

FELINE health topics

for veterinarians

JAN 20 2005

CONSIDERING OLDER CATS*

Page 1

COGNITIVE DYSFUNCTION SYNDROME*

Page 6

UPCOMING MEETINGS

- January 11, 2005
- March 13-15, 2005

Page 8

*Adapted with permission from the proceedings of the 16th Annual Fred Scott Feline Symposium held at Cornell on July 30-August 1, 2004

Considering Older Cats

Daniëlle Gunn-Moore, BVMS, PhD, MRCVS, RCVS
University of Edinburgh, Scotland

There are now more elderly pet cats than ever before. Cats are more popular than dogs as pets, and improvements in nutrition, health care and management have lead to many cats living to increasingly greater ages. In the United States of America, over the last 10 years, there has been a nearly two-fold increase in the percentage of pet cats of over 6 years of age (from 24 percent to 47 percent), a 15 percent increase in cats over 10 years of age, and the proportion of the feline population aged 15 years or older has increased from 5 percent to 14 percent.¹⁻³ While less data are available for cats in Europe, the average age has increased from 4.7 to 5.3 years and it is estimated that there are currently ~2.5 million 'senior' cats in the United Kingdom. Since this accounts for ~30 percent of the pet cat population the good management of these individuals is becoming an ever more important consideration for small animal veterinary practitioners and nutritionists.⁴⁻⁵

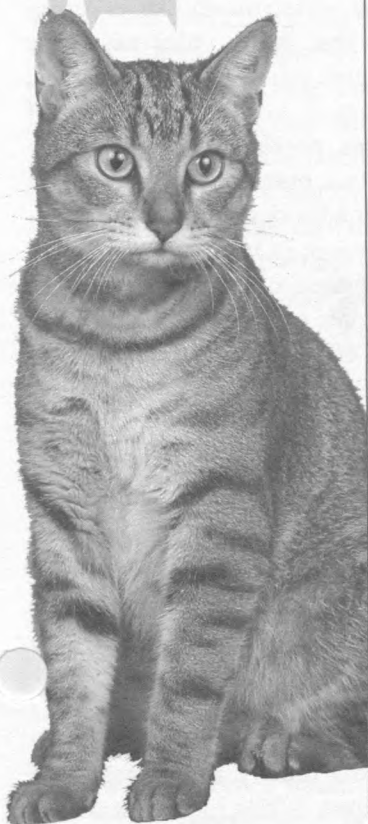
Defining the Age of Senior and Geriatric Cats

In order to determine the best ways to care for our older cats we first need to decide at what age a cat becomes 'senior,' and then at what age it becomes 'geriatric.' However, cats, like people, do not age consistently and chronological age does not always match physiological age. Some cats show obvious signs of old age after 10 years, while others appear almost unchanged until they reach 15-16 years. That said, it is gen-

erally considered that cats become 'senior' at about 7-8 years of age and progress to 'geriatric' by 12-15 years. Interestingly, some authors recommend that longer-lived breeds, such as Siamese, should be considered as 'senior' when they reach 11-12 years, while shorter-lived breeds, such as the Persian, may become 'senior' by 6-7 years. Table 1 shows the approximate correlation between cat and human ages.

It is only by understanding how cats change with age that we can try to care for them in ways that best support a long and healthy life. To do this we need to know how their advancing age is affecting their bodies. Some changes are obvious, like whitening of hair, general decline in body and coat condition, and failing senses (sight and hearing). However, other changes are less obvious, and these include alterations in the physiology of the digestive tract, immune system, kidneys, liver, brain, and skeleton. Thankfully, there are now an increasing number of studies investigating the effects of aging in cats, so we no longer need to rely on extrapolation from other species.

All aspects of a cat's life may affect its potential longevity and overall quality of life. However, perhaps the most important concepts to understand involve the complex interplay between concurrent physiological and pathological changes and how these affect the older cat's ability to maintain its body weight, accommodate to changes in its environment, fight off infection, and cope with disease. A number of these interacting factors will be discussed below.



Changes in Body Weight

Older animals often experience changes in their body weight. It is recommended that owners keep a regular record of their cat's weight and that this is checked at each clinic visit. This is because significant and/or rapid weight change can have very serious implications, irrespective of the underlying cause.

Until recently, it was assumed that older cats, like dogs and humans, have a significantly reduced energy requirement, and therefore a tendency toward obesity. Indeed, a slight trend towards a decreased maintenance energy rate (MER) has been shown in

cats of up to 10 years of age. However, there is also increasing evidence that there is a much greater tendency for geriatric cats (over 10 years of age) to be underweight.⁶⁻⁹ (See Table 2). The difference in the risk of mid-life obesity between cats and dogs probably results from their differing lifestyles. Dogs tend to be energetic when young, then slow down as they age. In contrast, cats are relatively inactive throughout most of their lives. It is probably because of this that they do not show a significant age-related decline in either MER or lean body mass to fat ratio.^{7,10,11}

Ideally, cats should be fed to maintain their optimal body weight, and probably the single most important aspect to feeding older cats is that their body weight should remain stable. Long-term studies have shown that neither obesity or excessive thinness increases mortality.⁸ While obesity itself reduces life span, it also increases the risk of many weight-related diseases, including heart disease, diabetes mellitus (DM), lameness (often due to arthritis), liver disease (e.g., hepatic lipidosis), and skin problems.¹²

Many older cats experience weight loss which can result from a number of different, often interacting, factors. These may include physiological aging changes, the presence of pathological disease processes, or behavioral alterations. Weight loss is often associated with inappetence and in older cats this commonly results from reduced senses of smell and taste, and/or oral pain associated with periodontal disease.¹³ In addition, older cats tend to be less efficient at digesting their food. This probably results from reduced intestinal function, gastric acid production, gastric and intestinal motility, and intestinal blood flow.^{14,15} Older cats may also have reduced pancreatic lipase activity and changes in the composition of bile.¹⁶ While these factors affect the digestion of all dietary components they

particularly affect the digestion and absorption of fats and proteins.^{9,16} There is a striking reduction in the apparent energy digestibility coefficients as cats age. These coefficients give an indication of how much benefit a cat derives from its food. In cats of less than seven years the coefficients range from 0.8-0.9. However, they can be reduced to as low as 0.65 in some older cats.⁹ Most cats will compensate for this by increasing their daily food intake. However, some individuals may need to increase their intake by as much as 25 percent.⁹ Due to the limitation of their stomach capacity this means that they need to eat many small meals a day. Weight loss is likely to result when more frequent meals are not offered or when eating is painful. To compensate for this many older cats may benefit from being fed a highly palatable, highly digestible, energy dense food and that it is offered in small amounts frequently.

Many of the specific nutrient requirements for older cats have still not been determined. It is often assumed that many older cats have some degree of sub-clinical disease, particularly of the kidneys. Because of this it has previously been recommended that older cats should be fed diets with a moderate protein restriction. However, in view of our current understanding of the high protein requirements of cats and the reduced digestive efficiency of old age, it is now felt that inappropriate restriction of dietary protein may risk the development of protein malnutrition. That is, of course, unless the cat has evidence of chronic renal insufficiency (CRI) when it is likely to benefit from moderate protein restriction, moderate phosphorus restriction, and potassium supplementation.¹⁷

Many compounds are currently being studied for their potential to improve the quality and duration of our cats' lives. While more research is



The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats every-

where by developing methods to prevent or cure feline diseases, and by providing continuing education to veterinarians and cat owners. All contributions are tax-deductible.

Director:

James R. Richards, D.V.M.

Veterinary Consultants:

Christine Bellezza, D.V.M.

Paul Maza, D.V.M.

Carolyn McDaniel, V.M.D.

Administrator:

Michael Lenetsky

Administrative Assistants:

Kathleen Mospan

Donald Personius

Pamela Sackett

Sheryl Thomas

Phone: (607) 253-3414

Consultation: 1-800-KITTYDR

Web: www.vet.cornell.edu/FHC

©2004 by Cornell University on behalf of the Cornell Feline Health Center, College of Veterinary Medicine, Ithaca, NY 14853.

All rights reserved. Permission to reprint selected portions must be obtained in writing. Cornell University is an equal opportunity, affirmative action educator and employer.

needed to determine the extent of any potentially positive effects, suggested compounds include increased levels of antioxidants and free-radical scavengers (e.g., glutathione, vitamins A, C, and E, taurine, carotenoids, and selenium), green-lipped mussel extract, various combinations of essential fatty acids, and many more.

Significant weight changes should always be investigated because weight loss is often the first sign of disease. Interestingly, while many of the diseases seen in older cats are associated with inappetence and a reluctance to eat, this is clearly not always the case. With hyperthyroidism and some of the mal-assimilation syndromes (e.g., inflammatory bowel disease, or early stage gastrointestinal lymphocytic lymphoma) weight loss may be accompanied by a good or even increased appetite. Therefore, owners need to know that any alteration in appetite—be it an increase or a decrease—can be significant.

Changes in Environment

Unfortunately, older cats often cope very poorly with changes in their daily routine. Their response to stress is often to stop eating, hide, and/or alter their toileting habits. Any change within the environment, the family, or even the diet can act as a source of stress. Because a diet change can, in itself, be stressful, it is important to make changes slowly, gradually introducing the new food in a separate bowl, while keeping the old food available. Unfortunately, in some very easily stressed cats diet changes cannot always be made. Because many older cats experience difficulty coping with alterations in their environment it is important to consider this when planning changes. Where possible these should be kept to a minimum, and when they have to be made they should be made slowly and with much reassurance. Some geriatric cats become progressively senile. These cats may benefit from having their area of

access reduced, while still containing all necessary facilities. This small area can then be kept safe and constant.

Sensitivity to Thirst

As cats age they have reduced sensitivity to thirst. This results in an increased risk of dehydration, especially when combined with excessive urination. The latter is commonly associated with either concurrent CRI or DM, and both of these conditions occur commonly in older cats. It is often advisable to feed older cats a diet with high water content. However, if cats are unwilling to eat wet food, then it may be helpful to try to increase their fluid intake using other methods. Drinking can be encouraged by ensuring constant access to water, using bottled water or pet water-fountains, or by giving fishy water or chicken/meat stock (ensure that no onion or onion powder has been added as cats can develop hemolytic anemia if fed too much onion).

Changes in Immune Function

The immune function of all mammals deteriorates with age. While there are only a few studies looking specifically at the effects of aging on the immune system of cats, these studies do appear to confirm that this is the case. Older cats have significantly lower numbers of total white blood cells (particularly CD4+ lymphocytes), while neutrophil counts are raised.¹⁹ These changes are likely to result in a reduced ability to fight infection or to screen for neoplastic cells. This may explain the increased risk of neoplasia in older cats. While studies are still at a very early stage, a number of dietary components are being investigated for their potential to support or even improve the immune function of older animals (e.g., vitamins A and E, selenium, zinc, magnesium, and co-enzyme Q10).²⁰⁻²³

The age-related risk of infection can perhaps best be demonstrated by looking at the age-related incidence of bacterial cystitis. Clinical signs suggestive

Table 1: Shows the approximate age correlation between cats and humans

Cat's Age	Approximate Human Equivalent
1	16
2	21
3	25*
4	29
5	33
6	37
Senior Cat's	
7	41
8	45
9	49
10	53
11	57
Geriatric Cat's	
12	61
13	65
14	69
15	73

*From then add 4 years for every year

of bladder disease include increased frequency of urination, straining to urinate, blood in the urine, or a blocked urinary tract. In cats under 10 years of age a bacterial cause is found in only 1-2 percent of cases.^{24,25} In the majority of these young cats no obvious cause can be found (although stress and diet may play a role), and some are found to have bladder stones. However, the situation in older cats with cystitis is very different, with almost 50 percent of cats over 10 years of age having a bacterial cause for their bladder inflammation.^{26,27} Some of

these infections are related to the general immune senescence associated with age. However, the majority are associated with CRI or DM, both of which are diseases that occur commonly in older cats and which are, in themselves, both locally and systemically immunosuppressive.

Chronic Renal Insufficiency

Older animals are susceptible to many diseases and diet has a role to play in the cause and/or management of many of them. Veterinary surgeons typically list the most common as kidney disease, hyperthyroidism, neoplasia, dental disease, diabetes mellitus, and arthritis. Arguably, the most significant of these is renal failure.

Advancing age has many ways of damaging cats' kidneys. Some of the factors include a tendency towards mild dehydration, an increased risk of infection (pyelonephritis or interstitial nephritis), and an increased risk of acute renal failure secondary to the administration of certain drugs. It is therefore not surprising that acute and chronic renal failure are both seen very commonly in older cats. However, these are not the only causes of renal failure and we now know that there are a number of dietary factors that can also be detrimental to kidney function. These include over-acidification of the diet, the addition of extra salt, the inclusion of high levels of ash, or the addition of too little potassium.²⁸⁻³¹ The presence of any of these factors can result in kidney failure, especially when fed to older cats. Interestingly, some of these factors are often included in diets that are marketed to help reduce the risk of struvite urolithiasis. Diets that are designed for this purpose should not therefore be fed to older cats. (That is, of course, unless a specific diagnosis of struvite urolithiasis has been made). Interestingly, while both struvite and oxalate uroliths are found quite commonly in younger cats, oxalate uroliths are seen most fre-

quently in older cats. This probably reflects the fact that older cats have significantly lower blood and urine pH levels, and this reduces the risk of struvite urolithiasis while increasing the risk of oxalate urolithiasis.²⁸ While we do know of some of the nutritional factors that are detrimental to kidney function, we are a long way from defining a diet that actually preserves it.

The Importance of Arthritis

Interestingly, most owners list the diseases that they see in their older cats in a different order to the list generated by veterinary surgeons. At the top of the list is arthritis, and this is followed by kidney failure, deafness, blindness, hyperthyroidism, bronchitis, and dental problems.³² The role of arthritic pain in reducing the quality of life for many older cats has probably been significantly underestimated. Many owners report having to adjust their house to assist their older cats; moving food and water bowls to lower surfaces, adding ramps to allow easier access to favored sleeping areas, and placing low-sided litter boxes within easy cat reach. The increasing importance of arthritis in our older cats is supported by finding radiographic evidence of degenerative joint disease in 90 percent of cats over 12 years of age.³³ The cause of arthritis is usually multi-factorial; trauma, diet (obesity), and genetics all play a role. Recognizing and addressing these causes, and presence of arthritis, can make a considerable difference to the quality of an older cat's life. While there is a clear role for diet and, in particular, for obesity in the cause of arthritis, a positive role of specific nutrients is still unclear. That said, the potential anti-arthritic properties of a number of different nutritional compounds are currently being studied (e.g., green-lipped mussels and various sources of chondroitin sulphate).

Senior Health Care Clinics

Many older cats develop clinical illness

and the diagnosis and treatment are often complicated by the concurrence of multiple interacting disease processes. Prompt and full investigation is essential if treatment is to be successful. Unfortunately, it is not always easy for owners to recognize the signs of ill health so it is important that they monitor their older cats for changes in food and water consumption, body weight, production of urine and feces, and behavior. The implementation of senior health care clinics by primary care veterinary practices can be very beneficial. While the clinics do need to be tailored to individual cats, in general they should include regular and thorough physical examinations (including assessment of body weight, systolic blood pressure, and retinal examination). In addition, a blood sample is usually collected for biochemical screening, thyroid level assessment and hematology and, where appropriate, serological testing for FeLV and/or FIV. A urine sample should undergo routine urinalysis, urine protein to creatinine ratio and, where possible, bacterial culture. Initially, most cats will only need to attend a clinic on a yearly basis. However, those cats showing significant aging changes may need to attend more frequently for repeated reassessment, monitoring, and treatment.

Changes in Physiology

Once disease has been diagnosed it is important to remember that changes in physiology also affect the pharmacokinetics of many drugs. Most drugs need to be metabolized in some way, and most drug metabolism occurs in the liver and/or kidneys. Liver disease, low levels of blood albumin (which binds to many drugs), and CRI all occur frequently in older cats. When coupled with mild dehydration (which is common in older cats) these can result in reduced clearance rates and marked elevations in circulating drug concentrations.⁹ When treating

geriatric patients the dose and dosing intervals of some drugs may therefore need to be altered. For example, the dose of metronidazole given for the treatment of suppurative cholangio-hepatitis may need to be significantly reduced while the dosing interval of aspirin given in the management of thrombosis associated with hypertrophic cardiomyopathy may need to be increased. However, it is not only drug overdose that needs to be considered. In humans, adverse drug reactions are two to three times more common in people over 60 years of age.²⁴ The situation is likely to be similar in cats, so we need to be observant when medicating our older cats.

Treat the Individual

While veterinary medicine can often

offer complex therapeutic options and sophisticated prescription diets it is important to remember that older cats are often poorly tolerant of the stress of hospitalization or excessive physical handling. It is essential that each cat be assessed and treated as an individual. In some cases investigations and interventions may have to be adapted or even abandoned if they are poorly tolerated for either medical or temperamental reasons. Also, once our patient's quality of life can no longer be maintained it is important that euthanasia be discussed and then performed as compassionately as possible.

While it is true to say that "old age is not a disease," it is important that we pay particular attention to our older cats, feed and care for them

Table 2: Shows the approximate correlation of cat age to body condition^{6,9}

Age of Cat	% too thin	% too fat
1-2 years	<10	20
2-10 years	<10	20-50
>12 years	30-50	<20

appropriately, and observe them closely so we can keep them well for as long as possible. 🐾

References

1. AAFP and AFM panel report of feline senior health care. (1999) Comp Cont Edu Small Anim Pract, June, 531-539.
2. Broussard JD, Peterson ME, Fox PR. (1995) Changes in clinical and laboratory findings in cats with hyperthyroidism from 1983 to 1993. JAVMA, 206(3):302-5.
3. Wolf A. (1995) BSAVA Pedigree Pet Foods Lecture Tour.
4. Morgan D. (2002) Comparative aspects of ageing. Vet Times, September, 11-12.
5. Venn A. (1992) Diets for geriatric patients. Vet Times, May issue.
6. Armstrong PJ, Lund EM. (1996) Changes in body composition and energy balance with ageing. Vet Clin Nut, 3:83-87.
7. Harper EJ. (1998) Changing perspectives on ageing and energy requirements: Ageing, bodyweight and body composition in humans, dogs and cats. J of Nut, 128:26275-26315.
8. Scarlett JM, Donoghue S, Saidla J, Wills J. (1994) Overweight cats: perspectives and risk factors. Int J of Obesity, 18: S22-S28.
9. Taylor EJ, Adams C, Neville R. (1995) Some nutritional aspects of ageing in dogs and cats. Proceedings of the Nutritional Society, 54:645-656.
10. Harper EJ. (1998b) Changing perspectives on ageing and energy requirements: Ageing, and energy intakes in humans, dogs and cats. J of Nut, 128:26235-26265.
11. Peachey SE, Harper EJ, Dawson JM. (1999) Effects of ageing on resting energy expenditure in cats. Vet Rec, 15:420.
12. Scarlett JM, Donoghue S. (1998) Associations between body condition and disease in cats. JAVMA, 212 (11):1725-1731.
13. Ingham KE, Gorrel C, Blackburn J, et al. (2001) Prevalence of feline odontoclastic resorptive lesions in a clinically healthy cat population. Proceedings of the Waltham International Symposium 'Pet Nutrition Comes of Age', Vancouver, Canada, August.
14. Polzin D, Osborne C, O'Brien T. Chapter 108. In: Ettinger S.J. ed. Textbook of Veterinary Internal Medicine. Philadelphia: W.B. Saunders, 1989:1962-2046.
15. Saltzman JR, Russell RM. (1995) Gastrointestinal function and ageing. In: Morley JE, Glick Z, Rubenstein LZ (eds) Geriatric nutrition, second edition, New York, Raven Press, pp183-189.
16. Harper EJ. (1998c) Changing perspectives on ageing and energy requirements: Ageing and digestive function in humans, dogs and cats. J of Nut, 128:26325-26355.
17. Elliott J, Rawlings JM, Markwell PJ, Barber PJ (2000) Survival of cats with naturally occurring chronic renal failure: effect of dietary management. J of Small Animal Practice, 41:235.
18. Campbell DJ, Rawlings JM, Koelsch S, et al. (2001) Age-related differences in leukocyte populations, lymphocyte subsets, and immunoglobulin (Ig) production in the cat. Proceedings of the Waltham International Symposium 'Pet Nutrition Comes of Age', Vancouver, Canada.
19. Chandra RK. (1992) Effect of vitamin and trace element supplementation on immune responses and infection in elderly subjects. Lancet, 340:1124-1127.
20. Han SN, and Meydani SM. (2000) Antioxidants, cytokines, and influenza infection in aged mice and elderly humans. J of Infectious Diseases, 182 (Suppl 1):S74-80.
21. Kubena KS, McMurray DN. (1996) Nutrition and the immune system: A review of nutrient-nutrient interactions. J of the American Diet Association, 96:1156-1164.
22. Roy M, Kiremidlian-Schumacher L, Wishe HJ, Cohen MW, Stotzky G. (1995) Supplementation with selenium restores age-related decline in immune cell function. Proceedings of the Society of Experimental Biology and Medicine, 209:369-375.
23. Schneider EL, Reed JD. (1985) Modulations of ageing processes: In Finch CE, Schneider EL (eds): Handbook of the Biology of Ageing, ed 2. New York, Van Nostrand Reinhold Co, pp45-76.
24. Buffington CAT, Chew DJ Kendall MS, DiBartola SP. (1997) Clinical evaluation of cats with non-obstructive lower urinary tract disease. JAVMA, 210:46-50.
25. Kruger JM, Osborne CA, Goyal SM, Wickstrom SL, Johnston GR, Fletcher TF, Brown PA. (1991) Clinical evaluation of cats with lower urinary tract disease. JAVMA, 199:211-216.
26. Bartges JW, Blanco L. (2001) Bacterial urinary tract infection in cats. Comp of Standard of Care, 3:1-5, 9.
27. Bartges JW (2002) What's new in feline LUTD? Proceedings of the European College of Veterinary Internal Medicine, Munich, Germany, 93-97.
28. Hawthorne A. (2002) Nutritional requirements of ageing dogs and cats. Waltham Focus, 12 (1 Special edition), 28-34.
29. Kirk C. (2002) Dietary salt and FLUTD: risk or benefit? Proceedings of the American College of Veterinary Internal Medicine, Dallas, USA, 553-555.
30. Hughes K, Slater M, Geller S, Burkholder W, Fitzgerald C. (2002) Diet and lifestyle variables as risk factors for chronic renal failure in pet cats. Preventative Veterinary Medicine, 55 (1), 1.
31. DiBartola SP, Buffington CA, Chew DJ, McLoughlin MA, Sparks RA. (1993) Development of chronic renal disease in cats fed a commercial diet. JAVMA, 202(5):744-751.
32. Halls V, personal communication, 2002.
33. Hardie E, Roe S, Martin F. (2002) Radiographic evidence of degenerative joint disease in geriatric cats (1994-1997). JAVMA, 220(5): 628-632.
34. Vestal RE, Dawson GW (1985) Pharmacology of ageing: In Finch CE, Schneider EL (eds): Handbook of the Biology of Ageing, ed 2. New York, Van Nostrand Reinhold Co, pp744-819.

Cognitive Dysfunction Syndrome: a Neurodegenerative Disease

Daniëlle Gunn-Moore, BVM&S, PhD, MRCVS, RCVS
University of Edinburgh, Scotland

With improvements in nutrition and veterinary medicine the life expectancy of pet cats and dogs is increasing. Accompanying this growing geriatric population there is an increasing number of pets with signs of apparent senility. It is generally accepted that cognitive and motor performance deteriorates with age, and experiments with cats have indicated that this deterioration usually occurs between 10-20 years of age. Recent studies suggest that 28 percent of pet cats aged 11-14 years develop at least one geriatric-onset behavior problem, and this increases to over 50 percent for cats of 15 years of age or older.

Cognitive dysfunction syndrome (CDS) is a neurodegenerative disease resulting in geriatric-onset behavioral problems. The clinical signs can include disorientation, altered interaction with the family, changes in sleep-wake cycles, changes in activity such as wandering and/or pacing, inappropriate urination/defecation, and/or inappropriate vocalization. Diagnosis is made on the basis of several altered cognitive signs. The cause of the syndrome in cats and dogs is still unknown. However, recent work points to the involvement of disease processes similar to those seen in humans suffering from neurodegenerative disorders, such as Alzheimer's disease (AD).

Histopathologically, there are two major hallmarks of AD; senile plaques and neurofibrillary tangles. Senile plaques (SP) are formed by the extracellular accumulation of the β -amyloid ($A\beta$) protein. Neurofibrillary tangles (NFT) are formed by the initially intracellular accumulation of the abnormally hyperphosphorylated form of the microtubule protein tau (in its unphosphorylated form tau is involved in forming the cytoskeleton of neurons). While there are a number

of theories suggesting how these deposits may be associated with neurological degeneration, it is currently believed that the accumulation of $A\beta$ into SP may initiate inflammatory change and neurotoxicity which then results in tau hyperphosphorylation, NFT formation and neurological dysfunction. In addition to $A\beta$ accumulation as SP it also accumulates around the meninges and blood vessels (ultimately resulting in cerebral amyloid angiopathy [CAA]). However, these changes are not pathognomonic of AD as SP and CAA are also seen in the brains of senescent humans who did not show clinical signs of AD, and the brains of many aged mammals. In addition, hyperphosphorylated tau is also present during postnatal development and arises in response to degenerative events such as ischemia or seizures.

Using sensitive immunohistochemical techniques it has been possible to show that the pattern of canine $A\beta$ accumulation parallels that in humans, being age-related, with plaques developing in several cortical and subcortical brain regions. In Beagles, the earliest and most consistent site of $A\beta$ deposition is the prefrontal cortex (at about 9-10 years of age), with the development of SP in the parietal and occipital lobes at a later age. Interestingly, deposition within the entorhinal cortex is not consistently observed until 14 years of age, except in a subset of dogs that show signs of early-onset cognitive impairment.

Studies have shown a direct correlation between the extent of $A\beta$ deposition and the extent of cognitive dysfunction in dogs, with the regions of the brain affected correlating with certain types of learning and memory deficits. Intriguingly, while all dogs naturally accumulate diffuse SP and CAA with age, some breeds appear to

develop them at an earlier age than others. In agreement with this, age-related cognitive dysfunction has been shown to vary between different breeds (and sources) of dogs.

The understanding of CDS in cats is even less advanced than in dogs. Immunohistochemical techniques have shown that while $A\beta$ is constitutively expressed within cat brains, the intensity of its accumulation within neurons and blood vessels appears to be age-dependent, as is the development of diffuse SP within the deep cortical layers. To date, the investigation of only 25 cats has been published, 23 of which were over 12 years of age. These studies appear to show that older cats are more likely to develop SP (only the 14 oldest cats were found to have SP). Our own study supports this finding: SP were seen in seven of nine cats over 10 years of age, but none of 10 younger cats. Interestingly, the SP appear to be even more diffuse than those seen in dogs, and quite unlike the well developed and circumscribed SP that are typical of humans. While NFT have not been seen in cat brains, immunostaining for hyperphosphorylated tau has been demonstrated, occurring concurrently within the neurons of some of the cats showing SP development, and providing evidence of possible pre-tangle formation in four older cats.

While the relationship between seeing SP and/or positive staining for hyperphosphorylated tau and behavioral or neurological dysfunction has not yet been well explored in cats, preliminary studies appear to indicate that there may be a correlation. For 17 of the cats previously assessed for SP the presence or absence of behavioral change was known: eight had behavioral changes consistent with CDS; seven of these were found to be positive, as compared to only three of the

nine cats without behavioral changes. For seven of the cats assessed for hyperphosphorylated tau the presence or absence of behavioral change was known: five of these had behavioral changes; two of which were positive for tau, compared to one of two cats without behavioral changes. Interestingly, amongst five cats with well documented CDS the severity of the behavioral changes did not appear to correlate particularly well with the extent of the SP formation.

Hence, while there are many similarities between CDS and AD, CDS should not be considered as a model for AD as there are a number of subtle differences between the two diseases. For example, as yet, NFT have not been detected in cats or dogs, possibly because they have isoforms of tau that cannot form paired helical filaments. Alternatively, it may be that these species do not usually live long enough to develop NFT. Further investigations are needed to confirm, for example, whether or not these changes only relate to progressive age, and/or to the presence of particular disease processes or disorders. In addition, the extent of the changes needs to be correlated with the clinical signs of CDS, and it remains to be seen whether or not particular breeds of cats may be predisposed.

Treatment Options

As yet, there is no published information relating to the successful treatment of cats with CDS. It may be possible to consider potential treatment options by extrapolation from work with humans with AD and/or dogs with CDS. There are a growing number of possible therapeutic options for AD; these include the use of selegiline (to manipulate the monoaminergic system), various cholinesterase inhibitors (to increase the availability of ACh at the neuronal synapses), or antioxidants (e.g., Vitamin E) and non-steroidal anti-inflammato-

Additional Reading

Ball, M.J., MacGregor, J., Fyfe, I.M., Papoport, S.I., and London, E. Paucity of morphological changes in the brains of aging beagle dogs: Further evidence the Alzheimer lesions are unique for primate central nervous system. *Neurobiology of Aging*, 1983, 4: 127-131.

Bobik, M., Thompson, T. and Russell, M.J. Amyloid deposition in various breeds of dog [abstract]. *Abstracts in Neuroscience*, 1994, 20: 172.

Chapman, B.L. and Voith, V.L. Behavioral problems in old dogs: 26 cases (1984-1987). *JAVMA*, 1990, 196(6): 944-946.

Campbell, S., Trettien, A. and Kozan, B. A noncomparative open-label study evaluating the effect of selegiline hydrochloride in a clinical setting. *Veterinary Therapeutics*, 2001, 2(1): 24-39.

Cummings, B.J., Su, J.H., Cotman, C.W., White, R. and Russell, M.J. β -amyloid accumulation in aged canine brain: A model of plaque formation in Alzheimer's disease. *Neurobiology of Aging*, 1993, 14: 547-560.

Cummings, B.J., Head, E., Ruehl, W., Milgram, N.W. and Cotman, C.W. The canine as an animal model of human aging and dementia. *Neurobiology of Aging*, 1996, 17: 259-268.

Hardy, J.A. and Higgins, G.A. Alzheimer's disease: The Amyloid cascade hypothesis. *Science*, 1992, 256: 184-185.

Head, E. Brain aging in dogs: Parallels with human brain aging and Alzheimer's disease. *Veterinary Therapeutics*, 2001, 2(3): 247-260.

Head, E., Callahan, H., Muggenburg, B.A., Cotman, C.W. and Milgram, N.W. Visual-discrimination learning ability and β -Amyloid accumulation in the dog. *Neurobiology of Aging*, 1998, 19(5): 415-425.

Head, E., McCleary, R., Hahn, F.F., Milgram, N.W. and Cotman, C.W. Region-specific age at onset of β -amyloid in dogs. *Neurobiology of Aging*, 2000, 21: 89-96.

Head, E., Moffatt, K., Das, P., Sarsoza, F., Poon, W.W., Landsburg, G. and Murphy, M.P. β -Amyloid deposition and Tau phosphorylation in clinically characterized aged cats. *Neurobiology of Aging*, 2004, In Press.

Head, E., Milgram, N.W. and Cotman, C.W. Neurobiological methods of aging in the dog and other vertebrate species. In: *Functional Neurobiology of Aging*. Hof and Mobbs (Ed), 2001, Academic Press, San Diego, pp 457-468.

Ikedo-Douglas, C.J., Zicker, S.C., Estrada, J., Jewell, D.E. and Milgram, N.W. Prior experience, antioxidants, and mitochondrial cofactors improve cognitive function in aged Beagles. *Veterinary Therapeutics*, 2004, 5(1):5-16.

Levine, M.S., Lloyd, R.L., Fisher, R.S., Hull, C.D. and Buchwald, N.A. Sensory, motor and cognitive alterations in aged cats. *Neurobiology of Aging*, 1987, 8: 253-263.

Moffat, K.S., Landsberg, G.M., Head, E. and Lindgren, B. An investigation of the prevalence of clinical signs of cognitive dysfunction syndrome (CDS) in cats. 2004, In preparation.

Nakamura, S., Nakayama, H., Kiatipattanasakul, W., Uetsuka, K., Uchida, K. and Goto, N. Senile plaques in very aged cats. *Acta Neuropathology*, 1996, 91: 437-439.

Ruehl, W.W., Bruyette, D.S., DePaoli, A., Cotman, C.W., Head, E., Milgram, N.W. and Cummings, B.J. Canine cognitive dysfunction as a model for human age-related cognitive decline, dementia, and Alzheimer's disease: Clinical presentation, cognitive testing, pathology and response to l-deprenyl therapy. *Prog Brain Research*, 1995, 106: 217-225.

Selkoe, D.J. Alzheimer's disease: Genotypes, phenotype, and treatments. *Science*, 1997, 275: 630-631.



ry drugs (e.g., ibuprofen) to reduce neuronal damage.

There have been a very small number of studies in dogs. These appear to suggest that high doses of mixed antioxidants and selegiline (l-deprenyl) may have beneficial effects. A four year study into the use of dietary antioxidants (vitamin E and complex antioxidants) revealed significant improvements in learning and memory. In a separate study selegiline has been shown to improve sleep/wake cycles and interaction with the family after it has been given for longer than a month (0.5-1.0 mg/kg po q24h). Interestingly, while selegiline appeared to provide symptomatic relief, it had little or no effect on disease progression.

Management

Since there are, as yet, no proven medical options for cats with CDS, it is nec-

essary to advise clients how best they can manage these cases. Affected cats often become stressed and cope very poorly with change: whether in their environment, their daily routine, their diet, or the members of the household with which they live. The cat's response to this stress is usually to stop eating, hide, and/or alter its toileting habits. Where possible, changes should be kept to a minimum. However, when a change cannot be avoided, it is very important that it is planned carefully and made slowly, with much reassurance. Some cats become progressively more senile. These cats may benefit from having their area of access reduced, while still containing all necessary facilities. This small area can then be kept safe and constant. 🐱

CONFERENCES

North American Veterinary Conference-Florida

January 11, 2005

Feline infectious diseases in cat populations will be the focus of the Shelter Medicine Track. Drs. Kate Hurley and Diane Addie will give presentations on URI, infectious diarrhea, virulent calicivirus, infection control programs, FIP, and other topics. For more information, visit: www.tnnavc.org.

American Association of Feline Practitioners-Puerto Rico

March 13-15, 2005

Mark your calendars for this event. Details are being finalized and information will be available at: www.aafponline.org.



Cornell Feline Health Center

Cornell University
College of Veterinary Medicine
Ithaca, New York 14853

