Common physical and functional changes associated with aging in dogs

Jan Bellows, DVM; Carmen M. H. Colitz, DVM, PhD; Leighann Daristotle, DVM, PhD; Donald K. Ingram, PhD; Allan Lepine, PhD; Stanley L. Marks, BVSc, PhD; Sherry Lynn Sanderson, DVM, PhD; Julia Tomlinson, BVSc, PhD; Jin Zhang, PhD

In the broadest sense, aging refers to the natural, progressive series of life stages beginning with conception and continuing through development, maturation, and senescence. Most often, however, the term is more narrowly used to refer to the complex set of biological changes occurring in older individuals that result in a progressive reduction of the ability to maintain homeostasis when exposed to internal physiologic and external environmental stresses. These changes ultimately lead to decreased vitality, increased vulnerability to disease, and eventually death.

Older dogs make up a substantial proportion of the pet dog population in the United States. One survey, for example, estimated that 30% to 40% of the 78 million pet dogs in the United States in 2007 were ≥ 7 years old, and a more recent survey suggested that the percentage of older dogs may be as high as 49%. Of course, the rate at which individual dogs exhibit overt signs of aging is affected by a number of factors, including breed, adult body size, genetic makeup, exposure to injuries and disease, and nutritional status. When all breeds are considered together, the mean lifespan of domestic dogs is approximately 13 years. However, body size substantially affects lifespan in dogs. Thus, because of their shorter lifespans, giant- and large-breed dogs (ie, dogs with a mature body weight ≥ 22.7 kg [50 lb]) should probably be classified as senior when they are 6 to 8 years of age and as geriatric when they are ≥ 9 years of age. Medium- and small-breed dogs (ie, dogs with a mature body weight < 22.7 kg) may be classified as senior when they are 7 to 10 years of age and as geriatric when they are ≥ 11 years of age. Regardless of the specific age cutoffs used, senior and geriatric dogs can all be considered to be aged and to likely have at least some changes associated with aging.

Some changes associated with aging can be considered favorable. For example, aged dogs often are well-behaved and have well-established habits. Other aging changes are neither positive nor negative, such as graying of the muzzle or a moderate reduction in activity level. Less desirable changes are those associated with illness, changes in mobility, or the development of behavioral problems. Collectively, deteriorative changes that negatively affect an aged dog's overall quality of life are referred to as senescence.

Several theories have been proposed to explain the phenomena of aging and senescence. Many of these focus on genetic controls, such as the somatic mutation and gene regulation theories. Others examine the impact of temporal changes on homeostatic mechanisms of various body systems or the accumulation of damaging products as a result of cellular aging. For example, the oxidative stress theory postulates that aging is linked to energy expenditure and the cumulative cellular damage caused by free radicals derived from external sources as well as internal sources such as mitochondrial respiration and immune cell reactions. However, none of these theories by itself explains all of the changes that are observed during aging, and many of the theories that have been advanced are not necessarily mutually exclusive. A more cogent view is that aging and senescence are multifaceted processes influenced by genetics and a myriad of internal and external environmental factors.

Naturally, many older dogs are cherished family members whose owners are committed to providing them with the best of care. When examining older dogs and when providing owners of older dogs advice regarding their care, veterinarians should have an appreciation of the types of changes that reflect typical age-related changes (ie, healthy aging) versus an under-
lying disease or abnormality. To that end, the present report reviews some of the most common health-related changes observed in older dogs as they age.

**General Physical Changes Associated with Aging**

Typical physical changes associated with aging in older, healthy dogs manifest as changes in behavior, appearance, and daily function, and it is these changes that are most often noticed by pet owners. Typical behavioral changes include changes in sleep cycle, responses to verbal commands, and interactions with family and other pets, which could reflect functional changes in cognitive and behavioral health. Appearance changes include a gray, dull, dry coat; loss of muscle mass; and development of cataracts and nuclear sclerosis, which could reflect functional changes in skin and coat, weight, body condition, and vision health. Functional changes include decreased activity and mobility and decreases in vision, smell, and hearing, which could reflect functional changes in musculoskeletal system and special senses health. These changes can happen in the absence of any disease process as part of normal aging.

**Cognitive and Behavioral Changes**

Age-related changes in the cognitive and behavioral domains can be expected in most dogs with advancing age. Some of the changes that occur in aged dogs without underlying systemic disease include changes in cognition, affect, sleep patterns, general activity, and motor performance; many of these changes likely result from underlying neurodegenerative processes.12–14

Formal, laboratory-based methods for assessing age-related changes in cognitive behavior in dogs have expanded greatly over the past 2 decades. Using methods adapted from cognitive assessment techniques in nonhuman primates, Studzinski et al15 and Tapp and Siwak16 developed the Toronto General Test Apparatus to identify cognitive impairment in dogs and evaluated age-related changes in cognitive abilities in Beagles across several cognitive domains. Age-related declines were reported in spatial memory, executive function, and concept learning. What emerged from these studies was the observation that older dogs could be separated into impaired and unimpaired animals. The performance of unimpaired dogs generally resembled that of their younger counterparts, whereas impaired dogs had notable impairments in 1 or more domains of behavioral performance. Impairments were also predictive of altered sleep-wake cycles, an increased likelihood of behavioral stereotypies, and decreased social contact with humans, which are consistent with behavioral changes reported in aged pet dogs.14 By contrast, unimpaired aged dogs had behavioral patterns that differed from those of both young and age-impaired dogs. Compared with young dogs, unimpaired aged dogs showed lower levels of activity as well as a shift from spending a lot of time interacting with humans to simply spending more time near humans.14

Analyses of biochemical and anatomic aspects of aging in dogs have revealed underlying neurologic changes related to cognitive and behavioral performance.14,15,17–21 Further investigation of these changes found a correlation between cognitive disorders in aged dogs and the accumulation of oxidative damage in brain cells.20,22 The brain appears to be particularly susceptible to the damaging effects of oxygen-free radicals.23 Overall, these findings suggest that biological processes of brain aging that affect the behavior of older dogs can start as young as 7 to 8 years of age.14

**Skin and Coat Changes**

With advancing age, several changes occur in the skin and hair coat of dogs. Cellular atrophy increases in both the epidermis and dermis. Follicles may also atrophy, resulting in areas of hair loss.24 The skin loses elasticity and becomes less pliable as a result of increased calcium content and pseudolastin in the elastic fibers. This loss of elasticity is often accompanied by hyperkeratosis of both the skin and hair follicles. Loss of melanocytes in the hair follicles and reduced activity of the enzyme tyrosinase result in the production of white hairs, which are often observed around the muzzle and face of older dogs.25 Changes in sebum production in older animals can result in scaly skin and cause the hair coat to become dry and dull. Highly sulfated GAGs are present in the basement membranes of hair follicles, and their concentration increases with age. A recent retrospective study26 documented that older dogs are more likely to have a diagnosis of cutaneous neoplasia, with 10 to 15 years being the most frequent age range and lipomas, adenomas, and mast cell tumors representing the most common types.

**Changes in Body Weight and Condition**

As animals age, their basal metabolic rate naturally slows. This decline is caused primarily by proportional changes in body composition that include decreased lean tissue and water contents and increased fat content. For example, a study27 comparing young and old dogs reported that the body fat percentage of young adults was between 15% and 20%, while that of older dogs was between 25% and 30%. Most, but not all, dogs voluntarily reduce physical activity as they enter their senior years. It is estimated that a dog’s total daily energy requirements may decrease by as much as 30% to 40% during the last third of its life as a result of reduced activity and decreased metabolic rate.28 For these reasons, some aging dogs are at increased risk for becoming overweight. However, a greater proportion of dogs > 12 years of age are underweight, compared with proportions for other age groups.29 This may be related to age-related sarcopenia in older dogs.

Some dogs do remain active and athletic well into their senior years. Because physical activity helps offset age-associated losses of lean body tissue, the basal metabolic rate in older dogs that remain active may not decrease substantially.

**Musculoskeletal Changes**

Lean body (muscle) mass and bone mass decrease as dogs age. Both the number and size of myocytes decrease with age.
Sarcopenia is a syndrome seen during aging in the absence of disease. The current definition of sarcopenia in people proposed by the European Working Group on Sarcopenia in Older People is “a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength with a risk of adverse clinical outcomes, such as physical disability, poor quality of life, and death.” In people, sarcopenia is associated with increased mortality rate and adverse effects on muscle strength, immune function, and quality of life. Although little information on the effects of sarcopenia in aging dogs is available at this time, it is a recognized syndrome in aging dogs, and there is every reason to believe that its effects on dogs are similar to those reported in people. A recent unpublished study of Labrador Retrievers found that healthy geriatric dogs (> 8 years of age) had significantly lower mean epaxial muscle area than did healthy young dogs (1 to 3 years of age).

Protein requirements sufficient to support protein turnover may actually increase in older dogs. A study comparing protein requirements in young versus older Beagles showed that older dogs required approximately 50% more protein than did young dogs to maintain nitrogen balance and maximize protein reserve. In addition, protein turnover was reduced in older dogs, even at the highest level of protein fed. Failure to recognize these nutritional needs as dogs age can accelerate the weight loss and sarcopenia that occur in geriatric dogs.

The cortices of the long bones become thinner, less dense, and brittle as dogs age. The composition of the articular cartilage matrix also changes with age. Specifically, a reduced number of chondrocytes leads to decreased production of GAGs, type 1 collagen, and chondroitin sulfate. As a result, aging cartilage gradually becomes less resilient and has limited ability to regenerate in response to intense activity or trauma.

Changes in the Special Senses

Advancing age may lead to a general decline in a dog’s ability to react to stimuli and to changes in the special senses, including vision, hearing, and olfaction.

The most common age-related change in the eyes of dogs (especially those that are > 6 years of age) is development of nuclear (lenticular) sclerosis, which appears as bilateral bluish-gray haziness in the nucleus of the lens. It is caused by compression of existing lens fibers as a result of new fiber formation, leading to increased density of the lens and an increase in the refractive index of the lens nucleus. Although many dog owners confuse the resulting bluish haze with cataracts, nuclear sclerosis does not usually affect a dog’s vision, except in severe cases. Night vision loss is gradual and very common in aging dogs; however, most owners and veterinarians blame the lens changes. Some dogs with a gradual onset of vision impairment do not demonstrate signs of these changes until their hearing is diminished, which illustrates the importance of hearing over vision in dogs.

Hearing impairment caused by cochlear degeneration is common in older dogs. Changes seen morphologically are quantitatively and qualitatively similar to those that occur in aging humans. Although there are generally no direct health risks associated with hearing loss, owners are often acutely aware of these changes and may be concerned for their dog’s safety and quality of life. In some dogs, age-related changes in cognitive function may manifest as apparent hearing loss.

Clinical changes in the sense of smell have not been documented in dogs as a manifestation of aging, although pathological changes have been demonstrated. Because dogs and humans age similarly, it has been hypothesized that cognitive impairment and olfactory function may be linked in dogs, as they are in humans. In fact, impaired olfactory function is associated with the risk of developing cognitive impairment in humans. On the basis of published data, it would be logical to assume that olfactory function in dogs would be diminished with advancing age. In a study of dogs > 14 years of age, olfactory epithelium was atrophied, as was the olfactory nerve layer. In addition, there were age-related vascular amyloidosis, astrocytic gliosis, and ubiquitin deposits within the olfactory bulb. An interesting difference between human and murine olfactory bulbs and canine olfactory bulbs is that dogs do not have β-amyloid deposition in this location, despite having it elsewhere in the cerebral cortex. β-Amyloid has been found in the olfactory epithelium of aging dogs. To clinically evaluate changes in olfaction in aging dogs, researchers in a study developed a novel paradigm to evaluate odor discrimination in dogs and identified a weak, though not significant, decline in odor discrimination with age. However, the paradigm needs to be evaluated with a larger group of dogs as well as with untrained dogs to rule out artifacts before any conclusions can be made. Nevertheless, given clinical information for other species, the histologic data, and the preliminary clinical data for dogs, it is likely that a dog’s sense of smell diminishes with age.

Oral and Gingival Changes

In dogs that do not have evidence of plaque, calculus (tartar), gingivitis, or periodontal disease, there are no changes to the visual appearance of the gingiva and dental hard structures as dogs age. Plaque normally attaches daily on the crowns of teeth unless mechanically or chemically removed. Calcium and phosphorus in the saliva then mineralize the plaque to produce calculus. It is common to find plaque and calculus on the teeth of healthy aged dogs.

Mouth size is a significant risk factor for periodontal disease in dogs. Clinically, larger aged dogs may have healthy mouths and teeth with little plaque and calculus accumulation, while smaller dogs may have greater accumulations of plaque and calculus, are more likely to develop periodontal disease at an early age, and tend to show more severe disease, compared with larger dogs. Reduced jaw size and crowding of teeth may be predisposing factors for dental disease in smaller dogs. In addition, toy-breed dogs are more likely to have malocclusion problems, which may facilitate the deposition of subgingival plaque that is more difficult to remove through either chewing or home care. As periodontal disease progresses, there is destruction and
loss of alveolar bone along the roots of teeth. Because smaller dogs have a lower ratio of mandibular size to tooth volume, compared with the ratio in larger dogs, the loss of bone has a greater impact.57

Owner intervention in preventing plaque accumulation can have a major impact on the establishment and progression of periodontal disease in dogs. If the owner strictly controls plaque, the periodontium remains healthy and the teeth should remain well-anchored in their alveoli. Conversely, if the owner does not establish a plaque control regimen, periodontal disease will usually occur, leading to gingival inflammation and, eventually, tooth loss.

**Gastrointestinal Tract Changes**

With advancing age in dogs, several structural and functional changes take place in the GI tract. These include reduced salivary and gastric acid secretion; decreased villus size, rate of cellular turnover, and colonic motility; and alterations in the intestinal microbiota.58 One study58 found that age and dietary fructooligosaccharide supplementation affect the intestinal microbiota in dogs. Another study59 found that the microbiota in the large bowel changes as dogs age. In a third study,60 the authors found a difference in metabolic activity in the feces of 4-year-old dogs, compared with that in feces of 10-year-old dogs. Age-related changes in fermentation products in that study59 suggested an alteration in bacterial metabolic activity or in the rate of intestinal absorption of these compounds. Although it has been theorized that aging of the GI tract leads to a decreased ability to digest and absorb nutrients, studies51-53 of healthy older dogs indicate that most dogs appear to maintain digestive efficiency as they age. This makes calculating energy provisions for aged dogs relatively straightforward. Because maintenance energy requirement decreases by approximately 20% and energy digestibility remains constant, aged dogs should be offered a reduction in energy equivalent to an approximately 20% decrement, although individual variations in metabolic rates exist.94

Using radiopaque markers and radioisotopic methods, researchers55 have demonstrated slowing of gastric emptying after consumption of large solid meals and a delay after consumption of large liquid meals in older people. Results of a study56 involving rats support the concept that changes in the aging GI tract result in increased satiety. The effects of age on the gut microbiota have been well studied in people. A recent study57 showed that although microbial composition and gut ecosystems are similar in young adults and seniors, they differ significantly from those of centenarians. Changes in the microbiota of centenarians are associated with inflammaging (a chronic, systemic inflammatory state) and a reduction in symbiotic bacterial species that have anti-inflammatory properties.

The liver is the central organ in the regulation of nutrient metabolism, xenobiotic metabolism, and detoxification. Evidence from humans and rodents has indicated that aging leads to marked changes in liver structure and function.65 The aged liver is characterized by decreases in weight, blood flow, regeneration rate, and detoxification rate, which are related to an increased risk of liver abnormalities in the elderly.66 Aged dogs are affected by many of the same chronic hepatic disorders seen in elderly humans, with age-related alterations in liver function influenced by diet. Molecular microarray analysis of liver tissue from aged and young-adult dogs revealed that genes related to inflammation, oxidative stress, and glycolysis were upregulated, whereas genes related to regeneration, xenobiotic metabolism, and cholesterol trafficking tended to be downregulated in aged liver tissue.69

In humans, age-related changes in exocrine pancreatic secretion include decreased flow rates and diminished production of bicarbonate and enzymes; however, functional and structural changes do not occur in everyone, nor do they progress continuously.66 These changes are generally not associated with clinical manifestations and do not require substitution treatment because the reduction in pancreatic secretions is typically well below the 80% to 90% decrease in exocrine function at which malabsorption occurs.60-62 There is also a decrease in secretin-stimulated secretions.60-62

**Cardiac Changes**

Normal vascular changes that occur with age in dogs include hyaline thickening of blood vessels and increased calcium deposition in the intima of the aorta and sections of the peripheral arteries.63 Together, these changes contribute to an increased load on the heart, which can eventually lead to the development of congestive heart failure.

Beginning in midlife, cardiac output gradually decreases and can decrease by as much as 30% in geriatric dogs.63 Maximum heart rate and oxygen consumption during exercise also decrease as animals age. For example, a study64 that compared cardiovascular responses during exercise between young and old dogs reported that aging was associated with a loss of cardiovascular reserve and adaptability. These changes are thought to contribute to cardiovascular disease in older dogs.

The effects of aging on contractile performance, stiffness, and contraction time of the left ventricle were evaluated in 8 young (mean ± SEM age, 27.5 ± 2.5 months) and 7 old (128 ± 20.5 months) Beagles.65 A major finding of this study showed that increasing age was associated with an increase in the stiffness of the left ventricle, both in systole and diastole, as well as a prolonged duration of contraction. A more recent study66 evaluated the effects of age on transmural and pulmonary venous flow in client-owned dogs comprising 27 breeds that ranged from very young (3 months of age) to very old (19 years of age). Results indicated that a gradual decrease in the rate of left ventricular relaxation, an increase in myocardial stiffness, and an enhanced late diastolic filling occur with aging in dogs. Although there are limited studies in dogs evaluating the effects of aging on cardiac function, there do appear to be some age-related changes that could adversely affect the ability of older dogs to respond to cardiac stress in the same way as younger dogs.

**Respiratory Tract Changes**

Aging changes in the respiratory system have been well characterized in humans and have been document-
ed, albeit to a lesser extent, in dogs as well. In humans, major age-related changes include decreases in pulmonary elasticity, respiratory muscle strength, and chest wall compliance. Alterations in pulmonary immune cell number and function, reduced diffusion capacity across the alveolar-capillary membrane, and dysfunction in pulmonary β-adrenoreceptors and airway reactivity have also been associated with aging in humans.

Similar changes are considered likely to develop with advancing age in dogs. Pulmonary alveoli enlarge and coalesce, leading to reduced lung elasticity and decreased surface area for gas exchange. In addition, control of breathing has been shown to be altered with age in dogs, with decreases in ventilation and responses to hypoxia during slow-wave sleep.

For the most part, even with this decrease in critical ventilatory functions, the respiratory system of older humans is capable of maintaining adequate gas exchange, and the same appears to be true for older dogs.

**Renal and Urinary Tract Changes**

Although a gradual decline in renal function is normal in older animals, a substantial loss of functioning nephrons must occur before changes in renal function become evident by routine assessment. With the exception of acute renal damage, most damage that occurs in the kidneys as dogs age is irreversible, and the healing of irreversibly damaged nephrons occurs by means of replacement fibrosis.

Renal histopathologic preparations usually show some combination of a loss of tubules with replacement fibrosis and mineralization, glomerulosclerosis and glomerular atrophy, and foci of mononuclear cells (small lymphocytes, plasma cells, and macrophages) within the interstitium. These changes are nonspecific, and as a result, the underlying cause of the renal damage is usually unknown. Compensatory hypertrophy occurs in the remaining viable nephrons and creates a large functional reserve early on in the process.

A study conducted over a period of 13 years evaluated clinical changes in renal function associated with age in Beagles. Results showed that nephrosclerosis was the most frequently diagnosed kidney lesion in older dogs. The data from that study also indicated that normal kidney aging may lead to nephron loss of up to 75% before clinical signs or conventional biochemical changes occur in older dogs. Animals with < 75% loss may be more susceptible to renal insult than younger animals still possessing renal reserve capacity.

Alterations in renal cortical and medullary GAGs are also seen in aging dogs. Glycosaminoglycans are among the most highly negatively charged molecules known, and their presence in the glomerular basement membrane helps maintain the membrane’s charge barrier properties, which prevent protein from crossing from the glomerulus into the glomerular filtrate. Hyaluronic acid in the extratubular stroma of the medulla contributes a gelatinous support for the tubular structure of the nephron and may slow translocation of sodium in the renal tubules. One study evaluated GAG composition of the renal cortex and medulla in healthy younger and older dogs. Results showed a significant reduction in the heparan sulfate content of the cortex (where all glomeruli are located) and a decline in hyaluronic acid content in the medulla in aging dogs. In the renal cortex, heparan sulfate concentration, which is the predominant GAG, gradually increased until the sixth year of age and then sharply decreased as dogs grew older. Heparan sulfate and hyaluronic acid were present in equal proportions in renal cortices of 1- and 3-year-old dogs; however, in the renal cortices of 10-year-old dogs, heparan sulfate formed only 30% of the total GAG content, which is only 0.75 times the hyaluronic acid content. The reason for the alterations in the GAG composition in the renal cortex as dogs age is not clear, but it may explain the frequency of proteinuria related to aging in dogs. In the renal medulla, chondroitin sulfate concentration, which forms a small proportion of the total GAGs, remained unaltered in young versus aging dogs. However, medullary heparan sulfate concentration, which formed a third of the total GAG content in 1- and 3-year-old dogs, steadily decreased as dogs aged. By 10 years of age, heparan sulfate formed only 14% of the total GAG content, and the ratio of hyaluronic acid to heparan sulfate, which is approximately 1.0 in younger dogs, increased to 3.9 in aging dogs.

**Changes to the Endocrine System**

Age-related alterations in adrenal cortex secretion, serum cortisol and aldosterone concentrations, and HPA axis regulation have been reported in dogs. The influence of aging on adrenal responsiveness in dogs has been well studied, with studies showing that aging is associated with increased HPA activity, characterized by increased plasma ACTH and cortisol concentrations and increased urinary cortisol excretion. Strasser et al theorized that increased cortisol concentration could point to an “age-related hyperrenocorticism and indicates a reduced stress resistance in older animals to equal stress than younger animals.” Other authors have assumed that sensitivity to negative glucocorticoid feedback at the pituitary, hypothalamus, and hippocampus levels is reduced in aging dogs. Basal activity of the HPA axis is controlled by mineralocorticoid receptors (predominantly located in the hippocampus) and glucocorticoid receptors (located in the pituitary gland and the hippocampus). The loss of mineralocorticoid and glucocorticoid binding sites with aging may explain the altered feedback regulation documented in elderly dogs. Healthy dogs between 11 and 14 years of age had a marked reduction in mineralocorticoid receptor-binding capacity (expressed as a percentage of the corresponding levels in dogs between 18 and 24 months of age) in the dorsal hippocampus, ventral hippocampus, septum, and hypothalamus.

The effects of advancing age on serum concentrations of T₄ and TSH, on T₄ responses to TSH, and on...
TSH responses to thyrotropin-releasing hormone have been studied in prepubertal, adult, middle-aged, and old Beagles. Serum T₄ concentrations were highest in puppies and decreased by 40% in older dogs. A longitudinal study completed over the lifetime of healthy Labrador Retrievers identified age-related decreases in total triiodothyronine (T₃), T₄, and free T₃ concentrations and age-related increases in T₄ autoantibody concentration. Baseline serum T₄ concentration is lower in some breeds, most notably sight hounds such as Greyhounds and northern breeds such as Siberian Huskies. Thus, a serum total T₄ concentration that is less than the lower reference limit can be a normal age- or breed-related phenomenon and should not be misinterpreted as evidence of hypothyroidism. In dogs, serum T₄ concentration can also be suppressed by a variety of factors, including nonthyroidal illness and administration of medications such as prednisone, phenobarbital, and sulfonamide antimicrobials. The reasons for the reduction in T₄ concentrations in older dogs are not well-understood, and this decrease could be related to decreased responsiveness of the thyroid gland to TSH, fibrosis or atrophy of the thyroid gland, decreased biological activity of TSH, and concurrent illness.

The pancreas and pancreatic function may also be affected by age. Age is a significant risk factor for glucose intolerance and diabetes mellitus in dogs. This may result from either a reduction in the number of insulin receptors or development of insulin receptor insensitivity. In addition, the change in body fat content that is associated with aging is strongly and positively correlated with changes in glucose tolerance. This reduction in insulin sensitivity may be ameliorated through weight loss or the prevention of becoming overweight. Improved glucose tolerance has been demonstrated with diet restriction in Labrador Retrievers undergoing a lifetime food restriction trial. A 25% reduction in food intake over the course of the dogs’ lives was associated with lower mean basal serum glucose concentration (9% lower) and plasma insulin concentration (33% lower) among the dogs that were food restricted, compared with values for their control-fed littermates.

There is also evidence that ovarian (endogenous estrogen) status contributes to healthy aging. Female Rottweilers tend to outlive male Rottweilers. However, ovary removal during the first 4 years of life abolished the female Rottweilers’ survival advantage.

Immune System Changes

The immune system is an interactive network of cells, proteins, and signaling molecules designed to provide protection from environmental pathogens, parasites, malignant cells, allergens, and toxins. Similar to changes reported in rodents and humans, the immune system in dogs undergoes complex remodeling with advanced age, also known as immunosenescence. Canine immunosenescence has been studied for more than 3 decades, and various changes in the immune system can be found in healthy aged dogs (Appendix). There are fundamental changes in both T-cell- and B-cell–mediated immunity in aging dogs. It is well-documented that old dogs (8 to 13 years of age) have lower lymphocyte proliferative response to specific antigens, including phytohemagglutinin, concanavalin A, and pokeweed mitogens, compared with responses in young dogs (2 to 4 years of age). A study of immune activation of lymphocytes in 40 young (1.5 years of age) and old (7 years of age) Fox Terriers and Labrador Retrievers found that both breeds demonstrated an age-related decrease in their ability to respond to various mitogens, but that the decrease was greater for Fox Terriers than for Labrador Retrievers.

Aging is also associated with changes in the distribution of lymphocyte subsets in the peripheral blood, including phenotypic changes in the absolute number, relative percentage, or ratio of T cells and T-cell subsets and B cells in the peripheral blood or in the expression of surface markers of activation or memory in these subpopulations. Age-associated changes in humoral immunity are reflected in the number and function of B cells and through antibody responses to antigens or vaccination. Increasing age has been associated with increased production of inflammatory mediators in mice and humans. The T-helper 1-to-T-helper 2 ratio changes to reflect a dominance of the T-helper 1 subpopulation in the peripheral blood as dogs age. There is also evidence of no significant changes in tumor necrosis factor-α activity and increased interleukin-1-like activity in older female dogs (age range, 8 to 13 years). On the other hand, the innate immune system is apparently less vulnerable to age, compared with the acquired immune system. There are subtle or no changes in natural killer cell activity and polymorphonuclear leukocyte phagocytic activity with age.

Conclusions

It is readily apparent that considerable changes occur in virtually every body system of dogs with advancing age. Some of these changes can greatly affect the health and well-being of older dogs and have a tremendous impact on their owners, both from the standpoint of cost of management and from the viewpoint of the daily pet-owner relationship. An appreciation of aging in dogs is critical for both clinical and research reasons. In this regard, it is imperative to be able to distinguish between what should be considered normal versus unhealthy aging changes. This distinction would clearly impact clinical management of aging dogs in that management could be adjusted on the basis of normal aging expectations. Research efforts in dogs could be focused on evaluating the effects of various interventions in healthy aging dogs and older dogs with evidence of disease. Additional effort is needed to define the clinical assessments required to differentiate healthy aging from disease for each of the systems identified.

References


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### Appendix

Summary of studies of immunosenescence in dogs.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Mean age or age range (y)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fox Terrier</td>
<td>11.5</td>
<td>Decreased mitogen responses to phytohemagglutinin, pokeweed mitogen, and concanavalin A</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>9.6</td>
<td>No changes in antibody response to sheep RBCs</td>
</tr>
<tr>
<td>Beagle, Labrador Retriever, and other breeds</td>
<td>12.1</td>
<td>No changes in antibody response to protein antigen</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>Lifetime</td>
<td>Lower CD8+, higher B cell</td>
</tr>
<tr>
<td>German Shepherd Dog</td>
<td>8–13</td>
<td>Decreased antibody response to sheep RBCs, lower CD4+:CD8+</td>
</tr>
<tr>
<td>Beagle, Labrador Retriever, and other breeds</td>
<td>12.1</td>
<td>Higher CD8+, lower CD4+:CD8+</td>
</tr>
<tr>
<td>Beagle</td>
<td>&gt; 5</td>
<td>Higher CD8+, no change in CD4+, lower CD4+:CD8+, higher B cell</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>Lifetime</td>
<td>No changes in antibody response to vaccine; no difference in IgM and IgG</td>
</tr>
<tr>
<td>German Shepherd Dog</td>
<td>8–13</td>
<td>No changes in IgG</td>
</tr>
<tr>
<td>German Shepherd Dog</td>
<td>8–13</td>
<td>Decreased interleukin-2, no changes in tumor necrosis factor-α, increased interleukin-1–like activity in female dogs</td>
</tr>
<tr>
<td>Beagle</td>
<td>&gt; 8</td>
<td>Inclined to T-helper 1 dominance</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>Lifetime</td>
<td>No difference in NK cell activity and polymorphonuclear leukocyte phagocytic activity</td>
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<td>No difference in polymorphonuclear leukocyte phagocytic activity and increased NK cell activity in female dogs</td>
</tr>
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</table>

NK = Natural killer.