**TCVM Treatment of Canine Cognitive Disorder**

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**SENILITY:** As we and our pets age, there is a natural reduction in many biological processes and a loss of tissue structure. This includes the CNS and the cerebral tissues. Neurochemicals change with a general reduction in certain chemical reactions. Neurons are gradually lost from the wear and tear of daily life. Researchers believe Cognitive Dysfunction Syndrome (CDS) is caused by physical and chemical changes that affect the brain function in older dogs; however, in dogs with CDS the signs of confusion or various other behavioral changes are greater than the normal alterations of aging. Most dogs age without the accentuated signs seen in CDS, yet the changes that lead to CDS take place in all dogs to some extent. In one study at the University of California-Davis, 62% of 11- to 16-year-old dogs showed signs in at least one category of CDS. In a pet owner survey, nearly half of dogs age 8 and older showed at least one sign associated with CDS.

**Pathophysiology**: Monoamine oxidase (MAO)s are widely distributed throughout the body and are sub-classified into 2 types, A and B, which differ in their substrate specificity and tissue distribution. MAO plays a role in the catabolism of catecholamines, (dopamine, and, to a lesser extent, norepinephrine and epinephrine) and serotonin. CDS is thought to result in part from reduced catecholaminergic nerve function and decreased dopamine levels in the CNS. The pathogenesis of the development of clinical signs associated with cognitive decline is considered to be partly a result of a decrease in the level of catecholamines in the CNS and deficiencies in neurotransmission. There is also evidence which points to hypothalamic dopamine deficiency playing a role in the pathogenesis of pituitary dependent hyperadrenocorticism in the dog.

In people, numerous studies have indicated that senility and Alzheimer’s disease are related to similar changes as occur in CDS. In those human conditions, oxidative free-radicals have been shown to play a key role in causing the pathologic changes seen. Anything which improves cerebral blood flow and enhances cerebral oxygen (cosmic Qi) delivery to the CNS will reduce the rate of progression and improve cognitive function. While people suffer more from cerebral vascular insufficiency than dogs and cats (people get atherosclerosis), animals still respond to the same treatments used in human beings. Recently, it has been suggested that glutamate levels increase in Alzheimer’s disease which results in stimulation of specific neural receptors that result in cytotoxic reactions. This glutamate-dependent receptor’s effects are blocked by antioxidants.

**Diagnosis:** The diagnosis of CDS is based upon the presentation of the clinical signs in a older patient and ruling out other causes to explain the presence of the condition. A work-up should include a thorough physical and neurological examination. A CBC, chemistry profile and UA may be helpful in recognizing any additional systemic factors which need therapy or which might contribute to the symptoms. Remember that CDS is a chronic and slowly progressive problem, not one that occurs over-night. Chest and abdominal radiographs and abdominal ultrasound may help look for other complication and diseases which might result in similar symptoms. Perineoplastic signs could mimic signs of CDS and the minimum database helps provide evidence which precludes systemic neoplasia as part of the process. A CSF tap is usually normal with the exception of a possible mild increase in CSF protein. An MRI can be helpful since many of these patients show signs of de novo hydrocephalus from cortical atrophy. If no other signs, except for behavior and the MRI changes are seen, then the tentative diagnosis of CDS is made.

**Treatment:** Anipryl is the first and only drug approved by the FDA for the control of clinical signs associated with canine Cognitive Dysfunction Syndrome. Most dogs are prescribed one tablet each day, preferably in the morning. (Anipryl can be given with food.) It's important to administer every tablet as directed since interruption of therapy could lead to the reappearance of signs.

In studies, pet owners reported that 69 to 75% of dogs improved in at least one clinical sign after one month of Anipryl therapy. Because CDS is a syndrome (a collection of signs), no two dogs will show exactly the same signs. Response to Anipryl may vary from dog to dog.

In the blinded, placebo-controlled study, owners reported that 69% of dogs improved in at least one clinical sign after one month of Anipryl therapy, compared to 52% of placebo-treated dogs. A second open label clinical study revealed that 75% of dogs improved in at least one clinical sign after one month of Anipryl therapy. Some dogs in both studies showed increased improvement for up to three months, indicating that some increased improvement may be seen with continued use. However, onset, duration and magnitude of response varied with individual dogs. In studies, the most common side effects were vomiting, diarrhea or changes in behavior such as hyperactivity and restlessness. Most side effects were mild to moderate.

Based upon IV administration of selegiline to 4 mixed breed female dogs, the plasma elimination half-life was estimated to be 60 10 minutes (mean SD) and the volume of distribution at steady-state (Vss) was estimated to be 9.4 1.6 L/kg (mean SD). The relatively large Vss suggests that the selegiline is extensively distributed to body tissues. The absolute bioavailability, F, of an oral solution was less than10%.

**Alternative Therapy:** Although Anipryl is recommended for treatment of CDS, I prefer to try other measures before resorting to it for the control of the condition. Aerobic exercise has been shown to improve cognitive function and should not be overlooked as a simple way to improve the pets cerebral functions. Antioxidants can be very useful including vitamin E, vitamin C, Vitamin A (or beta carotene) and selenium should be given. Vitamin E, however, should be given at therapeutic levels which are 50-100 IU/kg. Grape seed extract can be helpful as an antioxidant as well. Ginkgo biloba extract (2-4 mg/kg every 8-12 hours) can be very helpful and has been shown to provide long-lasting and effective help in human Alzheimer’s patients. Another antioxidant that has been demonstrated in studies to help in senile dementia and Alzheimer’s disease is acetylcysteine (25 mg/kg every 8 hours). Compared with vitamin E and C, acetylcysteine is even more potent as an antioxidant. In addition, coenzyme Q-10, soy lecithin, omega-3-fatty acids, gammalinolenic acid and vitamin B complex can be very useful in helping support CNS function, oxygen utilization, membrane stabilization and neurochemical production. If these measures do not help (and the diagnosis is correct), then Anipryl can be tried.

Westlab Pharmacy (1-800-4WESTLA) has 2 formulas to help with CCD. The first is prevention which should be added to all dogs nutritional building blocks as they age. However, when signs of CCD begin to develop, they have a therapeutic formula which contains higher doses of antioxidants and also Huperazine A which seems to stimulate forebrain function selectively and can help improve cognition and memory. Nothing will completely prevent further decline nor reverse severe CCD, but delaying the onset and reducing the early symptoms can greatly improve the quality of life for the pet and the owner.

**TCM Diagnosis and Treatment:** Neurodegenerative disorders are complex with an onset that is followed by progressive deterioration. Their clinical manifestations are determined by the location and the seriousness of neurodegenerative disorders. Its pathogenesis is a mixture of deficiency and excess conditions, represented by the deficiency of kidney essence or the blocking of the brain channel by blood stasis (an excess condition) - or both. Old age leads to kidney deficiency. The kidney fails to nourish the child (liver) leading to stagnation. The grandparent (kidney) fails to control the grandchild (heart) leading to shen disturbance.

As such, the cause of neurodegenerative disorders lays not so much in the brain (though it is the brain that shows the symptoms) as in the kidney, which according to TCM theories controls the bone and generates the marrow. From the point of view of disease differentiation through viscera and their interrelations, the root of the disease is due to the deficiency of the kidney and the bone marrow. While the blood stasis and the phlegm accumulation are considered as the symptoms, not the cause. Therefore, the keys to treating neurodegenerative disorders are to tonify the kidney, eliminate the phlegm, remove blood stasis and induce resuscitation.

According to TCM theories, the spirit (shen) resides within the heart and the brain. The spirit is affected by the overall mental and physical health of the animal. If the spirit is damaged, both the mental and the physical functions of the patient are greatly compromised. Deterioration in mental functions may result in delirium and dementia with the decline in physical functions resembling complications of stroke. Therefore, the treatment for neurodegenerative disorders should focus on awakening up the spirit (shen), opening up the sensory orifices and stimulating the brain. The selection of points is as follows:

**Local AP points:** GB-20, TH-17, BL-10, GV-20, & GV-21

**Special AP points:** GV-26, PC-6, LI-4, SP-6, & BL-40

**TCM herbal:** Shen calmer, Left side replenisher, and Right side replenisher