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Exceptional Longevity in Pet Dogs Is Accompanied by Cancer Resistance and Delayed Onset of Major Diseases

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To characterize extreme aged pet dogs as a first step in developing an animal model of exceptional longevity, we constructed lifetime medical histories for 345 Rottweiler dogs using information collected from owners and veterinarians. Extreme aged dogs (alive at the 95th percentile age at death for the study population, $\geq$13.3 years) were compared with a usual longevity group (9–10 years). Exceptional longevity in Rottweiler dogs was accompanied by a significant delay in the onset of major life-threatening diseases; 76% of extreme aged dogs remained free of all major diseases during the first 9 years of life. Only 19% of extreme aged dogs died of cancer versus 82% of dogs with usual longevity ($p < .0001$). The reduction in cancer mortality in oldest-old pet dogs mimics that seen in human centenarians and provides strong rationale for using this animal model to study comparative mechanisms of cancer resistance in the extreme aged.

THE oldest-old humans have been studied to identify the genetic and environmental determinants of exceptional longevity (1–3). The majority of centenarians have a significant delay in the onset of major life-threatening diseases, and this probably contributes to their exceptional longevity (4). Cancer is one of the most important aging-related diseases affecting Western societies. Cancer mortality rates increase with age throughout most of adulthood (5), however, they decline in advanced age (2,5–8). Although poorly understood, this pattern suggests that, compared to the general population, the oldest-old have a cancer-resistant phenotype.

The domesticated pet dogs living among humans represent an underutilized mammalian model to identify determinants of exceptional longevity. Because of the compressed life span of dogs compared with humans, pet owners are usually able to provide detailed information on medical history and environmental exposures throughout the life course, including early life events. In addition, biological samples are readily available from siblings and first generation relatives of extreme aged pet dogs living in the same or different environment. Pet dogs share with humans a high lifetime risk for the development of spontaneous cancers, and many of these cancers mimic their human counterparts in terms of biological behavior and response to treatment (9). Whether or not the oldest-old pet dogs, like humans, exhibit diminished cancer mortality compared with dogs with usual longevity has not been investigated.

The objective of this study was to characterize extreme aged pet dogs as a first step in developing an animal model of exceptional longevity. We tested the hypothesis that, like humans, extreme aged pet dogs have a reduced risk of age-specific cancer mortality compared with dogs dying at younger ages. Furthermore, we hypothesized that exceptional longevity in pet dogs is associated with a significant delay in the onset of other life-threatening diseases. To test these hypotheses, we conducted an historical cohort study of 345 Rottweiler dogs, a popular breed with a relatively high cancer incidence. Herein, we report the first detailed description of extreme aged pet dogs and discuss comparative aspects of exceptional longevity in pet dogs and humans.

Methods

Study Population and Data Collection

An historical cohort study was conducted of Rottweiler dogs living in North America. In November 1999, a questionnaire was mailed to 1,500 owners of Rottweiler dogs identified through 8 national Rottweiler breed specialty clubs [Medallion Rottweiler Club, Colonial Rottweiler Club, Delta Rottweiler Owners Club, Emerald Valley Rottweiler Club, Great Lakes Rottweiler Club, Gulfstream Rottweiler Club, Northstar Rottweiler Club, and Mile High Rottweiler Club]. In addition, the questionnaire was published in the national breed magazine, *The Rottweiler Quarterly* (10). Purebred Rottweiler dogs of any age alive on January 1, 1995 were considered eligible. With the assistance of their veterinarian, pet owners completed a 12-page dog health history questionnaire for each eligible dog relating to general owner and dog information, usual diet and dietary supplements, family history of cancer, exposure

to herbicides and pesticides, history of trauma, and health conditions (13 cancer-related and 27 noncancer-related) diagnosed by a veterinarian. Age at death and causes of death that were confirmed by a veterinarian were recorded. Data were obtained from owners of 737 purebred Rottweiler dogs. For this report, data on gender, neuter status, age at death, cause of death, and age at onset of major diseases were analyzed for the 345 dogs that were deceased at the time of the questionnaire. More detailed information on the reproductive history of female dogs (i.e., number of litters, number of puppies, age at whelping) was obtained through follow-up telephone interviews with owners. Successful interviews were obtained from 83% of attempted contacts.

Age Versus Cancer Mortality Risk

To evaluate the relationship between age and cancer mortality risk, the study population was divided into 7 groups based upon age at death (20th, 40th, 60th, 80th, 90th, and >90th percentiles, and extreme aged >95th percentile). Proportional cancer mortality (i.e., the percentage of deaths attributable to cancer) and age-specific cancer mortality rates (expressed as cancer deaths per 100 dogs) were calculated. Proportional cancer mortality was calculated by dividing the number of cancer deaths within each group by the total number of deaths within that group. Cancer mortality rate for each of the 7 age-at-death groups was calculated by dividing the number of cancer deaths within each age group by the total number of dogs that entered the age group. In order to graphically display the relationship between cancer and noncancer mortality rates over the life course, age-specific mortality rates were calculated at 2-year intervals from 0–14 years of age and expressed as the number of deaths per 100 dogs that entered the interval (Sigma Plot for Windows 1997, SPSS, Inc., Chicago, IL).

Age at Onset of Major Diseases in Dogs With Exceptional Longevity

A Kaplan-Meier survival curve was constructed for the 345 dogs in the study population. Twenty-one dogs whose age at death exceeded the 95th percentile for the population (i.e., ≥13.3 years) were selected as the Extreme Aged group. The 95th percentile cutoff (rather than the 90th or 99th percentile) was chosen because it allowed us to report the characteristics of >20 dogs with the most extreme phenotype. Extreme aged Rottweiler dogs were subdivided into three groups according to age at onset of major diseases (4): 1) *Survivors*—onset of at least one major disease prior to 9 years of age; 2) *Delayers*—free of all major diseases until after 9 years of age; and 3) *Escapers*—free of all major diseases until after 13 years of age. The cutoff of 9 years was used to identify dogs with a delay in onset of major diseases until after the median age at death for the study population. The cutoff of 13 years was used to identify Escapers who did not develop any major diseases until they were extreme aged. The cutoffs of 9 and 13 years of age in Rottweiler dogs correspond to 75 and 106-human year equivalents, respectively, based upon the algorithm of Patronek and colleagues (11). Major diseases included all diseases that are potentially life-threatening despite treatment, such as cancer, cardiopulmonary disease, gastrointestinal disease, neurological disease, renal disease, and infectious disease. Debilitating diseases, such as advanced osteoarthritis, were considered life threatening because they sometimes caused owners to euthanize their dogs.

Comparison of Extreme Aged Dogs and Dogs With Usual Longevity

To determine if extreme aged dogs differed from dogs with usual longevity, we selected a comparison group of 61 dogs who died within 6 months of the median age at death of the population (i.e., 9–10 years). To evaluate the association between gender, neuter status, and extreme longevity, Rottweiler dogs were categorized into four groups: castrated male, sexually intact male, spayed female, and sexually intact female. Differences in gender, neuter status, nulliparity (in females), and cancer mortality between the extreme aged and usual longevity groups were examined using Chi square or Fisher's exact test. For each dog, lifetime gonadal hormone exposure was expressed as the percentage of the dog's lifetime that it was sexually intact. A *t* test was used to compare duration of gonadal hormone exposure and other reproductive parameters (age at first litter, age at last litter, number of litters, number of offspring) between extreme aged dogs and the usual longevity group. All data analyses were performed using standard computerized statistical software (SPSS Version 10.0; SPSS, Inc.), and differences were considered to be statistically significant at $p < .05$.

Results

Study Population

Gender, neuter status, and cause of death for the 345 Rottweiler dogs are shown in Table 1. Cancer was the most commonly reported cause of mortality in this cohort, accounting for 69% of deaths. A Kaplan-Meier survival curve for the 345 Rottweiler dogs of the study cohort is shown in Figure 1. Median age at death was 9.5 years (range = 1.3–15.0 years). Twenty-one dogs whose age at death was ≥13.3 years (95th percentile age at death) were identified as the Extreme Aged group.

Gender, Neuter Status, and Reproductive History of Extreme Aged Dogs (Table 2)

The female:male ratio was 2.0:1 and 1.3:1 among extreme aged dogs and dogs in the usual longevity group, respectively ($p = .38$). Nineteen of 21 (90%) extreme aged dogs were neutered. There was no significant difference in the percentage of dogs in the extreme aged and usual longevity groups that underwent gonadectomy ($p = .31$ for females, $p = .67$ for males) or in the duration of lifetime gonadal exposure ($p = .27$ for females; $p = .41$ for males). Nulliparity was not significantly associated with extreme longevity; 19 of 31 (61%) dogs in the comparison group and only 5 of 14 (38%) extreme aged dogs were nulliparous ($p = .17$). Similarly, age at first or last whelping and number of offspring did not differ significantly between the extreme aged and usual longevity groups.

Table 1. Characteristics of 345 Rottweiler Dogs

Median age at death (range)	9.5 (1.3–15.0)
Gender and Neuter Status	
Intact female	29 (8.4%)
Spayed female	157 (45.5%)
Intact male	71 (20.6%)
Castrated male	88 (25.5%)
Cause of Death	*Number of dogs* (%)
Cancer	238 (69.0%)
Appendicular bone sarcoma	74 (21.4%)
Lymphosarcoma	33 (9.6%)
Other cancers	131 (38.0%)
Gastrointestinal disease	22 (6.4%)
Neurological disease	15 (4.3%)
Cardiopulmonary disease	14 (4.1%)
Musculoskeletal disease	11 (3.2%)
Old age	10 (2.9%)
Renal disease	8 (2.3%)
Endocrine disease	8 (2.3%)
Other (includes hematologic, infectious, trauma, behavior)	11 (3.2%)
Unknown	8 (2.3%)

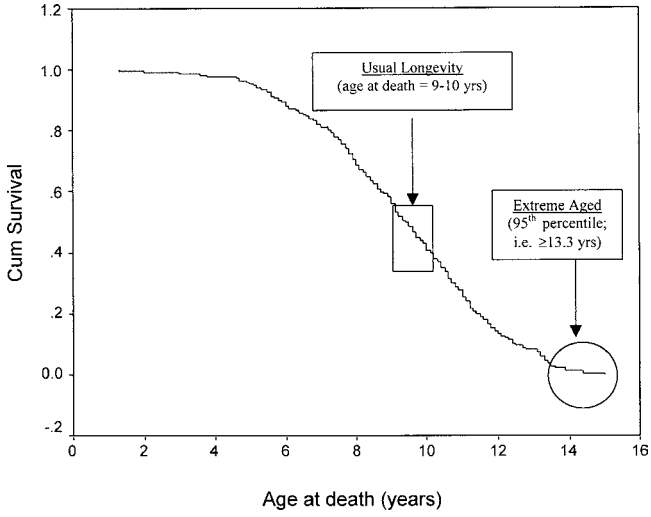

Figure 1. Kaplan-Meier Survival Curve for 345 Rottweiler dogs in the population. The circle represents those dogs defined as Extreme Aged (i.e., the dogs among the 95th percentile of age at death). The rectangle represents dogs in the usual longevity group (i.e., those dogs that died within 6 months of the median age at death for the study population).

Age at Onset of Major Diseases in Extreme Aged Dogs

There was considerable heterogeneity among extreme aged dogs in the age at onset of major diseases. The majority of extreme aged dogs had a delayed onset of all major diseases compared with the general population (Table 3). Specifically, 76% of extreme aged dogs were free of all major diseases until >9 years of age, the median age at death of dogs in this study cohort. Furthermore, 57% of extreme aged dogs had no history of a major disease during the first 13 years of life (Escapers). Only 24% of extreme aged dogs were categorized as Survivors, reaching extreme age despite suffering onset of a major disease at <9 years of age.

Diminished Cancer Mortality Risk in Extreme Aged Dogs

Age-specific cancer mortality rate and proportional cancer mortality were used to evaluate the relationship between age and cancer mortality risk in the study population. Age-specific

Table 2. Gender, Neuter Status, and Female Reproductive History of 21 Extreme Aged Dogs and 61 Dogs with Usual Longevity

Factor	Extreme Aged	Usual Longevity	*p* Value*
Age of death	≥13.3 years	9–10 years	
Gender			
Female	14 (66.7%)	34 (55.7%)	.38
Male	7 (33.3%)	27 (44.3%)	
Gender and neuter status			
Spayed female	14 (100%)	30 (88.2%)	.31
Intact female	0	4 (11.8%)	
Castrated male	5 (71.4%)	15 (55.5%)	.67
Intact male	2 (28.6%)	12 (44.5%)	
Duration of gonadal exposure			
% of lifetime sexually intact			
Male	56.4 ± 35.9%	69.1 ± 36.2%	.41
Female	34.1 ± 20.0%	44.3 ± 31.6%	.27
Female Reproductive History			
Pregnancy			.17
No	5 (38.5%)	19 (61.3%)	
Yes	8 (61.5%)	12 (38.7%)	
Age at first whelping	3.5 ± 0.8 years	3.2 ± 1.4 years	.61
Age at last whelping	5.0 ± 1.5 years	4.9 ± 1.4 years	.86
Number of litters	1.9 ± 1.0 litters	2.3 ± 0.8 litters	.35
Number of offspring	13.1 ± 7.2 offspring	11.1 ± 9.0 offspring	.61

Note: *Chi square, Fisher exact, or *t* test.

Table 3. Classification of 21 Extreme Aged Rottweiler Dogs Based Upon Age at Onset of Major Diseases

Category	Number (%) of Dogs
Survivor	
Onset of at least one major disease prior to 9 years of age	5 (24%)
Delayer	
Free of all major diseases until after 9 years of age	4 (19%)
Escaper	
Free of all major diseases until after 13 years of age	12 (57%)

cancer mortality rate per 100 dogs increased with age until approximately 10 years of age and then declined (Figure 2). In contrast, the rate of noncancer deaths within the population increased sharply after 8 years of age (Figure 2). When the population was divided into seven groups based upon age at death, the highest cancer mortality rate was 32.1 deaths per 100 dogs at risk in dogs that died between 10.3 and 11.4 years of age (Table 4). In contrast, cancer mortality rate for dogs in the Extreme Aged group was only 19.0 deaths per 100 dogs at risk. Proportional cancer mortality was also lowest in the extreme aged group. The percentage of deaths attributable to cancer was highest in dogs that died before 10.3 years of age. When the causes of death in extreme aged dogs and in dogs with usual longevity were compared, extreme aged dogs had significantly lower proportional cancer mortality (Table 5). Cancer accounted for only 19% of deaths in extreme aged dogs compared with 82% of deaths in dogs with usual longevity ($p < .0001$).

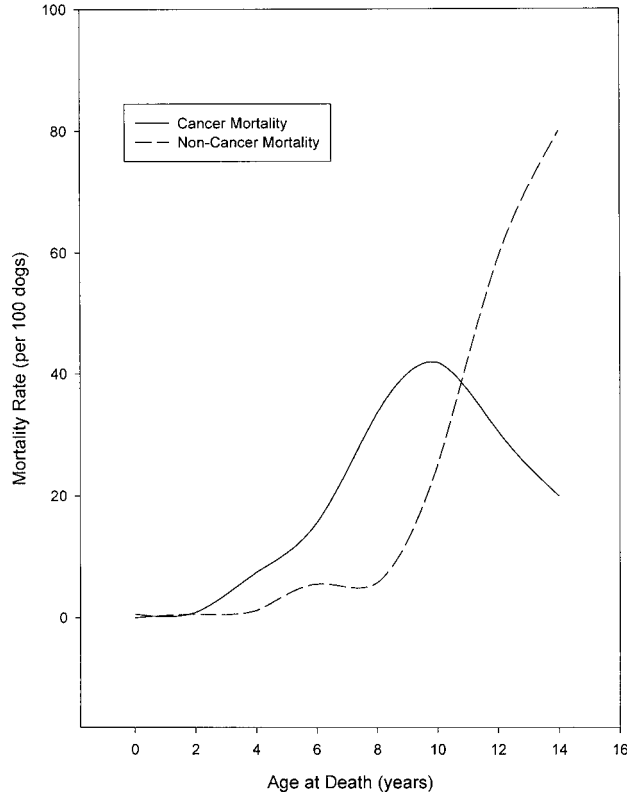

Figure 2. Comparison of age-specific cancer and noncancer mortality rates for 345 Rottweiler dogs. Age-specific cancer and noncancer mortality rates were calculated at 2-year intervals from 0–14 years of age and expressed as the number of cancer or noncancer deaths per 100 dogs that entered the interval.

Discussion

The study of extreme aged pet dogs provides an opportunity to probe the determinants of exceptional longevity in a domesticated mammalian population living in the same environment as humans. In this historical cohort study, we characterized the extreme aged Rottweiler dogs that survive at least 25% longer than other Rottweilers as a first step in the development of an animal model of exceptional longevity. Similar to the oldest-old humans, the majority of extreme aged dogs experience a delayed onset of major life-threatening diseases. In addition, we found a lower risk of cancer mortality in extreme aged dogs that mimics that seen in human centenarians.

There is a sizeable difference in the life span of small and large breed pet dogs (11–14). Therefore, we studied the relationship between age at onset of clinical disease and exceptional longevity within one breed. We used owner-reported questionnaire data to establish the age at onset of major diseases in 345 purebred Rottweiler dogs that were deceased at the time the questionnaire was submitted. Rottweiler dogs were selected to evaluate longevity and cancer mortality because they represented a popular breed with a relatively high risk for cancer. Comparison of cancer incidence among the 25 most popular dog breeds in the Veterinary Medical Data Base showed that the percentage of Rottweilers with a diagnosis of cancer was greater than 17 other breeds but less than 7 breeds (D. J. Waters, unpublished observations). An analysis of cancer-related mortality among 20 dog breeds in Denmark showed that the percentage of Rottweilers dying of cancer was greater than 16 breeds, but less than 3 breeds (15). The 69% overall cancer incidence in this cohort may overestimate the true incidence of cancer in Rottweilers, because owners of dogs with cancer were more motivated to submit questionnaires.

When life expectancy of men and women is compared, a consistent female survival advantage is apparent (16). It is not surprising, therefore, that a majority of human centenarians are females (17–20). Similarly, females outnumbered males (2:1) among extreme aged Rottweiler dogs. For both genders, there was a nonsignificant trend toward shorter duration of gonadal exposure (i.e., earlier neutering) in extreme aged dogs compared with dogs with usual longevity. Studies in dogs (21,22) and humans (23) have shown that gonadectomy increases longevity, but the exact mechanism is unknown. None of these studies examined the relationship between exceptional longevity and lifetime gonadal exposure.

A complex association between reproduction and longevity has been suggested from studies of flies and women. In selection experiments with *Drosophila*, the ability to produce eggs later in life correlated with longer life expectancy (24,25). Perls and colleagues (26,27) reported that exceptional longevity in women was associated with successful reproduction after 40 years of age. Perls

Table 4. Cancer Mortality Rate and Proportional Cancer Mortality in 345 Rottweiler Dogs

Factor	Age-at-Death Percentile						
	20th	40th	60th	80th	90th	>90th*	Extreme Aged >95th
Age range	1.3 to 7.3	7.4 to 8.7	8.8 to 10.2	10.3 to 11.4	11.5 to 12.4	12.5 to 15.0	≥13.3
Number of cancer deaths	56	55	59	42	16	10	4
Number of noncancer deaths	16	12	16	21	17	25	17
Cancer mortality rate (cancer deaths per 100 dogs at risk)†	16.2	20.1	28.6	32.1	23.5	28.6	19.0
Proportional cancer mortality (% of all deaths attributable to cancer)‡	77.8	82.1	78.7	66.7	48.5	28.6	19.0

Note: *These 35 dogs include the 21 extreme aged dogs in the >95th percentile.
†Cancer mortality rate = number of cancer deaths/100 dogs within the population that entered the age group.
‡Proportional cancer mortality = number of cancer deaths/total number of deaths within the age at death percentile.

hypothesized that late reproductive success may reflect a slower than normal rate of aging in these individuals (28). Other studies suggest a possible trade-off between reproduction and longevity in females. When egg production in female *Drosophila* was prevented, flies were spared a wave of mortality later in life (29). Similarly, in a study of the British aristocracy, Westendorp and Kirkwood (30) showed that nulliparous women were more likely to achieve advanced age (i.e., 80 years) than childbearing women. In Rottweiler dogs, neither late reproductive success nor nulliparity were found to be significant predictors of exceptional longevity. Late reproductive success may not be a reliable surrogate for high physiologic reserve or slow rate of aging in pet dogs, since pet owners decide whether or not breeding and whelping take place in advanced age. However, pet dogs seem ideally suited to determine if nulliparity influences exceptional longevity, because a large percentage of pet dogs undergoes elective ovariohysterectomy early in life (59% of female dogs in this cohort were nulliparous).

The ''compression of morbidity hypothesis'' (31) predicts that individuals whose longevity approaches the limits of maximum life span will compress the onset and duration of life-threatening diseases to the final years of life. Observations from human centenarians support this hypothesis. In the New England Centenarian Study, Hilt and colleagues (32) found that 90% of centenarians were functionally independent at 90 years of age, an age at which the majority of individuals within their birth cohort were deceased. Similar to human centenarians, pet dogs exhibiting exceptional longevity appear to experience a significant delay in the onset of major life-threatening diseases. A comparison of age at onset of major diseases in extreme aged Rottweiler dogs and human centenarians shows that 76% of extreme aged dogs and 62% of human centenarians (4) can be classified as Delayers or Escapers, i.e., individuals who do not suffer from any major diseases until after the median age at death of the population (Table 6). In fact, 57% of extreme aged Rottweiler dogs in our study were categorized as Escapers, reflecting their ability to remain free of major diseases until reaching extreme age. In contrast, Escapers comprised only 19% of human centenarians (4). The practice of elective euthanasia by pet owners may provide a selection pressure resulting in the higher percentage of Escapers among extreme aged dogs. Pet owners have the option to euthanize their dog when its quality of life is severely diminished by serious diseases, instead of pursuing palliative or potentially curative treatment. Thus, extreme aged pet dogs may represent a more penetrant phenotype of disease resistance than extreme aged humans, who often

Table 5. Cause of Death in 21 Extreme Aged Dogs and in 61 Dogs With Usual Longevity

Cause of Death	Extreme Aged	Usual Longevity
Cancer	4 (19.0%)*	50 (82.0%)
Noncancer	17 (81.0%)	11 (18.0%)
Cardiopulmonary disease	1 (4.8%)	3 (4.9%)
Gastrointestinal disease	3 (14.3%)	5 (8.2%)
Renal disease	1 (4.8%)	0
Neurological disease	3 (14.3%)	0
Musculoskeletal disease	4 (19.0%)	1 (1.6%)
Old age	3 (14.3%)	1 (1.6%)
Unknown	2 (9.5%)	1 (1.6%)

Note: *Differs significantly from usual longevity group at $p < .0001$.

Table 6. Comparison of Extreme Aged Rottweiler Dogs and Human Centenarians

Factor	Extreme Aged Rottweiler Dogs	Human Centenarians
Age at Death	≥13.3 years*	≥100 years
Gender		
Female	67%	80%†
Cause of Death		
Cancer	19%	4%†
Noncancer	81%	96%†
Delay in Onset of Major Diseases‡		
Survivor	24%	38%§
Delayer	19%	43%§
Escaper	57%	19%§

*Chronologic age of 13.3 years in a Rottweiler dog is equivalent to 109 human years (11).
†Data obtained from *Vital Statistics of the United States*, 1990 (5).
‡Based upon lifetime medical histories, extreme aged dogs and human centenarians were subcategorized using the method of Evert *et al.* (4): *Survivor* = onset of at least one major disease prior to median age at death for the population; *Delayer* = free of all major diseases until after median age at death; *Escaper* = free of all major diseases until after reaching extreme age.
§Data obtained from Evert *et al.* (4).

receive heroic life-saving medical interventions (e.g., organ transplant, joint or heart valve replacement) and are not euthanized following the diagnosis of a debilitating age-related disease.

Although cancer is a disease strongly associated with aging, age-specific cancer mortality rates in humans usually decline in the tenth decade of life (5). Limited data from human centenarians suggest that the oldest-old humans seldom develop lethal cancers (2,5–8,28,33–35). In an autopsy study of persons aged 97–106 years, cancer was responsible for only 6% of 114 deaths (33). According to the 1990 Vital Statistics of the United States, only 4% of centenarians had cancer as the cause of death reported on their death certificate (5). In Rottweiler dogs, the cancer mortality rate increased with age throughout adulthood, but declined after 10 years of age. Furthermore, dogs with exceptional longevity were much less likely to die of cancer than dogs with usual longevity. This raises the possibility that cancer resistance genes are over-represented in the extreme aged of both species, where they may influence longevity by protecting the host from malignant disease. The mechanism of cancer resistance in extreme aged humans and dogs has not been clearly defined. The observed cancer resistance may reflect a universal resistance of host cells to malignant transformation, either through efficient DNA repair or by mechanisms that protect cells from exposure to DNA-damaging agents (36). Alternatively, there may be widespread transformed foci in these elderly hosts that remain dormant, submacroscopic, and clinically occult (37). Finally, cancer-resistant individuals may develop benign neoplasms or nonlethal malignant neoplasms, and their reduced cancer mortality can be attributed to protection against the development of tumors with aggressive biological behavior (38).

Could the apparent resistance to cancer mortality in dogs with exceptional longevity be partially explained by a bias toward early euthanasia of cancer-bearing dogs within the usual longevity group? It is unlikely that dogs classified in the usual longevity group were prematurely euthanized for their cancers. On average, dogs in the usual longevity group lived longer after cancer diagnosis than extreme aged dogs (median survival = 3.6 months and 2.4 months, respectively). It would appear that if there was bias, it would be for earlier euthanasia of extreme aged dogs following cancer diagnosis, perhaps reflecting comorbidity in dogs of advanced aged. Ultimately, the fate of dogs with usual longevity was largely determined by their susceptibility to develop clinically aggressive cancers that were diagnosed at 8–9 years of age. In contrast, all extreme aged dogs that died of cancer were free of a cancer diagnosis until at least 11 years of age. Although the practice of euthanasia abbreviated the natural life span of more than 75% of dogs in this study, in many instances longevity was likely shortened only by days to months. Treatment of most cancers affecting adult Rottweilers extends survival only 4 to 12 months. Because more than 80% of dogs in the usual longevity group died of cancer, it is highly unlikely that dogs in the usual longevity group would have survived an additional 3+ years to reach extreme age had euthanasia not been practiced.

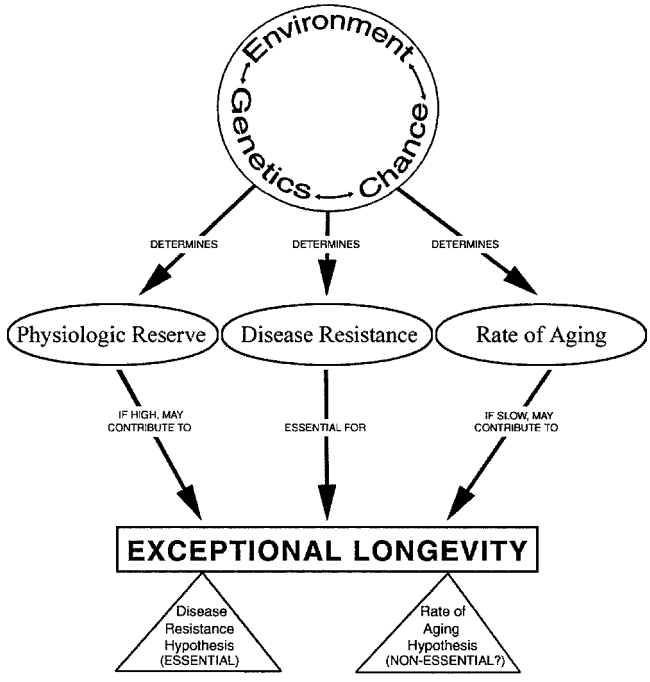

Figure 3. A conceptual model of factors that contribute to exceptional longevity.

A limitation of this study is that few causes of death were verified by necropsy. However, the reliability of these data is likely comparable to that of human mortality studies based on death certificates. Veterinarians assisted owners in providing accurate information on disease history and cause of death. There is no reason to suspect that the cause of death (i.e., cancer versus noncancer) was preferentially misclassified in extreme aged dogs versus dogs with usual longevity.

Exceptional longevity is a complex trait reflecting genetic, environmental, and stochastic influences. Based upon our current understanding of extreme aged humans and pet dogs, we propose that disease resistance is an essential determinant of exceptional longevity (Figure 3). In the extreme aged, disease resistance may be manifested as disease avoidance, delayed onset of clinical disease, or a decrease in mortality from specific diseases. Recent findings in *Caenorhabditis elegans* (39) lend further support to the important contribution of disease resistance to exceptional longevity. High physiologic reserve likely contributes to exceptional longevity because it may delay the clinical onset of diseases or ameliorate the deleterious effects of comorbid conditions. It remains unproven whether rate of aging (i.e., the rate of organismal senescence) is a significant determinant of exceptional longevity. To date, there are no definitive data supporting the hypothesis that a slow rate of physiologic decline is essential to achieve exceptional longevity in dogs or humans. Future studies that collect data on an array of physiologic parameters (e.g., muscle strength, cardiovascular compliance, neurologic processing, inflammation/immune response) are needed to determine whether individuals reaching extreme age demonstrate a significantly different rate of physiologic decline than individuals with usual longevity. Such studies are

feasible in dogs because of their relatively short life span compared with humans.

Summary

Human centenarians and extreme aged pet dogs have significantly lower cancer mortality compared with the general population. In both species, the majority of extreme aged individuals demonstrate an ability to delay the onset of life-threatening diseases. Pet dogs living in households with humans offer an outbred mammalian population with which to systematically study the genetic and environmental determinants of longevity. The relative cancer resistance of extreme aged pet dogs observed in this study provides strong rationale for future investigations using pet dogs to determine the mechanisms of cancer resistance in the oldest-old.

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