When we get a puppy, we hope that puppy will be with us a lifetime. Dogs and cats are living longer, expert medical care is readily available and the human-animal bond is strong. 66.7 percent of dog owners say they view their beloved dog as a member of the family. Old age is inevitable and sometimes, age related cognitive decline is inevitable. There are many correlations between human Alzheimer disease and Cognitive Dysfunction Syndrome. According to the Alzheimer Association: “Alzheimer’s Disease is the sixth leading cause of death in the United States. More than 5 million Americans are living with the disease”. Just as Alzheimer disease in elderly people is not the same as age related cognitive decline: Cognitive Dysfunction Syndrome in senior dogs is not the same as age related cognitive decline. A clinical trial in Australia is calling for dogs with CDS to participate in a program which may hold promise for people. Researchers will transplant stem cells created from the skin of a dog’s belly into its hippocampus, in the hope memory function will be improved. Michael Valenzuela explained to ABC news “These new cells survive in the brain, they grow into brain cells and they actually form connections with the animal’s own brain and improve overall memory function”.

Client’s will have first-hand experience with a human loved one being affected with either age related cognitive decline or Alzheimer disease and they will welcome opportunities to reduce the effect of age related cognitive decline for their pet’s.

CANINE COGNITIVE DYSFUNCTION (CDS)

CDS is a neurodegenerative disorder of senior dogs which is characterized by both cognitive changes and neurophysiological pathologies. Memory impairment, poor problem solving skills, social disconnect, confusion and day-night reversal may occur and increase as the condition progresses. The development and validation of tests for assessing cognitive function (many at CanCog Technologies [www.cancog.com]) including discrimination, oddity, reversal, and spatial memory has been instrumental in documenting age related cognitive differences.

The associated neurodegenerative changes include:

- Reduction in brain mass
- Increased ventricular size
- Meningeal calcification
- Demyelization
- Neuroaxonal degeneration
- Reduction in neurons
- Increased accumulation of diffuse beta amyloid plaques with perivascular infiltrates
• Depletion of catecholamines, increase in monoamine oxidase B (MAOB) activity resulting in a decline in the cholinergic system.\textsuperscript{5}

Common clinical signs of cognitive decline in pets are represented by the acronym \textbf{DISHA}\textsuperscript{5,7}

\begin{itemize}
  \item \textbf{D}isorientation
  \item \textbf{I}nteractions with people or other pets
  \item \textbf{S}leep-wake cycles
  \item \textbf{H}ousesoiling
  \item \textbf{A}ctivity changes (initially decline then increased restless or repetitive locomotion)
\end{itemize}

\textbf{PREVALENCE OF COGNITIVE DYSFUNCTION SYNDROME}

CDS is probably under-reported and under-diagnosed. Sadly, the problem behaviors may be mistaken for behavioral problems, which means not only is the primary problem of CDS not addressed, the pet may be put through unnecessary and misguided training programs. Medical conditions may mimic or confound the diagnosis.

There are many cognitive dysfunction screening checklists available.\textsuperscript{5,7} The primary care clinician should consider incorporating a screening program into senior pet visits to aid in identification of patients suffering from cognitive decline. In one study of dogs aged 11–16 that did not show signs of medical problems: 28\% of 11–12 year-old dogs and 68\% of 15–16 year old dogs showed at least one sign of CDS.\textsuperscript{13} Another study looked at both the prevalence of canine CDS and the diagnosis by the veterinary practitioner. While the prevalence of CDS as diagnosed by questionnaire from a primarily internet based survey (\textit{n} = 497). The prevalence of CDS in dogs aged: 8–10 years (3.4\%); 10–12 years (5\%); 12–14 years (23.3\%); and >14 years (41\%). Only 1.9\% of these patients were diagnosed by the primary veterinarian: the overall prevalence averaged 14.2\%.\textsuperscript{14} Veterinarians should be thinking about the effects of cognitive dysfunction on pets and how these concerns may manifest in every day conversations.

\textbf{DIAGNOSIS OF COGNITIVE DYSFUNCTION SYNDROME}

There is not a definitive test for CDS and the clinician must rely on owner reports and descriptions of behavior changes.\textsuperscript{5,7} In the laboratory memory function may be evaluated but the average pet owner is not well equipped to note when their dog’s memory is failing. Common symptoms such as night time waking or confusion may also be under reported or under recognized until the impairment is extreme. Annual screening is recommended for both early identification and education of clients regarding these symptoms.

\textbf{TREATMENT AND MANAGEMENT OF COGNITIVE SYNDROME}

Even for humans, there is not a cure: according to the Alzheimer Association, “It is the only cause of death among the top 10 in America without a way to prevent it, cure it or even slow its progression.”\textsuperscript{3} Epidemiological studies in humans suggest that the best results for reducing the incidence of Alzheimer’s disease is a life-long or long term commitment to a diet high in
antioxidants. Prevention may truly be the best medicine. Combination antioxidant therapy may be more effective than single component supplementation.

The signs and symptoms of CDS may be lessened and the progression diminished by use of medications, supplements, pheromones, diet or mental enrichment. A senior diet, Canine b/d, Hills Pet Nutrition, has been shown to improve the signs and slow the progress of cognitive decline. It is supplemented with a combination of fatty acids, antioxidants (vitamins C and E, b-carotene, selenium, flavonoids, and carotenoids), as well as DL-a-lipoic diet and L-carnitine, which are intended to enhance mitochondrial function. In a laboratory study, the combined effect of the enriched diet plus the enriched environment provided the greatest improvement.

Another commercially available diet, Vibrant Maturity 7+ Formula Dog Food, (Nestlé Purina PetCare), is a diet that includes enhanced botanical oils containing medium-chain triglycerides (MCT) to provide ketone bodies as an alternate source of energy for aging neurons, dual defense antioxidant blend of Vitamins E & A along with minerals zinc and selenium. Vibrant Maturity has also been shown to significantly improve cognitive function in senior dogs by providing an efficient fuel source for the senior dog’s brain.

Dietary supplements may provide an efficient way to include antioxidants in a pet’s diet. These supplements may be especially beneficial if initiated before the onset of clinical signs of cognitive impairment but there are no long term clinical trials to support this extrapolation.

Senilife® (CEVA Animal Health) includes a combination of antioxidant ingredients: phosphatidylserine, pyridoxine, ginkgo biloba, resveratrol, and natural vitamin E which may reduce the effects of neurodegenerative aging and the associated behavior changes. Phosphatidylserine, a membrane phospholipid, has been shown in canine clinical trials to reduce the severity of clinical signs associated with CDS. CanCog conducted a clinical trial with an earlier formulation of Senilife which found the performance accuracy was improved in the treated group compared with baseline, and dogs receiving the supplement in the first portion of the study maintained their improved performance. Gingko biloba extract contains flavonoids and ginkgolides which are active as antioxidants and appear neuroprotective.

S-Adenosyl-L-methionine, is found in all living cells and is formed from methionine and ATP. SAMe may help to maintain cell membrane fluidity, receptor function, and the turnover of monoamine transmitters, as well as increase the production of glutathione. In a placebo-controlled trial in dogs, greater improvement in activity and awareness was reported in the SAMe group after 8 weeks. SAMe is available in canine formulations: Novifit® by Virbac and both Denosyl® and Denamarin® (a combination of SAMe and Sibylin) by Nutramax Laboratories.

Selegiline (Anipryl, Pfizer Animal Health) and Selgian (CEVA Animal Health), are approved for the treatment of CDS in dogs. Selegiline is a selective and irreversible inhibitor of MAOB in the dog. Selegiline is considered to be neuroprotective, potentially by increasing efficiency of superoxide dismutase and catalase for improved free radical scavenging, which may decrease nerve damage/degeneration. Selegiline may enhance dopamine and other catecholamines in the cortex and hippocampus. Period to effect is often 2 to 6 weeks. CDS is a progressive disorder
and regression is inevitable. Patients which improve while taking selegiline should continue receiving this medication life long. Selegiline should not be used concurrently with other monoamine oxidase (MAO) inhibitors including amitraz (Mitaban® by Upjohn, Preventic® by Virbac). Extreme care should be exercises with selective serotonin reuptake inhibitors, tricyclic antidepressants, narcotics, dextromethorphan, buspirone, trazodone, or tramadol.

Other cognitive enhancers are utilized in human patients which may be beneficial for canine patients include: memantine and amantadine. Drugs that may enhance the noradrenergic system, such as adrafinil and modafinil, might be useful in older dogs to improve alertness and help maintain normal sleepwake cycles (by increasing daytime exploration and activity). However, dose and efficacy in dogs has not been well established or widely utilized.

**NIGHT TIME WAKING: SPECIAL CONSIDERATIONS**

Commonly the primary owner concern is nighttime waking. This may be an urgent and even life-threatening concern as owner’s faced with many consecutive nights of sleep deprivation and a feeling of hopelessness may elect euthanasia. Promptly reducing anxiety and reestablishing normal sleep-wake cycles may be sufficient to ease the crisis of sleep deprivation. Melatonin, may be useful as part of a bedtime routine ritual and may be best given 30 minutes before bedtime. Optimally melatonin should not be redosed at other times of day when used to establish nighttime sleeping patterns. Some medications, such as diphenhydramine, phenobarbital, or trazodone may offer sedation effects if given at or near bed time. If the dog is receiving antihistamines or phenobarb for other indications these may be best administered at bedtime. The senior dog may be more susceptible to the sedative effects of medications and even if the dog has been on these medications for years, ask if these medications cause daytime sedation.

Determine if the dogs is having difficulty settling at night or if he dog wakes up in the middle of the night since these patterns will suggest alternative responses. For the dog or cat that has difficulty settling at night but then sleeps well, situational use of anxiolytics that may promote sleep may be beneficial as adjunctive therapy to behavior modification. Benzodiazepines maybe useful because of rapid onset of short-acting anxiolytic and sedative effects. In senior pets, especially if liver function might be compromised, clonazepam, lorazepam, or oxazepam might be preferable to alprazolam or diazepam since these do not have active intermediate metabolites. The dog that goes to sleep and then wakes up in the middle of the night may be experiencing pain, elimination urges, confusion or even seizures. Consider a trial of gabapentin an adjunctive therapy for pain management. Gabapentin may also have mood stabilizing effects and anticonvulsant properties which may be useful. Provide a comfortable sleeping area with an Adatil® Diffuser for support of emotional wellbeing. Some elderly dogs benefit from a heated bed which may provide comfort for neuromuscular disorders. Assure clients they may attend to their pet’s needs in the night and that “ignoring” such bad behavior is not required. If a little reassurance helps a confused pet settle in the night, then this is a humane and kind strategy. Some clients feel they must ignore their pet in the night and this may result in more confusion and anxiety in a dog that is experiencing cognitive distress. Certainly punishment or reprimand for behaviors caused by confusion is contraindicated. A day time routine that includes fresh air, sunshine and exercise may help reset the day time – night time cycle for all family members. Excessive or extreme increases in exercise should be avoided.
Mentally stimulating interactions are preferable. Shared activities which celebrate the special bond and relationship with a senior pet are preferable to imposition of strict obedience regimes.

The senior pet shares a unique bond and relationship with their family. Identification and management of problem behaviors due to age-related cognitive decline or CDS ensure these issues are addressed with the compassion our old dogs deserve.

REFERENCES