evaluation is due.

These programs provide a wonderful opportunity for us to truly provide the finest care available for older animals and to bond more and more with our clients. Our clients should be made aware of the fact that there are actually many specialists available whenever necessary to be involved, along with the primary care veterinarian, in their pet's medical care.

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LEVELS OF GERIATRIC WELLNESS PROGRAMS

Level I

Complete history to include the pet's medical, surgical, vaccination, dietary, behavioral and travel history

Complete physical examination (includes orthopedic exam, ophthalmic evaluation that at a minimum includes a Schirmer tear test and direct ophthalmic exam, and identification of any lumps and bumps that might require intervention).

Complete blood count

Major blood chemistry profile and thyroid evaluation

Complete urinalysis and urine culture (cystocentesis samples are to be obtained whenever possible)

Fecal examination

Nutrition consultation (identification of exactly what the pet is eating, how many meals are fed per day, etc.)

Conference with owner(s) to fully review findings, make recommendations, and answer questions (in person whenever possible, but telephone consultation at a minimum, with clients having an opportunity to ask any questions that they may have)

Send summary letter to client within 2 weeks of completion of the diagnostic evaluation and conference, explaining in writing the information provided in the conference and making clear our recommendations on when follow-up evaluations are indicated

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Level II

Complete history to include the pet's medical, surgical, vaccination, dietary, behavioral and travel history

Complete physical examination (includes orthopedic exam, ophthalmic evaluation that at a minimum includes a Schirmer tear test and direct ophthalmic exam, and identification of any lumps and bumps that might require intervention or just client observation)

Complete blood count, blood chemistry profile, thyroid evaluation

Complete urinalysis and urine culture (cystocentesis samples are to be obtained whenever possible)

Fecal examination

Thoracic and abdominal radiographs (5 views minimum)

Blood pressure

Additional tests as needed to further evaluate abnormalities identified on screening tests (e.g., bile acids assay)

Nutrition consultation

Conference with owner(s) to fully review findings, make recommendations, and answer questions (in person whenever possible, but telephone consultation at a minimum, with clients having an opportunity to ask any questions that they may have)

Send summary letter to client within 2 weeks of completion of the diagnostic evaluation and conference, explaining in writing the information provided in the conference and making clear our recommendations on when follow-up evaluations are indicated

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Level III

Complete history to include the pet's medical, surgical, vaccination, dietary, behavioral and travel history

Complete physical examination (includes orthopedic exam, ophthalmic evaluation that at a minimum includes a Schirmer tear test and direct ophthalmic exam, and identification of any lumps and bumps that might require intervention)

Complete blood count, blood chemistry profile, thyroid evaluation

Complete urinalysis and urine culture (cystocentesis sample)

Fecal examination (zinc sulfate flotation)

Thoracic and abdominal radiographs (5 view minimum)

Additional imaging (ultrasound, CT, MRI as indicated)

Electrocardiography

Blood pressure

Nutrition consultation

Conference with owner(s) to fully review findings, make recommendations, and answer questions (in person whenever possible, but telephone consultation at a minimum, with clients having an opportunity to ask any questions that they may have)

Send summary letter to client within 2 weeks of completion of the diagnostic evaluation and conference, explaining in writing the information provided in the conference and making clear our recommendations on when follow-up evaluations are indicated

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Aging Interventions

Caloric Restriction

Restricting calorie intake to extend life has been extensively studied and reviewed in the literature. It may be the only strategy that yields reproducible results across numerous strains of rodents. Weanling Simonsen albino rodents were randomly assigned to seven dietary regimens. One group was fed ad libitum throughout life and the other six were fed 80% or 60% of an ad libitum calorie intake. Dietary restriction was also initiated at weaning or 12 weeks after weaning and continued for 12 consecutive weeks or a lifetime. Diet restriction extended life in both sexes compared with all ad libitum controls, with the greatest gains in longevity in males fed ad libitum for the first 12 weeks, then restricted to 60% ad libitum intake for life. The mean survival time for males and females was 927 and 943 days, respectively. Lifetime ad libitum controls experienced the worst outcome with mean survival for males and females 706 and 756 days, respectively.

Another study examined male SPF Fischer rats fed ad libitum until 6 weeks of age. The animals were randomized to either a continued ad libitum group (group A) or a restricted diet group (group R) that consumed about 60% of group A's mean caloric intake. Group R had significantly increased longevity over group A (986 +/- 25 days vs 701 +/- 10 days) and lower body weights. Weight and longevity were not directly correlated. The authors were unable to determine what factor(s) increased the life of the rats, the consumption of fewer calories, the resultant lower weight, or both. Food restriction was also associated with a decreased frequency of disease. Of interest, lean body weight declined only after the onset of terminal disease despite calorie restriction.

The findings from these two studies are particularly interesting considering that calorie restriction began within the first 6 months of life. This is generally considered the normal growth period for most rat strains. Another study explored the relationship between the time calorie restriction was initiated and longevity in the same rat strain. All animals were fed ad libitum from 4-6 weeks. Calorie restriction occurred from 6 weeks of age to 6 months or 6 months to death. Rats that were fed ad libitum from 4-6 weeks and then restricted to 60% of the mean ad libitum intake of the control group had significantly longer lives than other diet groups (median 1057 vs 941 days in the second-longest-lived group fed ad libitum for 6 months; range 701-1057 days).

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Similarly, in previous studies the body weights in these two longest-lived groups were lower than those in the three other groups. The results were consistent with those in the previous study with the same animal strain. It was surprising that calorie restriction at 6 weeks was equally effective at extending life as calorie restriction at 6 months. The optimum timing, sequence, and magnitude of calorie restriction for life extension remain controversial.

L-Deprenyl

The association of shortened life expectancy and the benefits of levodopa on the progression and mortality of patients with Parkinson's disease are well documented. Deprenyl, a central nervous system-selective monoamine oxidase inhibitor, has emerged as a potential method for slowing the progression of dopaminergic neuron degeneration associated with aging and Parkinson's disease. One of these studies examined the effect of deprenyl on survival of patients with Parkinson's disease. After controlling for baseline demographic differences, significant gains in life expectancy occurred. These results show deprenyl's ability to spare dopaminergic neurons and favorably modify the natural course of Parkinson's disease. Its effect on biologic aging and life span in humans remains unclear, however, experiments in several different rodent strains have been conducted.

Older age is associated with a decline in sexual activity in rodents and humans; however, considerable variability exists in both at comparable ages. This exemplifies the dissociation between chronologic and physiologic or biologic age. Stratification of rodents by sexual activity in longevity studies ensures some control over this variability. Theoretically, the effects of life extension interventions on sexual activity in rats would more closely reflect modulation of biologic aging, with minimal confounding by chronologic age. Generally, rodents treated with deprenyl experience an improvement in sexual activity from baseline.

Subcutaneous administration of deprenyl (0.25 mg/kg 3 times/week) to 66 2-year-old male rats significantly improved sexual activity, learning, performance, and survival compared with saline-treated controls. Animals receiving deprenyl that were noncopulators at baseline, had statistically significant gains in life expectancy versus control counterparts (187.90 $\pm$ 3.27 vs 142.74 $\pm$ 0.38 wks, $p < 0.001$). Treated animals that were sluggish at baseline (mounting or intromission) had significant gains in longevity over controls and over treated noncopulators (214.05 $\pm$ 3.07 vs 152.00 $\pm$ 0.92 wks, $p < 0.001$). The sluggish rats had the longest lives. The

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aggregate mean survival in the deprenyl and saline groups were 197.98 $\pm$ 2.36 and 147.05 $\pm$ 0.56 weeks, respectively ($p < 0.001$). The longest-lived baseline noncopulating rat treated with deprenyl died at 216 weeks of age. This result is extraordinary since the technical life span of these animals was 182 weeks. The longest-lived rat was from the baseline sluggish group and lived 226 weeks. These results are noteworthy because the majority of treated rodents exceeded the technical life span in all baseline sexual performance groups.

The relationships between sexual activity and longevity with and without deprenyl were consistent with another study with a different rodent strain. Longer-lived Wistar-Logan rats at age 28 weeks were administered the same saline--deprenyl regimen as the study discussed above. Extension of life span beyond the technical life span in this strain (3.5 yrs) was similar. However, all animals that lived beyond the technical life span accounted for approximately 64% of all baseline high-performers treated with deprenyl. Baseline high-performers receiving deprenyl had significant gains in survival over their low-performing counterparts (185.30 $\pm$ 1.96 vs 152.54 $\pm$ 1.36 wks, $p \sim 0.001$). This was also observed in saline-treated rats (151.24 $\pm$ 1.36 vs 134.58 $\pm$ 2.29 wks, $p < 0.001$). Significant effects of deprenyl on longevity compared with saline controls were also observed within groups stratified by sexual performance.

Results consistent with the previous two studies were observed in experiments using short-lived male Fischer 344 rats. These two studies also evaluated the effect of deprenyl-induced dietary restriction. Average body weight measured in 8-day sequences throughout the study period declined steadily in control rats. Animals treated with deprenyl demonstrated the greatest fluctuations, with a downward trend after approximately 120 days. However, those in the deprenyl-treated group were significantly heavier than saline-treated controls, with significant gains in longevity. This excludes the possibility that life extension was caused by deprenyl-induced dietary restriction.

This was also the case in another study in which the same strain of rats was injected with deprenyl 0.5 mg/kg 3 times/week. Although the magnitude of the effects on survival was significant in both studies using Fischer rats, the gains in life expectancy were less pronounced. This is likely the result of variability in life span among different rat strains.

In a study in dogs, eighty two beagle dogs ranging in age from 2.8 to 16.4 years and in weight from 6.3 to 15.8 kg were allotted to 41 pairs and administered placebo or 1 mg/kg deprenyl orally once daily for 2 years and 10 weeks. When survivorship for all dogs in the study was

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analyzed there was no significant difference between the deprenyl and placebo treated groups, most likely due to the (expected) survival of virtually all young dogs in both groups for the duration of the study. To assess whether L-deprenyl treatment begun in later life might enhance canine longevity in a fashion similar to that documented in rodents, they also examined survival in a subset of elderly dogs who were between the ages of 10 and 15 years at the start of tablet administration and who received tablets for at least 6 months. In this subset, dogs in the deprenyl group survived longer ($p < 0.05$) than dogs in the placebo group. Twelve of 15 (80%) dogs in the deprenyl group survived to the conclusion of the study, in contrast to only 7 of 18 (39%) of the dogs who received placebo ($P=0.017$). Furthermore, by the time the first deprenyl treated dog died on day 427, 5 placebo treated dogs had already succumbed, the first on day 295. Specifically with respect to dogs, the findings reported herein suggest daily oral administration of 1 mg/kg deprenyl prolongs life when begun in relatively healthy dogs 10-15 years of age and maintained for the duration of the individual's life, but in any event for no less than six months. A similar double blind, placebo controlled study is now underway in pet dogs over the age of 10 years. This study will be completed within the next 18 months.

Considering the profound effects of deprenyl administration on both human and animal models, the exact mechanism by which it may extend life requires further investigation. Several hypotheses exist, including decreased dopamine degradation and re-uptake and decreased production of reactive dopaminergic neuron cytotoxins from dopamine degradation. Enhancement of oxidant scavenger mechanisms has also been proposed with regard to increased SOD and catalase activities. Increased activity of the catecholaminergic nervous system and blocking of CNS apoptosis have also been suggested. The DATATOP study was begun to test the hypothesis that deprenyl would decrease the production of harmful radicals that may accelerate dopaminergic neuron decline. However, the agent's significant benefits on the progression of early Parkinson's disease were independent of vitamin E administration.

Improvements in learning ability and sexual activity were strongly associated with deprenyl in animal models. Perhaps the effects are not limited to central nervous system (CNS) activity. Deprenyl may modulate the neuroendocrine milieu, which might affect longevity. Despite the consistency in animal study results, conclusions about its life extension potential in humans are premature. Optimum dosing strategies in animals and data on long-term deprenyl administration in healthy human subjects are unavailable. The potential benefits of dopaminergic interventions to extend life, improve well being, and decrease the frequency of age-related CNS illnesses needs further study. ■

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References:

Morse DR, Rabinowitz H: A unified theory of aging. Int J Psychosom 37: 5-24, 1990.

Ruehl WW, Entriken TL, Muggenburg BA, et al: Treatment with l-deprenyl prolongs life in elderly dogs. Life Sciences 11: 1037-1044, 1997.