Virtually any medical condition can present with behavioral signs. In fact, behavioral changes may be the first or only sign of sensory decline, cognitive dysfunction syndrome, or pain. Behavior signs might be due to neurologic, sensory, endocrine, metabolic, gastrointestinal or musculoskeletal disorders. Therefore veterinarians should be proactive in asking pet owners about behavior problems or changes in behavior at each visit and encouraging them to seek guidance as soon as signs arise.

While it is essential to consider the effects of disease on behavior, acute and chronic stress can also impact both health and behavior. When the pet's behavior is unacceptable to the owners, not only might the pet be stressed, but the owners' responses including punishment, anger, frustration, and inconsistency can further add to the pet's anxiety and stress. To complicate the picture further medical problems are also a source of stress.

**Medical Causes of Behavior Signs**

a) **Neurological**

When there are neurologic deficits, mental status is altered or there is increased sleep, circling, head pressing, seizures, emesis, or altered eating and drinking, a neurologic diagnosis can be made. However, behavior signs may arise in the absence of neurologic signs. Changes in behaviour, personality, or mood, decreased responsiveness to stimuli, or loss of previously learned behavior including housetraining indicate forebrain disease. Altered responsiveness to stimuli can also arise from sensory or motor dysfunction.

Epilepsy is a differential diagnosis when pets are presented with motor or sensory signs or altered mood or temperament. Seizures may be generalized with convulsions and loss of consciousness or focal with motor or sensory signs and no loss of consciousness. Bizarre behaviors including fly biting, chewing, swallowing, staring, tail chasing and aggression may arise from focal seizures. Behavior causes must also be differentiated from other episodic events including tremors, narcolepsy, syncope, and cervical pain. Behavior pathology with alterations in serotonin metabolism have also been identified in aggressive cases especially in English Cocker and Springer Spaniels.1,2

b) **Cognitive dysfunction syndrome**

In senior pets, cognitive dysfunction syndrome is characterized by behavioral signs including disorientation, alterations in social interactions and sleep-wake cycles, housetsoiling, a decrease in activity or an increase in repetitive activities, an increase in fear and anxiety and deficits in learning and memory. Once signs are identified, a diagnosis of CDS is made by excluding all other medical causes. The development and validation of tests for assessing cognitive function (e.g. memory, discrimination, reversal) have been instrumental in documenting age related deficits in learning and memory in both dogs and cats. These functions are highly dependent on the frontal lobe, which shows atrophy and beta amyloid accumulation prior to other brain areas.

Early detection allows for early intervention to optimize clinical improvement and slow further decline. Veterinarians and staff must therefore be pro-active in informing clients of the importance of reporting these signs, and in screening for problems at each visit. In dogs frontal volume decreases, ventricular size increases and there is demyelination, meningeal calcification, increased lipofuscin, neuroaxonal degeneration and a reduction in neurons.3,4 There is also evidence of age-associated brain pathology in cats including neuronal loss, increased ventricular size, cerebral atrophy and widening of the sulci although perhaps not as marked as in dogs.5 Perivascular changes including microhemorrhage or infarcts may also be the cause of some of the signs of CDS.5-7 With increasing age there is also an increase in oxidative damage.5,8 A decline in the cholinergic system has also been identified in dogs and cats.9,10 With increasing age there is increased accumulation of diffuse beta amyloid plaques and perivascular infiltrates which has similar pathology to Alzheimers disease.7

Based on a recent internet survey, the prevalence of CDS ranged from 5% of dogs 10-12 years of age to 41% over 14 with an overall prevalence of 14.2%. However, a diagnosis was made in only 1.9%.11 In a study of cats aged 11 and older, 35% were diagnosed with CDS; 28% of 95 cats aged 11 to 15 and 50% of 46 cats over 15.5 Environmental enrichment together with drugs, supplements and dietary therapy may improve clinical signs and slow the progress of cognitive decline. (See drug and natural therapeutic notes)

c) **Metabolic and Endocrine**

Endocrine diseases, including hyper- and hypothyroidism, hyper and hypoadrenocorticism, androgen producing adrenal tumors and functional tumors of the ovaries or testes may be associated with changes in behavior. The decline in function in any organ (e.g. liver, kidneys) will also affect behavior, but other concurrent...
medical signs would be expected. In particular diseases affecting the urogenital system can cause or contribute to urinary housesoiling.

While classical signs of hypothyroidism include thin coat, sebhorrea, lethargy, bradycardia, and increased heat seeking, it has also been suggested that the early stages of hypothyroidism in dogs might be associated with fear based behaviors, hyperactivity, poor learning, anxiety and aggression especially toward family members.12 However, TT4 varies with age, breed and diurnal variation and is reduced by stress, disease and some drugs. In one study that compared TSH and TT4 levels in dogs with behavior problems and those without, TT4 was actually higher in the dogs with behavior problems, while in a second study comparing dogs referred for aggression compared to dogs with other behavior problems, no profiles were consistent with hypothyroidism.13,14 In a recent placebo controlled study, dogs with aggression were placed on thyroid supplementation or placebo if they had a free T4 that was low or in the bottom 20% of normal, if the TT4, TT3 or fT3 was low or in the bottom 30% of normal or if there were thyroid autoantibodies.12 While both groups improved, there was no significant difference between groups. While treatment is warranted in dogs with clinical signs and low thyroid levels confirmed by elevated TSH or low fT4 by equilibrium dialysis, replacement therapy has questionable value in cases where hypothyroidism is not confirmed and could potentially lead to hyperthyroid levels that might contribute to irritability, reactivity, restlessness, anxiety, and aggression.

d) Gastrointestinal / Ingestive
Medical problems and drug therapy can increase or decrease appetite or drinking and can lead to picas. Any medical condition affecting stool output, volume or consistency could contribute to fecal soiling. Unusual oral behaviors including licking, sucking, pica, smacking lips, or gulping can be a compulsive behaviors but medical differentials including partial complex seizures and gastrointestinal disorders must first be ruled out. Fly snapping and environmental licking might be caused by GI disorders.15,16

e) Pain
Behavioral measures are an important means of measuring pain. Clinical signs vary with whether the pain is acute or chronic and the cause of pain (e.g. dental, musculoskeletal, urogenital, neurologic or post-surgical). Since animals have adaptive mechanisms which may mask signs of pain, the absence of overt signs does not mean an absence of pain. In addition, physical examination and physiologic parameters may not be reliable measures of pain. Therefore behavioral measures including a change from normal behavior including activity, social interactions, play, or vocalization; a change in temperament (e.g. aggression, avoidance) or the expression of abnormal behaviors (e.g. housesoiling) might be an indication of pain.17 For veterinary staff the recognition of pain in hospitalized patients requires observational measures including behavior/demeanor, body postures, vocalization, activity, mobility, attention to surgical site and interactive measures including approach, stroking palpation. Upon discharge owners should monitor for changes in mobility and behavior. For chronic pain associated with osteoarthritis in dogs, there may be alterations in gait, mobility, behavior and demeanor which might be consistent with orthopaedic and radiographic findings. In cats with degenerative joint disease, changes in lifestyle (including activity and mobility) and behavior (including grooming and temperament) are more commonly identified than alterations in gait or lameness.18 In fact, lameness and alterations in gait may be absent since cats, are small and agile and pain is often bilateral.

The Stress Response
Stress is an altered state of homeostasis caused by physical or emotional factors that trigger behavioral, psychological, endocrine and immune effects designed to handle stress. In dogs and cats, exposure to mild stress and handling early in life stimulates hormonal, adrenal and pituitary systems that result in animals that perform better in problem solving, have greater resistance to disease and can better withstand stress later in life.

The first component of the stress response is the HPA axis, in which the hypothalamus releases corticocotrophic releasing hormone (CRH), which stimulates the release of ACTH. The second component is the sympathetic-adrenal-medullary system which releases noradrenaline and adrenaline. Noradrenaline is associated with sensitization and fear conditioning. In cats, transient hyperglycaemia is often reported. If stress is persistent or chronic there is continued stimulation of the HPA axis and catecholamine system, leading to effects on the immune system and on stress related diseases. One study found higher plasma levels of dopamine and 5HT in pets with stress compared to controls.19 Increases in dopamine may enhance aggressive behavior and lead to an increase in stereotypic and grooming behaviors. In one canine study, lowered prolactin was associated with acute fears and phobias, with higher prolactin with chronic stress, stereotypic behaviors, fear aggression and autonomic signs. Therefore, there can be marked differences on health and behavior between acute and chronic stress.
Stress and Physical Health

In humans there may be a correlation between stress and poor health, poor immune function, cardiovascular disease, skin disease, asthma, gastrointestinal disorders, and cellular aging. Similarly in pets, stress may alter immune function, and has been shown to contribute to gastrointestinal diseases, dermatologic conditions, respiratory and cardiac conditions, behavioral disorders and a shortened lifespan.20

Cats with feline interstitial cystitis (FIC) have altered bladder permeability during stress when compared to cats in an enriched environment.21 An increase in plasma noradrenaline has been demonstrated in cats with interstitial cystitis. In a recent study of a colony of cats, sickness behaviors including the gastrointestinal and urinary tract, skin, and behavior problems were all associated with environmental stressors. Cats with FIC that received MEMO (multimodal environmental modification) had a significant reduction in FIC, respiratory disease, fearfulness, and nervousness and less inflammatory bowel disease and aggression.22 In a placebo controlled study there were less bouts of FIC when a Feliway™ diffuser was installed. In another study behavioral risk factors for FIC included moving house, movement blocked by other cats, living with dogs, or living with another cat with which there was conflict. Behavior therapy led to significant improvement over placebo.

Stress and anxiety can alter bacterial flora, inhibit gastric emptying, increase colonic activity, and increase intestinal permeability leading to irritable bowel syndrome, inflammatory bowel disease, gastrointestinal reflux, stress induced hypersensitivity, and heartburn. In pets, acute fear and anxiety can lead to a decrease in appetite or anorexia, diarrhea, vomiting or colitis. Pica, polyphagia, and polydypsia may also be stress induced.

Stress can affect reproductive health by decreasing sperm quality, inhibiting sexual interest, erection and ejaculation in males and inhibiting ovulation and decreasing fertility in females.

Although stress leads to an immune response intended to enhance defence mechanisms, in some individuals stressors may contribute to inflammatory dermatoses. This brain skin connection is comprised of psycho-neuro-endocrino-immunological factors which under stress may play a role in the pathogenesis of dermatoses such as atopic dermatitis, psoriasis, and urticaria.23 In humans with atopic disease stress may lead to increased levels of IgE and eosinophils, and an over-reactive sympathetic adreno-medullary system. In humans, there may be a link between stress and increased epidermal permeability.24 A similar increase in pets might exacerbate atopic disease.25 In one study of dogs with recurrent pyoderma, psychogenic factors were identified. In dogs stress has been associated with onset of pruritus that resolved with behavior therapy.26

With age and disease the interplay of health and behavior is further exacerbated since there is an increase in tissue hypoxia, alterations in cell membranes, increased production and decreased clearance of free radicals, a decline in organ function, sensory function, and mental function, and a gradual deterioration of the immune system. These changes reduce the pet’s ability to respond to stressful events and maintain homeostatic balance, thus resulting in increased susceptibility to tumours, disease, and behavior problems. This is consistent with a study where environmental stress had greater effects on health and behavior in senior cats.

Stress and Behavioral Health

Chronic anxiety and stress may also lead to behavioral disorders in humans including panic disorders, separation anxiety, social, and other phobias, obsessive-compulsive disorders, generalized anxiety disorders, post-traumatic stress disorders, impulse control disorders, and sleep disorders which may all have animal correlates. When pets are in conflict (competing motivations), frustrated (where the pet is unable to achieve its goals) or when the behavioral needs of the pet are not addressed, displacement behaviors such as self-trauma, spinning, tail chasing or hyperesthesia might be exhibited. These signs are more likely to arise in pets that are anxious or reactive and those that are genetically predisposed. Behaviors that arise in response to a specific stimulus might be resolved if inciting factors can be avoided and owner responses are consistent and predictable.

Behavior becomes compulsive when it does not provide a mechanism for the pet to settle, the signs arise outside the original context and interfere with normal daily function. Pet owners may further aggravate the problem by reinforcing or punishing. Also problematic are inconsistent owner responses which add to conflict. They may have a neurologic (locomotory, hallucinatory), ingestive (pica) or dermatologic (self-trauma) presentation. Compulsive disorders have genetic and breed predispositions such as with tail chasing in German Shepherds, spinning in Bull Terriers, wool sucking in Oriental cats and flank and blanket sucking in Dobermans, for which a genetic locus has been identified.27 There is likely an alteration in serotonergic activity for most compulsive disorders in dogs and cats. As in humans with OCD, drugs that inhibit serotonin reuptake are most effective.28,29 However other neurotransmitters have also been implicated including altered dopaminergic or glutamatergic pathways or opioid receptors.30-32
12. Dodman NH et. al. The effect of thyroid replacement in dogs with suboptimal thyroid function on owner directed aggression; a randomized, double-blind placebo-controlled trial. J Vet Behav 2013 8, 225-230

