AGING IN CATS
Common physical and functional changes

Practical relevance: Aged pets comprise a significant proportion of the small animal veterinarian's patient population; in the USA, for example, it was estimated that over 20% of pet cats were 11 years of age or older in 2011. Certain changes associated with aging are neither positive nor negative, but others are less desirable, associated with illness, changes in mobility or the development of unwanted behaviors. These changes can greatly affect the health and wellbeing of the cat and have a tremendous impact on the owner.

Clinical challenges: Regular veterinary examinations are essential for evaluating the health of older patients and for providing owners with guidance regarding optimal care. With the exception of overt disease, however, it is difficult to definitively determine if a cat is displaying changes that are appropriate for age or if they reflect an abnormal process or condition.

Goals: This is the first of two review articles in a Special Issue devoted to feline healthy aging. The goals of the project culminating in these publications included developing a working definition for healthy aging in feline patients and identifying clinical methods that can be used to accurately classify healthy aged cats. This first review provides a thorough, systems-based overview of common health-related changes observed in cats as they age.

Evidence base: There is a paucity of research in feline aging. The authors have drawn on expert opinion and available data in both the cat and other species.

Introduction

Aging is defined as a complex set of biological processes resulting in the progressive reduction of an individual’s ability to maintain homeostasis when exposed to internal physiologic and external environmental stressors. These changes lead to decreased vitality, increased vulnerability to disease and eventual death.

Some of the changes associated with aging may be thought of as favorable; for example, aged cats often are well behaved and have well-established habits. Other changes are neither positive nor negative, such as graying of the coat or a moderately reduced activity level. Less desirable changes are those associated with illness, changes in mobility or the development of unwanted behaviors. Collectively, deteriorative changes that may negatively affect an aging pet’s overall health and quality of life are referred to as senescence.

A variety of theories have been proposed to explain the phenomena of aging and senescence. Several of these focus on genetic controls, such as the somatic mutation and gene regulation theories. Others examine the impact of temporal changes in homeostatic mechanisms of different body systems or the accumulation of the damaging products 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 from external

Aging is a multifaceted process influenced by genetics and a myriad of internal and external environmental factors.
sources as well as internal sources, such as mitochondrial respiration and immune cell reactions. While not mutually exclusive, neither of these theories solely explain all of the changes that are observed during aging. A more cogent view is that aging and senescence are multifaceted processes influenced by genetics and a myriad of internal and external environmental factors.

The rate at which an individual cat exhibits signs of aging may be influenced by breed, genetic make-up, exposure to injuries and disease, physical environment, stress and nutritional status. With good care, many cats live into their late teens and early 20s. A suggested classification for aging cats is to consider them as ‘mature’ or ‘middle-aged’ at 7–10 years, ‘senior’ at 11–14 years and ‘geriatric’ at 15+ years. These classifications are based on epidemiological data; each cat should be evaluated as an individual.

Aged pets comprise a significant proportion of the small animal veterinarian’s patient population. Of the 74.1 million pet cats in the United States in 2011, it was estimated that 20.4% (15.1 million) were 11 years of age or older. Naturally, many of these patients are cherished family members with owners who are committed to providing them with the best of care (Figure 1). Regular veterinary examinations are essential for evaluating the health of older patients, and for providing owners with guidance regarding optimal care including, when needed, nutritional, behavioral or medical interventions.

With the exception of overt disease, it is difficult to definitively determine if an aged cat is displaying age-related changes that are appropriate for age (ie, healthy aged cat) or if they reflect an abnormal process or condition. Effectively characterizing these aged cats as healthy or not requires a thorough, systems-based overview of health-related changes observed in cats as they age. The objective of this review is to provide that overview.

**General physical changes**

Typical age-related physical effects in healthy cats, as noticed by most pet owners, manifest as changes in behavior, appearance and daily function (see box). These changes can happen in the absence of any disease process, as part of normal aging.

**Cognitive and behavioral health**

The classic signs of aging noted by cat owners are commonly behavioral and related to changes in the musculoskeletal system, sensory systems and cognitive function. Pet owners often characterize these changes as just part of the aging process and may not mention them to their veterinarian, yet identification of these signs by veterinary health care professionals may permit timely intervention that can improve quality of life for the patient. Changes in behavior that possibly are not related to systemic disease include changes in attitude, activity, appetite, sleep and cognitive ability, and are often the result of underlying neurodegenerative changes.

Over the past two decades, relatively robust evidence has been compiled for cognitive decline in senior dogs, and a growing body of evidence supports similar changes in the cat (see box on page 535). Like dogs, an aging cat may show cognitive and behavioral changes without any underlying or concurrent systemic disease.

Decline in cognitive ability in aged dogs is supported by neuropsychological testing. Only limited neuropsychological testing results are available for the aged cat. One such study evaluated the responses of cats, divided into three age groups (young adult, 3.0–3.8 years; old, 7.7–9.0 years; senior, 10.5–15 years), to a battery of cognitive tasks; these were modeled on tasks and apparatus developed to assess cognitive function in dogs. The subjects showed significant age-dependent decline in learning in T-maze tasks, in both discrimination learning and reversal learning. Additionally, there were significant differences between adult and aged cats on a matching task. These data establish age-related differences in the ability of cats to learn certain cognitive tasks, which suggests that advancing age in cats is associated with a

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<th>Physical changes with aging</th>
<th>Cognitive and behavioral health</th>
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| Behavior changes<br>Altered sleep cycle, altered vocalizations, reduced stress tolerance, changes in elimination habits and changes in interaction with family members and other pets could reflect functional changes in cognitive and behavioral health. | Cognitive and behavioral health  
Change in activity patterns (either increased or decreased), decreased mobility and a decline in vision, sense of smell and hearing could reflect functional changes in musculoskeletal and special senses’ health. |
| Appearance changes<br>Non-neoplastic iris pigment changes, lenticular sclerosis, iris atrophy, decreased skin elasticity and brittle thickened nails could reflect functional changes in skin and coat, weight/body condition and visual health. |  |
Brain imaging research on elderly cats has identified cerebral atrophy, increased ventricular size and widening of the sulci – all signs noted in dogs with cognitive dysfunction syndrome (CDS). Changes in the cerebellum and piriform lobes have also been found and these may lead to changes in information processing and deficits. Comparative studies of the brains of aged (16–21 years) and young (<4 years) cats have revealed amyloid accumulation and tau abnormalities in clinically characterized aged cats, but not young cats. Additional feline studies have linked the presence of beta-amyloid with cognitive disturbances (Figure 2), including spatial and temporal confusion, inappropriate vocalization and confused wandering behaviors. Oxidative stress and free radical formation contribute to cognitive decline in the dog and are thought to do likewise in the cat.

An aging cat may show cognitive and behavioral changes without any underlying or concurrent systemic disease.

In addition, the effects of solar exposure may be more evident in older cats. A positive correlation between age and the degree of photodamage was found in cats chronically exposed to sunlight.

Skin and coat health

With advancing age, various changes occur in the skin and coat of cats (Figure 3). These include epidermal, dermal and follicular atrophy and hyperkeratosis, which may result in a thinning haircoat and focal alopecia. Loss of melanocytes in the hair follicles and reduced activity of the enzyme tyrosinase result in the production of white hairs; however, paradoxically whiskers may turn black. Changes in sebum production, along with reduced self-grooming activity, can lead to scaly skin and cause the coat to become dry or oily and dull. Decreased skin elasticity and brittle claws have also been noted in apparently healthy older cats.

Figures 2 and 3 show the changes in cognitive and behavioral functions in aging cats, including histopathology of the brain and skin and coat alterations.
exposed to natural solar radiation. In those cats, non-neoplastic photodamage was characterized by subepidermal edema and sclerosis, telangiectasia, squamatization of basal keratinocytes and increased epidermal thickness. Such solar keratotic lesions may progress to squamous cell carcinoma, which is primarily a cancer of older cats, the median age of affected cats being 10–12 years.

In general, neoplastic skin changes are more likely to be seen with advancing age in cats. In addition to squamous cell carcinomas, the more common skin tumors observed in older cats include benign basal cell tumors, basal cell carcinomas and fibrosarcomas.

**Weight and body condition**

Maintenance of a healthy body weight and body composition throughout the life cycle is well accepted to reduce the risks associated with morbidity and mortality in all mammals. Despite this, overweight, ranging from mild to severe (obesity), represents one of the most common health conditions in cats. While obesity is technically defined as having excess body fat (>12% body fat), in practical situations it is diagnosed as body weight that is >20% above ideal.

Weight gain is often unrecognized by the owner and under-reported by the veterinarian. Given the insidious nature of body composition changes, it is important that body composition is tracked throughout a cat’s life. Although body weight and fat:lean ratio are generally accepted to either plateau or maintain both weight and lean mass in cats through adulthood, and thereafter experience weight gain or loss of lean body mass up through 11 years of age; however, minor increases in blood urea nitrogen (BUN) and creatinine (data shown in Table 1) without concomitant changes in protein breakdown. Changes in BUN and creatinine are non-specific, and are not always renal in nature. Slight changes in these parameters may be related to changes in diet or lean body mass. Cumulatively, these data suggest that practitioners should first seek to limit weight gain and maintain lean mass in cats throughout adulthood, and thereafter maintain both weight and lean mass in cats >11 years of age.

Energy expenditure and intake are the variables contributing to energy balance. Many factors affect energy expenditure and intake, including age, body size, activity level, nutrient digestibility, neutering, health status and environmental conditions. These factors need to be considered for individual cats.

<table>
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<th>Table 1</th>
<th>Association between blood urea nitrogen (mg/dl) and age in cats in a controlled animal facility*</th>
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<td>Gender</td>
<td>Age (years)</td>
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<td>Male</td>
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*Data were generated from results for 627 healthy cats, including 211 cats aged 7–10 years and 149 cats aged 11+ years, housed at the Iams Pet Health and Nutrition Center between 2002 and 2011. CI = confidence interval
Data suggest that practitioners should seek to limit weight gain and maintain lean mass in cats throughout adulthood, and thereafter maintain both weight and lean mass in cats >11 years of age.

National Research Council and the Association of American Feed Control Officials base maintenance energy requirements (MER) and recommendations, respectively, for adult cats on data from unstressed, healthy adult laboratory animals that are of typical body weight and condition, undergoing modest amounts of exercise and housed in a thermoneutral environment to which they have been acclimated. These criteria may not adequately represent client-owned cats and/or cats >11 years of age. Indeed, Bermingham et al demonstrated that there is a significant effect of age and season on energy expenditure, but when standardized for lean body mass, energy expenditure, as evaluated in the summer, was not different between young and old cats. However, when dietary energy intake required to maintain body weight is used to determine MER, daily energy requirements appear to increase in cats 10–12 years old and more dramatically in cats >12 years old.

Studies report conflicting findings on the relative food intake of senior cats. Peachey and Harper demonstrated that food and energy intake of senior cats was not different from that of young adults when fed a wet food. However, the small number of cats (n = 6) in the study may not have been sufficient to detect numerically small, but physiologically significant, differences. In addition, there was a tendency for senior cats to consume less energy per meal than young cats, and this could contribute to an overall negative energy balance and weight loss over time. Conversely, Taylor et al reported that senior cats (10–14 years) had significantly greater energy intakes compared with younger cats.

The Bermingham study found that older cats had a lower total metabolizable energy intake in the winter compared with the summer, but that energy requirements based on energy expenditure were similar between summer and winter in older cats. The overall challenge in detecting any differences in energy intake is compounded by the small quantities of food consumed by most cats and the high energy density of most diets. While it takes quite a large change in body weight (at least 2 lb or 1 kg) to fall into a new feeding guideline amount (typically 1/4 to 1/3 cup) for most commercially labeled dry cat foods, a much smaller change in daily intake (<15 g or 1/8 cup) can result in significant increases or decreases in weight over time. Unlike humans and dogs, many cats do not have outdoor access; this may limit their ability to adequately compensate for energy intake excess or deficiency with concurrent changes in physical activity. There is a great need for additional research to better elucidate the relationship between food intake and energy balance in senior cats.

Diet digestibility can also impact energy balance. Studies that have examined age as a variable have suggested either lower or similar energy digestibility in older cats compared with younger cats. A reduction in digestibility of fat and energy may result in an energy imbalance and, in turn, loss of body and/or muscle condition. More frequent meals may improve digestibility and availability of nutrients. Recent research has suggested that increased feeding frequency and water intake increase physical activity, which can help maintain lean body mass. Therefore, for management of senior cats consideration might be given to increased frequency of feeding and methods to encourage increased intake of fresh, high quality water.

Musculoskeletal system health

The major changes in the musculoskeletal system that occur with age are a decrease in lean body mass (muscle, bone, skin, organs), deterioration of joint components and functional decline. These changes occur with normal aging and are distinct from changes in these systems that are induced by disease.

A decrease in lean body mass, deterioration of joint components and functional decline occur with normal aging and are distinct from musculoskeletal changes induced by disease.
Sarcopenia is a syndrome seen during aging in the absence of disease. The European Working Group on Sarcopenia in Older People defines sarcopenia in humans as 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. The term frailty has also been used in relation to age-related deterioration in the musculoskeletal system. Frailty is a multisystem impairment associated with increased vulnerability to stressors and describes individuals that are at increased risk of adverse health outcomes. Frailty is related, but not synonymous, with comorbidity and disability. In the human literature, there is controversy regarding the exact definitions of sarcopenia and frailty. Regardless, there appears to be increasing interest in understanding the mechanisms behind age-related deterioration of the musculoskeletal system, how to phenotype it and how to slow the process.

In contrast to humans, little work has been performed in this area in the cat, but most clinicians recognize a similar decline in musculoskeletal function with age. And, as discussed earlier, loss of lean body mass has been shown to be related to decreased survival in cats. A longitudinal analysis of cats suggested that absolute lean mass declines at a steady rate for many years prior to death, while absolute fat is maintained until around 3 years before death, from which time it increasingly declines. Various studies have highlighted the high prevalence of degenerative joint disease (DJD) in cats (Figure 5), even those of a young age, and the fact that this is not necessarily associated with clinical signs. Thus, many cats may have radiographically detectable DJD, apparently without any associated clinical signs, and so may still present as healthy individuals. Additionally, cartilage deterioration occurs in cats before radiological features of DJD are seen. This mirrors what is seen in aging humans. Again, the important aspect here is that DJD may be present in the healthy cat without causing any clinically evident signs.

Clinically apparent, age-appropriate changes in the cat may include some muscle loss, decreased muscle strength, decreased agility and flexibility, DJD (not associated with pain) and decreased bone density and cortical thickness. Such age-related changes are most likely to be seen after 10 years of age.

Degenerative joint disease may be present in the healthy cat without causing any clinically evident signs.
Special senses health

Aging cats often experience a decline in their sense of smell, hearing and vision. This decline can result in changes in how the individual responds to stimuli, people and the environment.

The most common visually apparent change in healthy aged cats is an increase in the density of the central portion of the lens as it ages. Known as lenticular (nuclear) sclerosis (Figure 6), this does not typically affect vision (except perhaps in low lighting) but is often noted by owners as a bluish haze in the lenticular tissue.46 Commonly in an aged cat there will be changes in the iris tissue, resulting in atrophy and the appearance of scalloping along the iris edge.47 Although likewise this does not appear to affect vision, these senile changes may progress with age and result in a slower pupillary response to changes in light. Benign deposition of melanin in the iris may also occur, and is difficult to distinguish from diffuse iris melanoma in the early stages.48

Hearing may become impaired in the senior cat, especially at higher frequencies. It is speculated that this hearing loss may result in confusion, anxiety and increased vocalization in some senior cats. To the authors’ knowledge, there is no documented evidence of loss of hearing with age.

It is likely that olfaction diminishes with age in the cat, as it does in other species. The loss of smell may manifest most obviously as changes in eating habits; cats use smell not only to find their food, but are attracted to, and more likely to eat, certain foods based on their aroma.49 Although changes in olfaction have been noted in dogs and humans with advancing age, no such information is available for the cat.

Oral and gingival health

The oral cavity of a healthy aged cat is defined by the absence of periodontal disease, tooth resorption, oropharyngeal inflammation, oral masses and fractured teeth.

The appearance of individual teeth often changes as cats age. The outer enamel layer of the tooth is non-living and remains approximately the same thickness throughout life. Young cats have wide pulp chambers and thin dentin walls compared with older cats. As cats age, the dentin walls thicken, resulting in greater tooth density with a yellow, tan or ‘off-white’ appearance. Elderly cats occasionally develop sclerotic dentin and pulp chamber shrinkage, which may result in a glassy or transparent appearance to the teeth (Figure 7).50

Figure 6 Lenticular sclerosis in an aging cat. Courtesy of David A Wilkie

Figure 7 Partially transparent dentin covering the maxillary fourth premolar of a 14-year-old domestic shorthair cat. Courtesy of Jan Bellows
Plaque biofilm attaches continuously on the crowns of feline teeth unless mechanically or chemically removed. Calcium and phosphorus in the saliva mineralize the plaque to produce calculus. It is common to find minimal plaque and calculus on healthy aged feline teeth. In some cats, the plaque irritates the gingiva, allowing pathogenic gram-negative bacteria (*Porphyromonas* species, *Prevotella* species, *Peptostreptococcus* species, *Fusobacterium* species) to survive subgingivally. By-products of these bacteria stimulate the host’s immune system to release cytokines and prostaglandins that weaken and destroy the tooth’s supporting tissues, resulting in oropharyngeal inflammation. The progression of periodontal disease depends on the complex regulatory interaction between bacteria and immune modulators of the host response.

Breed type is a significant risk factor for oral disease in cats. Clinically, the aged domestic shorthair cat may have a healthy mouth with little plaque and calculus accumulation, while brachycephalic cats (e.g., Persian, Himalayan) may present with a greater accumulation of plaque and resulting oropharyngeal inflammation caused by tooth crowding.

According to the Banfield Pet Hospital State of Pet Health 2011 Report, 68% of cats over 3 years of age are affected by dental disease. Increasing age also positively correlates with the severity of periodontal disease as measured by the intensity of gingival inflammation, quantity of calculus deposited, and the degree of bone resorption and tooth mobility.

**It is common to find minimal plaque and calculus on healthy aged feline teeth, though breed is a risk factor for oral disease in cats.**

**Gastrointestinal health**

A number of progressive physiologic changes involving the gastrointestinal (GI) system are appreciated in aging humans. This is despite the tremendous physiologic reserve supporting food digestion, and nutrient absorption and metabolism, which minimizes the clinical effects of many age-related changes until they are considerable. Although relatively few feline studies have focused on anatomic or functional changes, similar effects of aging may occur in cats.

Appetite can be reduced in aging cats because of many factors, including common dental issues that can result in pain, altered taste or olfaction, or compromised ability to prehend, masticate or swallow (see also ‘oral and gingival health’ above). Other possible contributing factors, based on what is known in humans, are outlined in the box below.

Morphologic and functional esophageal studies have disclosed neuronal loss and reduced amplitude of peristaltic waves in geriatric humans. Even in apparently healthy geriatric humans, inverse correlations between age, esophageal sphincter pressures, and amplitude and velocity of peristaltic esophageal waves have been shown. It is anticipated that similar changes occur in geriatric cats. These changes decrease clearance of esophageal contents and predispose to the dysphagia and gastroesophageal reflux that may be provoked by non-digestive disorders.

Reduced nutrient digestibility in humans, and also confirmed in cats (see below), associated with aging may be the result of alterations in bile composition, reduced pancreatic enzyme availability, delayed gastric emptying or altered enteric transit. Rapid transit times can lead to maldigestive malabsorption, while slower transit can promote bacterial overgrowth and stool dehydration and predispose to constipation. Numerous studies in humans and senescent rodents suggest that the number of enteric neurons declines in nearly all regions of the GI tract during ‘normal’ aging.

Possible contributors to appetite decline

In humans, age-related alterations in the density and size of taste buds influence appetite, and over a lifetime there is continuous damage to the nasal epithelium, culminating in loss of olfactory receptors. Atrophy or thinning of the oral mucosa associated with aging can make the oral cavity more susceptible to dehydration and reduce tissue resilience to masticatory trauma. Finally, reduced salivary flow rate has been reported in elderly humans, and can reduce the effectiveness of mastication and predigestion of food and influence taste and appetite.

Such changes have not been documented to the authors’ knowledge in cats, but they may potentially contribute to the variable appetite noted in otherwise healthy aging cats.

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These degenerative losses involve both the myenteric and submucosal plexus, are slowly progressive and correlate with altered function (motility, coordinated contractions). A study in healthy young and senior (11.6 ± 1.4 years) female cats revealed a trend for slower GI transit in the senior cats, with far more variability among individuals than observed in the young cats. Indeed, a large clinical study of apparently healthy geriatric and young humans showed that only colonic transit was significantly influenced by age. These findings support the proclivity for chronic constipation that has long been recognized as clinically important in aging cats. Dehydration undoubtedly also plays a role in this problem.

Advanced age is known to alter physiologic control systems regulating thirst and satiety (Figure 8), and homeostatic mechanisms controlling hydration. Although geriatric humans may consume adequate fluids on a daily basis in controlled environments, they may experience decreased thirst sensation and consequently a reduced fluid intake when challenged by fluid deprivation, a hyperosmotic stimulus or exercise in warm/humid conditions. Studies show that full restoration of fluid balance is slower compared with younger individuals. Similar responses may exist in aging cats, explaining their risk for constipation when challenged with dry coarse foods, limited exercise or illnesses leading to dehydration.

Studies suggest that aging can influence digestibility of energy and other nutrients in cats. Although results among studies are inconsistent, lower apparent digestibility values for protein, fat, carbohydrate and energy in older vs younger cats have been detected. Greatest inter-individual variability was also found in old cats (13.3 ± 0.6 years) compared with younger age groups. Collectively, these studies suggest that age-related changes in digestion or absorption occur, but are variable among cats. The inter-individual variability is not surprising because differences between chronologic and physiologic aging are well recognized in other species and likely exist in cats.

Studies in multiple species have suggested age-related changes in enteric microbiota, and cats are no exception (see box below). The reported reduction in bifidobacteria by Jia et al may confound the GI signs related to the changes in digestion and absorption and the propensity for constipation in older cats. This work indicates that future studies should investigate microbial changes at the family level, rather than genus or species level, in order to determine whether alterations in microbiota could also impact feline weight or metabolism. Age-related change in hepatobiliary function has been detected in humans and some other animals, but not confirmed in cats. One change that has been documented in older cats, however, is accumulation of lipofuscin in hepatocytes. Lipofuscin, often called age pigment, is considered a hallmark of aging, with accumulation inversely related to longevity. Pathophysiologic mechanisms associated with lipofuscin accumulation include age-related oxidative stress and reduced ability to eliminate reactive oxygen intermediates. It is not clear, however, whether this histologic finding correlates with an age-related, clinically significant change in hepatic function in older cats.

**Age-related changes in enteric microbiota**

A study of geriatric cats revealed that the predominant fecal bacteria included Actinobacteria (ie, *Bifidobacterium* species, Coriobacteriaceae) and Firmicutes (ie, *Clostridium* species, *Eubacterium* species, lactic acid bacteria), similar to findings in investigations of healthy kittens and adult cats. However, the *Bifidobacterium* population has been reported to be significantly lower in older cats, and one study documented large variations in samples acquired from the same animals. Patil et al reported that, compared with young and adult cats (1–9 years), elderly cats (9–14 years) had significantly lower concentrations of bifidobacteria and higher concentrations of *Clostridium perfringens*. The reduction in bifidobacteria can be attenuated through dietary interventions such as changes to form (wet vs dry) or specific nutrient levels (fat, docosahexaenoic acid, vitamin E, methionine).
Cardiac health

Disorders of the cardiovascular system are among the most commonly encountered disease entities in aging cats.75,76 Similar to dogs and humans, normal vascular changes including increased calcium deposition within the aorta and peripheral arteries occur with advancing age;77 although cats tend to develop fibrosis of the intima rather than atherosclerosis. Accordingly, there is appropriate concern for the stress that this might place on the aging feline heart. Routine monitoring of systolic blood pressure (SBP) is recommended as part of the geriatric health screening process for feline patients over 8 years of age (Figure 9), even when underlying causes for hypertension (eg, chronic renal disease, hyperthyroidism) are not suspected. There is published evidence to show a trend towards higher SBP as feline patients age (see box below); systemic hypertension, however, does not appear to be a normal age-associated finding. Auscultatory findings suggestive of underlying cardiac disease in a feline patient include murmurs, gallop rhythms and arrhythmias. Multiple studies in apparently healthy cats and cats with cardiomyopathy have repeatedly shown, however, that cardiac auscultation is insensitive for detecting underlying cardiac disease. As these studies have revealed, heart murmurs are commonly auscultated in older feline patients on routine physical examination, despite there being no evidence of underlying heart disease on subsequent echocardiographic investigation.81-84 Many of these patients appear to develop a murmur as a result of stress and anxiety producing increased blood flow through the right ventricular outflow tract. Thus, while a murmur in an older cat should not be ignored, many of these patients have physiologic murmurs that are not caused by underlying cardiac pathology.

Auscultation of an arrhythmia in an older feline patient is not as common as a murmur, and, likewise, this finding does not necessarily indicate underlying heart disease. Previous studies of healthy feline patients have shown that cats over 6 years of age have extrasystolic rhythms (atrial premature and ventricular premature complexes) recorded and auscultated more commonly than younger cats.85,86 Results of 24 h Holter monitoring tests have confirmed that healthy older cats commonly have ventricular premature complexes.85,86

A gallop rhythm is a dysrhythmia that occurs when there is reduced compliance of the left ventricle during either early or late ventricular diastolic filling. Although gallop rhythms are auscultated in many cats with myocardial disease, it is also noteworthy that older feline patients (>10 years of age) may occasionally have a gallop rhythm that is related to an aging, stiff ventricle, in the absence of significant cardiovascular disease. Reduced ventricular compliance and delayed relaxation of the left ventricle is a frequent finding in human geriatric patients,87 while no studies specifically looking at diastolic function in geriatric cats have been published, similar changes appear to occur commonly.

Therefore, a murmur, arrhythmia or gallop rhythm does not necessarily indicate underlying heart disease and may be an age-associated change. In cats with abnormal auscultatory findings, an echocardiogram is recommended to rule out an underlying morphologic problem. In the event of a normal echocardiogram, a gallop rhythm is still

Age-related changes in systolic blood pressure

One study of 203 apparently healthy cats assessed using an oscillometric technique in conjunction with a tail cuff noted increased blood pressure after 11 years of age.78 Another study in 50 healthy adult cats of various ages (range 1.5-16 years) with blood pressure assessed by the more widely used technique of Doppler ultrasonic sphygmomanometry found no significant correlation between SBP and age.79 A more recent and larger study of 100 apparently healthy cats, 6 years of age and older, assessed blood pressure by Doppler and showed an SBP of 133.6 ± 21.5 mmHg for the group as an average.80 When this same population of cats was divided into different age groups, middle-aged cats (6-10 years) had an SBP of 128.3 ± 16.7 mmHg, while cats >10 years of age had an SBP of 140.4 ± 25.0 mmHg.

There is a trend towards higher systolic blood pressure as feline patients age.
clinically relevant, as age-associated changes in diastolic filling (rather than heart disease) may make these patients more sensitive to volume overload during intravenous fluid administration. A recent study evaluated sleeping and resting respiratory rates in healthy cats and cats with subclinical heart disease and determined that cats with multiple or mean sleeping respiratory rate measurements >30 breaths/minute likely warrant additional evaluation.

The most common cardiac disease in cats over 6 years of age is hypertrophic cardiomyopathy (HCM). Because this is a disease that causes concentric hypertrophy, thoracic radiographs are not very helpful in assessing whether the auscultatory findings are caused by physiologic murmurs or underlying cardiac pathology. One of the newer methods of screening for heart disease in both human and veterinary medicine involves use of cardiac biomarkers, specifically N-terminal pro-brain natriuretic peptide (NT-proBNP). Increased NT-proBNP levels in older human patients are confounded by several aging-related physiologic changes, including reduction in body mass and kidney function, and anemia. Thus, until the effect of aging on NT-proBNP in feline patients is specifically studied, interpretation of this test may be challenging in the geriatric cat population.

Echocardiography is considered the ‘gold standard’ for diagnosing and staging feline cardiac disease. Although there are many different phenotypes of HCM, one particular pattern of hypertrophy is often seen in feline patients >10 years of age and is felt to represent an age-associated change, as opposed to actual underlying HCM. Many geriatric cats (with or without auscultatory abnormalities) have a focal area of thickening at the level of the left ventricular outflow tract. When following these patients longitudinally, there does not appear to be progression of the echographic change. The authors believe that this small septal bulge is likely related to the change in the angulation of the aortic root (which also occurs in geriatric human patients), rather than disease.

Respiratory health

Although aging changes in the respiratory health of geriatric humans have been well characterized, less is known about respiratory changes in old cats. In older humans, age-related changes include a decline in pulmonary elasticity, respiratory muscle strength and chest wall compliance. Alterations in immune function, in pulmonary beta-adrenoceptors and in airway reactivity associated with aging have also been described.

One study compared radiographic patterns and airway reactivity between groups of young (1–2 years) and senior (12–13 years) clinically healthy cats. A significantly higher proportion of senior cats showed broncho-interstitial patterns on radiography when compared with the young cats. The presence of this pattern radiographically in older feline patients is thus believed to be a normal aging change (Figure 10). Additionally, airway reactivity appears to be decreased in older cats, as suggested by the finding that naturally occurring asthma is typically reported in young to middle-aged cats, and not in elderly cats.

Renal/urinary health

Aging is a commonly associated risk factor for the development of chronic kidney disease (CKD) in cats. The reported prevalence of CKD in older feline populations varies, ranging from 28% in cats >12 years up to 80.9% in cats aged 15–20 years. IRIS staging in a randomly selected population showed a CKD prevalence of 50% in cats up to 20 years of age, with 27.9% of affected cats in stage 1 disease, 65.1% in stage 2, 7.0% in stage 3 and 0% in stage 4. This same study found a higher prevalence of CKD (68.8%) in a population of cats with DJD, with the majority of affected cats being in stage 2 (65.9%). In both the randomly selected and DJD populations, the prevalence of CKD was similar in cats up to 14.9 years, but it significantly increased after 15 years of age. In both populations, the most advanced stage seen (stage 3) was limited to cats ≥10 years. The prevalence rates in this study were higher than previously reported, but this may partially be due to the inclusion of earlier stages of CKD than in previous
reports. The underlying association between CKD and DJD is not known, but warrants further investigation to elucidate possible common immune and inflammatory mechanisms.

Among aged cats with CKD, tubulointerstitial fibrosis is the most prevalent pathology, with glomerular disease secondary to neoplasia or infectious disease seen less commonly.

One study evaluating a population of cats with CKD found older cats (>7 years) to be over-represented (52.9%) compared with the total older cat hospital population (12.7%). Morphologic diagnoses included chronic tubulointerstitial nephritis (52.7%), renal lymphoma (16.2%), renal amyloidosis (9.5%), chronic pyelonephritis (9.5%), chronic glomerulonephritis (8.1%), polycystic renal disease (2.7%) and pyogranulomatous nephritis secondary to feline infectious peritonitis (1.3%). Infectious and familial causes were more commonly seen in younger cats, while non-specific causes were more commonly seen in the older population. Another study evaluating an older population of cats (>9 years) showed a correlation between interstitial inflammation and fibrosis scores, suggesting that non-specific tubulointerstitial lesions could represent a slowly progressing inflammatory process resulting in eventual fibrosis. 

While the inciting cause for non-specific tubular inflammation and fibrosis has yet to be identified, it has been suggested that these changes could represent a survival-driven adaptive process. In an evaluation of 676 adult colony cats, cats that died of tubulointerstitial renal disease (38% of the population) lived significantly longer (11.67 years) than those that died from other causes (10.0 years). Glomerular changes occurred less frequently (11% of the population), and cats with glomerular changes died at a younger age (9.96 years), compared with those without glomerular changes (12.23 years). Of the cats that died of non-renal causes, life span was greater when histological renal changes were present. Based on these findings, the investigators hypothesized that age-associated renal changes may be a defensive, life-preserving adaptation. Additional research in this area is needed to understand the association between renal changes and age, and the impact or association with other disease processes over time.

There is a significant increase in SBP with increasing age in cats with CKD. When compared with cats with CKD, healthy controls had a lower risk (hazard ratio 0.2) of developing hypertension. The investigators of this study defined hypertension in cats as SBP ⩾ 170 mmHg on two consecutive visits, or SBP ⩾ 160 mmHg with concurrent evidence of hypertensive retinopathy or choroidopathy.

It has been suggested that non-specific tubular inflammation and fibrosis in aged cats could represent a survival-driven adaptive process.
Endocrine health

At the present time, there is very little information about normal age-associated changes of the endocrine system of cats. Unlike their canine counterparts, there are no published studies showing alterations in adrenal responsiveness. Pituitary, reproductive and thyroid hormones, renin, angiotensin and aldosterone concentrations, and pancreatic, hepatic, renal and GI hormone levels have likewise not been evaluated longitudinally in the healthy cat.

One paper, as well as unpublished work carried out in a private clinical diagnostic laboratory (Central Lab for Veterinarians, Langley, Canada), establishing regional age-group reference intervals, showed that thyroxine (total T4) levels are low in kittens, are maintained at adult levels between 1 and 5 years of age, and increase mildly above 5 years of age (S Lester, 2013, personal communication). Studies are lacking to verify whether a gradual increase in total T4 levels is normal in cats >10 years of age; however, this may contribute to the common finding of weight loss in cats >12 years of age.

There are two studies evaluating age and glucose regulation in cats. When adjusted for body weight, there was no difference in insulin sensitivity between young (0.8–2.3 years) and mature (4.0–7.0 years) cats. Body weight gain was more likely than feeding a dry-type diet to induce insulin resistance and dysfunctional secretion. Similarly, the second study found that diet had little effect on metabolic parameters. These data suggest that aging may predispose cats to insulin resistance, contributing to the risk of development of diabetes in older cats, especially if they are obese.

Hypertension is seen commonly in older cats. Age-related changes in blood pressure may be normal; however, as mentioned earlier, studies present contradictory results. There are numerous endocrine mechanisms implicated in the development of hypertension, many of which are related to disease (e.g., hyperthyroidism, CKD, hyperaldosteronism). Because hypertension is associated with so many pathologies of the older cat, blood pressure measurement should be incorporated into the examination of all older cats.

Table 2: Immunosenescence and inflamming in cats

<table>
<thead>
<tr>
<th>Reported age-related changes</th>
<th>Mean age or age range (years) ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower total WBC, lymphocyte and eosinophil counts; lower T cells, B cells and NK cells</td>
<td>10–14</td>
</tr>
<tr>
<td>Decreased mitogen response to Con A and PHA</td>
<td>9.92 ± 0.89; 10–14; 10–14</td>
</tr>
<tr>
<td>Decreased delayed-type hypersensitivity response to sRBC</td>
<td>9.92 ± 0.89</td>
</tr>
<tr>
<td>Decreased antibody response to sRBC</td>
<td>No range</td>
</tr>
<tr>
<td>Reduced blood CD4+ T cells</td>
<td>10–14</td>
</tr>
<tr>
<td>Reduced blood CD8+ T cells</td>
<td>10–14</td>
</tr>
<tr>
<td>Increased serum immunoglobulins IgA and IgM</td>
<td>10–14</td>
</tr>
<tr>
<td>Increased monocyte production of proinflammatory cytokine (IL-1β, IL-6, IL-12 p40) mRNA</td>
<td>8–10</td>
</tr>
</tbody>
</table>

Con A = concanavalin A; NK = natural killer; PHA = phytohemagglutinin; sRBC = sheep red blood cells; WBC = white blood cells
## Acknowledgements

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## KEY POINTS

- Considerable changes occur in virtually every body system of the cat with advancing age.
- Some of these changes can greatly affect the health and wellbeing of the cat and have a tremendous impact on the owner, both from the standpoint of the pet-owner relationship and the cost of management.
- An appreciation of normal aging in cats is critical from both a clinical and research perspective. In this regard, it is imperative to be able to distinguish between what would be considered ‘normal for age’ vs unhealthy aging changes.
- Importantly, this distinction would impact clinical management of the aging cat in that the aggressiveness of the approach could be adjusted based on normal aging expectations.
- Research efforts in cats could be focused on evaluating the effect of intervention on either a normal aging cat or disease processes.
- This article has reviewed systems-based, age-related changes and considerations regarding health vs disease as an initial step toward defining healthy aging in the cat. Additional effort will be needed to define the clinical assessments required to determine healthy aging vs disease within each of the systems reviewed.

## Conflict of interest

JB, SC, AHE, DFH, BDXL and MS all were paid for their contributions by Procter & Gamble Pet Care. LD, EAF, AL, SP and AKS have financial and personal interest in the Procter & Gamble Company; LD and EAF were employees of the company at the time of coauthoring this review. SP is an employee of Royal Canin, Mars Incorporated.

## References


## Additional Studies

Additional studies are needed to better understand the clinical implications of immunosenescence and inflammaging within aged feline patients and how these processes influence the response to infectious and inflammatory conditions.

## Immunosenescence

When compared with their younger counterparts (2.65 ± 0.02 years), older cats (9.92 ± 0.89 years) have been shown to have a suppressed lymphocyte blastogenic response to concanavalin A (Con A) and phytohemagglutinin (PHA). Further studies have demonstrated similar suppressed lymphocytic response to Con A and PHA mitogens in older cats (10–14 years) compared with younger controls, with an age-associated decline in CD4+ and CD5+ T cells. In addition to the reduced mitogenic response, older cats were also observed to have a lower delayed type hypersensitivity response to sheep red blood cells (sRBC) when compared with younger controls. The same research group additionally reported lower antibody titers to sRBC in aged cats compared with younger controls (unpublished data).

## Inflammaging

One study evaluating the transcription of cytokine genes within cultured monocytes of cats (15 months to 10 years) demonstrated increased production of proinflammatory cytokine mRNA (IL-1, IL-6, IL-12 p40) in both younger and older cats compared with middle-aged cats. This same study also showed a trend toward a progressive decline in IL-10 mRNA transcription with age.


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