2020
PROCEEDINGS

ANNUAL CONFERENCE

of the
American Holistic Veterinary Medical Association

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The Board of Directors extends its thanks to all those members who made this event possible. A special thank you goes to our Conference Program Committee, for their efforts and expertise in selecting the program for this year’s conference.

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The Council of Elders (COE) reminds us of our holistic roots with their morning Inspiration.

Many thanks for all the members:

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- International Veterinary Acupuncture Society
- RAIVE
- Veterinary Botanical Medical Association

We could not get very far without volunteers, before the meeting, and at the conference.

We extend our thanks to them as well.
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Promoting Wellness and Longevity Strategies
PJ Broadfoot, DVM

Objectives
To touch on lifestyle and therapeutics that engender vitality in the pets entrusted to our care, including dietary concerns, weight control.
To review wellness supplements that could potentially improve the long-term prospects for quality life.

It has been believed that maximum lifespan depends primarily on genetics, dependent on the damage that free radicals cause to DNA, which leads to degenerative diseases such as diabetes, arthritis, cardiovascular issues, dementia, and organ failures. Aging, more accurately, is the process of accumulation of various health hazardous chemicals in the body with age, such as free radical and reactive oxygen species; a multifactorial and tissue-specific process that involves diverse alterations regarded as the “hallmarks of aging”, which include genomic instability, telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion and altered intracellular communication, all of which increase the risk of disease and death.

Exercise and Weight Restriction and Dietary Concerns
The most reliable intervention which consistently increases life-span is calorie restriction (CR), in which the animal is kept on a diet which is 30% to 70% less calories compared to normal diets which not only extends the 'average life-span', but prolongs the 'health-span'- the number of years an organism can live without any major chronic disease. Dogs were fed to maintain a body condition score less than 5. The study revealed that the median life span (the age at which 50 percent of dogs in the group died) of the lean-fed dogs was extended by 15 percent or nearly two years. Median life span was 11.2 years for the control group versus 13 years for the lean-fed dogs. By age 10, only three lean-fed dogs had died, compared to seven control dogs. At the end of the twelfth year, 11 lean-fed dogs were alive with only one control dog surviving. Twenty-five percent of the lean-fed group survived to 13.5 years, while none of the dogs from the control group lived to 13.5 years. The lean-fed dogs maintained a significantly leaner body condition from 6 to 12 years of age than the control group dogs, with mean body condition scores between 4 - 5 (ideal) and 6 - 7 (overfed), respectively. On average, the lean-fed group weighed less, had lower body fat, and after a certain age, experienced a two-year delay in the loss of lean body mass as they aged, compared to the control group dogs. The control dogs exhibited more visible signs of aging, such as graying muzzles, impaired gaits and reduced activity, at an earlier age than the lean-fed dogs. The quality of vitamins, minerals, protein, carbohydrate, lipids and other factors in the diet is not compromised, thus supplemental nutrition is recommended. After a period of time on this diet, several biomarkers of aging return to normal levels and the animal looks and is healthy. In humans, a recent study found that obese children have telomeres that are 24% shorter than non-obese children, thus lean mass is health sparing.

Oral Health
Periodontal disease is common and often overlooked in a total wellness program. Moderate to severe periodontitis increases the level of systemic inflammation, which may be the common thread tying many disease processes together. Studies have shown that people with gum disease
had 23% shorter telomeres. Those with longer telomeres had no gum disease, and correspondingly lower markers of inflammation. Mounting evidence supports a strong association between periodontal disease and cardiovascular risk, as well as other systemic organ disease, including autoimmune responses, cerebrovascular, and peripheral arterial diseases. A critical component of chronic periodontal disease involves “Stealth infections,” which hide in biofilm communities, comprised of microorganisms encased within a self-produced matrix of exoproteins and exopolysaccharides, which strongly attach themselves to body tissues, including oral surfaces. The extracellular polymeric substance (EPS), or 'slime', covering and cementing of biofilm colonies, protects the bacteria from antibiotics, bacteriocins (produced by probiotics), antibodies, and other medicines/herbs which might kill it. An estimated 80% of all infections are biofilm related, as biofilm formation is the preferred “bacterial lifestyle”. EPS acts as diffusion barrier, protecting the microbes hiding behind the EPS matrix. Honey is now being revisited as an alternative treatment due to its broad-spectrum antibacterial activity and the inability of bacteria to develop resistance to it. A range of well-characterized New Zealand manuka-type honeys, in which two principle antibacterial components, methylglyoxal and hydrogen peroxide, were quantified, can eradicate biofilms of a range of Staphylococcus aureus strains, with higher anti-biofilm activity as the proportion of manuka-derived honey, and thus methylglyoxal, in a honey blend increases. Honey was able to penetrate through the biofilm matrix and kill the embedded cells in some cases. Interestingly, there are now some studies looking at the wildflower honeys of Arkansas!

**Microbiome**

Both the upper and lower parts of the human digestive tract harbor a complex ecosystem of bacteria, fungi, protozoa, and viruses, referred to as the microbiome. It begins to form in utero, developing after birth to become a stable, fully functioning microbiome, until the physiological changes associated with senescence lead again to substantial shifts in its composition. The lower part of the digestive tract gets “inoculated” every day with bacteria from the oral cavity, and microbial species detected in the oral and fecal microbiota overlap in about 45% of tested individuals and oral bacteria can disseminate all over the body via the blood stream. Dysbiosis of the oral microbiome is not only connected with oral diseases, but has been also implicated in the pathogenesis of autoimmune, inflammatory, and neoplastic diseases (e.g., heart disease, respiratory illnesses, psoriasis, psoriatic arthritis, and carcinogenesis at various sites). Periodontal diseases are characterized by localized infections and inflammatory conditions and directly affect teeth supporting structures which are the major cause of tooth loss. Several studies have demonstrated the involvement of autoimmune responses in periodontal disease with evidence of involvement of immunopathology. Bacteria in dental plaque induce antibody formation. Lymphocytes, cytokines and complement system are reported to have an important role in the progression of periodontal disease.

**Stress and Anxiety/Reduction**

Stress not only affects mental and emotional states, it can contribute to many serious chronic and deadly health conditions. This direct connection has been termed psychoneuroimmunology. Chronic stress may have a profound effect, by shortening of DNA telomeres, predisposing to chronic diseases and cancer, and is associated with cellular aging, or senescence. Several factors, including stress, increase the reduction in telomere size and aggravate the senescence process. Scientists have discovered that the multiple biochemical pathways of chronic stress dampen
telomerase activity and accelerate telomere-shortening. Maintaining their health is essential in preventing aging.

Ashwagandha, Withania somnifera, a.k.a. Indian ginseng is considered the foremost adaptogen in Ayurvedic medicine. Ashwagandha supports endurance, calm strength, and enduring vitality. Ashwagandha (Withania somnifera) is an adaptogenic herb, helping the body adapt to stress. It is rejuvenating, helping to balance endocrine functions, including adrenal, thyroid and reproductive. Active constituents are slightly sedative in nature and calm the nervous system. It helps support a healthy immune system and rebuilds the body’s energy reserves.

Aphanizomenon flos aquae (blue green algae), and dark chocolate contain Phenylethylamine (PEA) a naturally occurring alkaloid chemical compound neurotransmitter derived from the amino acid phenylalanine. It exists naturally in the central nervous system and is responsible for the emotional experience associated with pleasure and mental awareness; it supports mental energy, mental clarity, concentration, and attention, and is a known natural mood enhancer.

Velvet Antler (VA)-Mood/Stress components: Monoamine-oxidase inhibitor enhance mood by preventing the breakdown of neurotransmitters such as norepinephrine and serotonin, allow them to be available longer to the brain. A natural form of MAO and serotonin is present in VA. Serotonin is integral also to healthy activity of platelets, and while no data was found on deer velvet for thrombocytopenia or thrombosis, it is theoretically a viable use for this supplement until the research is done. Some fascinating data shows that serotonin can help a damaged liver to regenerate, and it may be a matter of time before VA is studied for this purpose! Gamma-aminobutyric acid (GABA): a non-essential amino acid that helps promote normal brain function by helping to block stress-related messages from reaching receptor sites in the central nervous system. This helps reduce feelings of anxiousness and may be helpful for treatment of disorders linked to emotional stress, such as reduced sex drive, as it plays a key role in regulating sex hormones, and in stress induced hypertension. Individuals with enlarged prostate glands may benefit from GABA supplementation. L-Dopa: is an important amino acid that is the precursor of dopamine.

Dopamine helps brain functions like sleep, mood, learning, behavior, and regulating prolactin production from the pituitary. Dopamine is also involved in the HGH loop cycle, mainly by increasing the response of the hypothalamus towards release of growth hormone in the bloodstream. Aromatic l-amino acid decarboxylase (AAAD): involved in the synthesis of dopamine, a neurotransmitter crucial in cognitive, neurobehavioral and motor functions. Mice given VA showed improvements in measurements of senility.

Hormesis
Despite the fact that the phenomenon of hormesis has been known for almost a century, and is central to the tenets of homotoxicology, it is still controversial how useful hormetic treatments are, in preventing age-related diseases and increasing life expectancy. There are some provocative findings suggesting that hormesis could be an important strategy for improving health, when exposure to a mild stress can increase tolerance to a subsequent stress challenge. For example, low level activation (“hermetic levels”) of the ionotrophic glutamate receptor in brain neurons (which triggers endogenous neuronal survival pathways) might be effective for
preventing neurodegenerative disorders as well as a therapeutic tool for augmenting cell survival following such damaging, potentially fatal disorders as stroke. Data on mice indicate that caloric restriction (specifically short-term starvation) as an activator of hormesis, increases the stress resistance of normal, but not glioma or neuroblastoma cells \textit{in vivo} to high doses of etoposide, a chemotherapy drug. Alternate day dieting improves normal cell and tissue survival in cancer patients treated with oxidative damage-producing chemotherapy drugs. An intriguing idea for employing hormesis to improve health is based, in large part, on the observation that cancer incidence is lower in countries where there is a high infectious disease burden. Hormetic phenomenon has been reported for several different kinds of stress including heat, oxidative stress, ionizing radiation, starvation, as well as treatment with various different chemicals and synthetic compounds. The challenge is selecting the optimal dose, since all treatments are toxic if either the dose or the length of exposure exceeds a critical value.

\textbf{Senescence}

A cellular stress response that results in the stable arrest of old, damaged or pre-neoplastic cells. Oncogene induced senescence is tumor suppressive but can also exacerbate tumorigenesis through the secretion of proinflammatory factors from senescent cells. Drugs that selectively kill senescent cells, termed “senolytics,” have proved beneficial in animal models of many age-associated diseases. Oubain (Strophanthus), a cardiac glycoside, is a senolytic agent with broad activity. Cardiac glycosides synergize with anti-cancer drugs to kill tumor cells. Oubain also eliminates senescent pre-cancerous cells. Thus, cardiac glycosides may be effective anti-cancer drugs acting through multiple mechanisms. Given the broad range of senescent cells targeted by cardiac glycosides, they have the potential to be used against age-related diseases! Strophanthus extracts, as a hormetic response, have opposite effects whether the substance is given in concentrated or very diluted (potentized) form. At very low levels, Strophanthus stimulates the so-called sodium/potassium pump which enables more potassium to enter the cells. Given the broad range of senescent cells targeted by cardiac glycosides, their use against age-related diseases warrants further exploration.

\textbf{Homotoxicology}

In addition to the above mentioned senolytics, which suggests Strophanthus Comp, and Placenta comp. premature aging formulas which address various impregnation and degeneration phases, include: Galium Heel as the foremost suggestion, along with the following: Barijodeel, Chelidonium-Homaccord, Cralonin (senile heart), Ginseng comp (for revitalization), Vertigoheel (dizziness) and shown to improve peripheral circulation, Selenium-Homaccord (deficiency of memory), Traumeel tablets (regeneration of the sulphide enzymes), Aesculus comp (improvement of the peripheral cerebral circulation), Syzygium comp (for diabetes mellitus), Aurumheel drops for hypotonia and circulatory insufficiency, Molybdän comp (trace element donor), Testis comp ampules (for males) or Ovarium comp (for females), Cerebrum comp (vegetative regulation and cerebral functions), Cor comp (coronary/circulatory functions), Discus comp ampules (skeletal system, also attrition phenomena of the joints, arthrosis, osteochondrosis etc.) Zeel (arthrosis), Hepar comp (hepatic function), Mucosa comp (remedy for affections of the mucosa), Solidago comp (remedy for disorders of the renal functions), Thyreoidea comp (stimulation of the thyroid functions, e.g. in precancerous dermatosis). Also critical to this system of medicine, are the mitochondrial catalysts: Coenzyme comp ampules (improvement of the enzyme functions), for recognizable precancerous dermatosis; Ubichinon comp ampules and
Glyoxal comp (contains methyl glyoxal and oxalaldehyde -carbonyl group series which, according to Koch, have a far-reaching action on many degenerative diseases: Deblocking blocked energy-producing systems of the cells, depolymerization of homotoxins and carcinotoxins, by action of free radicals, via quinones and through free carbonyl groups. Glyoxal and methylglyoxal, catalysts, are intriguing in that they act as photoamplifiers resulting in increased production of light and re-establishment of coherence. Methyglyoxal D6&D9 have a wavelength of 300 nm.

**Antioxidant Therapies**

Bodies are composed of trillions of highly specialized cells, that vary greatly in structure and function. Free radicals are produced in cells due to normal respiration and assimilation of sugar. Atoms normally contain an even number of paired electrons. During chemical reactions, electrons become unpaired momentarily, allowing the reaction to occur. If for some reason, an electron becomes separated, it will cause an imbalance and become a free radical. This unbalanced free radical can damage cells that do not have sufficient enzyme coatings. These enzyme coatings are formed by catalase, reductase, glutathione peroxidase and superoxide dismutase. In healthy cells, these enzymes prevent cell damage from free radicals. When cellular health declines, free radicals are able to attack and cause damage, resulting in degenerative disease. The oxidation products from biomolecules such as nucleic acids, lipids, proteins, sterols, and sugars increase with age. Plants have indefinite life span due to the presence of various antioxidants in the green parts of the plant, whereas the animal body does not have any integral mechanism to synthesize antioxidant enzymes. A major age promoting factor is reactive oxygen species (ROS) and free radicals, such as singlet oxygen, hydroxyl radicals, and hydrogen peroxide and superoxide anions. The aging process accelerates with the increase in oxidative stress because the level of prooxidants increases against antioxidants. The antioxidative nutraceuticals can be used for reducing the level of ROS and free radicals, leading to the deceleration of aging process. Damage caused by free radicals can be limited by supplementation with free radical scavengers, such as Vitamin E, Vitamin C, Vitamin A and beta carotene, and selenium.

**Sulphur**

Sulfur is an essential macronutrient which can be found in nearly all mammalian proteins, the building blocks of the body’s tissues and organs. Structural proteins particularly high in sulfur include collagen and keratin. Deficiency may contribute to age-related problems like wrinkles, sagging skin, thin and fragile hair or painful joints. Sulfur in the body is mostly found in two amino acids – cysteine which can be synthesized by the body, and methionine which cannot. Supplementation should include organic sulphur, which is critical for the production of many essential amino acids, such as glutathione for respiration and methionine for liver function. The best sources are blue-green algae, wheatgrass juice and aloe vera, as well as fresh fruit and vegetables, and raw milk. There has also been extensive medical testing on the use of MSM in the diet. Some diseases once considered irreversible, such as emphysema, have been overcome through use of supplemental MSM, along with skin and hair issues, diabetes, arthritis, candida, chronic fatigue syndrome, and low energy, amongst others. MSM helps with the oxygenation of cells and free radical scavenging and is thus anti-aging.
HGH
Human Growth Hormone (hGH or HGH) a.k.a. Somatotropin is abundant in young and growing creatures and declines with age. HGH is a peptide hormone that stimulates growth, cell reproduction, and cell regeneration. GH also stimulates production of IGF-1 and increases the concentration of glucose and free fatty acids. It is a type of mitogen which is specific only to the receptors on certain types of cells. GH is an amino acid, single-chain polypeptide that is synthesized, stored and secreted by somatotropic cells within the lateral wings of the anterior pituitary gland. In humans, levels of natural HGH at age 60 is 80% lower than the amount it is producing at age 20. A group of patients put on HGH demonstrated slowed signs of aging by an average of ten to twenty years, compared to the control group. HGH benefits only if natural HGH production is deficient. Supplements containing real HGH in pills and capsules do not exist. Oral supplements contain amino acids and herbs that stimulate production of HGH naturally: Amino acids: Arginine can triple HGH levels, even into old age and foods rich in arginine are sesame seeds, lobster, elk, moose, goat and ostrich. Ornithine is as effective as arginine, can as much as triple HGH levels, especially when used in combination with arginine, lysine, and glutamine. Lysine plus arginine is much more effective than just arginine alone. Glutamine: is the amino acid used most during times of stress, and it's the key to metabolism and maintenance of muscle, cell division, and cell growth. It increases energy and mental alertness, boosts immunity, lowers cholesterol, lowers blood pressure, reduces instances of arthritis, diabetes, heart disease, and more. Pyroglutamate is an amino acid present in large amounts in the human brain, cerebrospinal fluid, and blood, shown to be effective in alcohol-induced memory loss, and in improving memory functions in subjects affected by age-related memory decline. Tyrosine is used by the thyroid gland for the production of Thyroxine, another vital hormone shown in clinical studies to help reduce fatigue and depression, as well as regulate growth and metabolism. L-Valine is found in high concentration in the muscles and must be acquired through food or dietary supplements. It has a stimulating effect and is needed for muscle metabolism, repair and growth of tissue and maintaining the nitrogen balance in the body. GABA, or Gamma-Aminobutyric Acid, is classified as a neurotransmitter, which means it helps nerve impulses cross the synapses (gaps) and communicate better and has a number of positive effects on the nervous system. GABA promotes relaxation, restful sleep and a sense of well-being, as well as lowers the blood pressure.

Herbs that Stimulate Hgh Production
Tribulus Terrestris Extract - used as traditional medicine to treat sexual dysfunction and male infertility. Studies have confirmed the herb's beneficial effect and have suggested that Tribulus acts by increasing the level of dehydroepiandrosterone (DHEA).

Astragalus Root Extract- often used to enhance metabolism and digestion, strengthen the immune system and help wounds and injuries heal. It is also believed to help improve the function of the lung, adrenal glands and the gastrointestinal tract, increase metabolism, sweating, and reduce fatigue.

Ginkgo biloba extract increases endothelial progenitor-cell (EPC) numbers and functional activity. Increased EPC numbers and activity are associated with the inhibition of EPC senescence, which involves activation of telomerase. Ginkgo biloba extract dose-dependently
prevented the onset of EPC senescence and increased proliferation of EPCs, which may be important for potential cell therapy.

**Silymarin** Rapamycin, an antiproliferative agent used on drug-eluting stents, induces endothelial progenitor cells (EPCs) senescence through telomerase inactivation and may impair the reendothelization of an injured arterial wall, leading to thrombosis. Silymarin, a complex of flavonolignans with hepatoprotective and antioxidative properties, can protect EPCs against rapamycin-induced senescence. Silymarin increased telomerase activity 3-fold, reduced the number of senescent cells, and increased EPC proliferative activity (up to 64%) in comparison with cells cultured with rapamycin alone. Moreover, silymarin partially prevented impairment of tubular-like structure formation in Matrigel by rapamycin. Thus, silymarin counteracts the inhibitory effects of rapamycin in EPCs. Silymarin may protect EPCs against the antiproliferative effects of rapamycin and restore their reconstructive ability.

**Turmeric** (curcumin)- the “one-stop shop” herb for longevity! It prevents telomere shortening and may promote elongation by increasing telomerase expression; preserves brain health by preventing age-related brain damage; reduces oxidative stress; promotes mitochondrial homeostasis; increases AMPK activity.

**Panax Ginseng** increases resistance to the effects of stress and improves circulation and mental functioning. Stress reactions include increased acidity of the body chemistry, back pain, Crohn's disease, depression, chronic diarrhea, digestive disorders, hair loss, headaches, hypertension or high blood pressure, impotence, insomnia, TMJ syndromes, nervous and anxiety disorders, obsessive compulsive behaviors, various skin conditions, and ulcers. Ginseng is great for people who have thirst, hot flashes, people who crave excess sweets and have excess hunger.

**Functional Foods**
Published studies for decades, correlate diet and some chronic diseases, and have shown the extraordinary possibilities of foods to improve health. Main objectives of functional food science, called Nutritional Genomics or Nutrigenomics, is to identify beneficial interactions amongst foods or specific ingredient, and prove the mechanisms of action. The science is aimed at generating true wellness- helping to improve vitality and extend both quantity and quality of the lives of our patients.

**Deer Velvet Antler (VA)** is a typical traditional animal medicine, used for 2000 years as a healing substance and is widely beneficial, including stimulating HGH production. A powerful source of natural IGF-1 is thought to be VA from Cervus Elaphus, a deer raised commonly in New Zealand. It is also a natural source of glucosamine, chondroitin and collagen, which are components of scaffolding of the matrix. VA has been reported to have pharmacological activity, such as immunomodulatory, anti-inflammatory, wound-healing, anticancer and antiaging effects. Lung inflammation is characterized by damage to the alveolar-capillary barrier and increased lung tissue permeability, thereby resulting in pulmonary edema, the infiltration of neutrophils into the alveolar space, and hypoxia, which finally affect breathing function. A study investigated an aqueous extract of velvet antler (AVA) in mice with induced lung inflammation. Inhibition of NO, TNF-α, IL-1β, IL-6, and IL-10 productions, with improvement of histological alterations and enhanced antioxidant enzyme activity in lung tissues was seen. AVA treatment in
concentration dependent manner significantly reduced ROS production, and reduced pulmonary edema, proinflammatory cytokine production, and phosphorylation of NF-κB/P65, IκB-α, and MAPKs signaling pathways. The protective effect of AVA may be related to its ability to depress ROS generation, enhance antioxidant status, and regulate proinflammatory cytokine production, and could be considered as a promising ingredient in functional foods or nutraceuticals against inflammatory diseases.

**Ozone**, A very small amount of ozone is necessary to trigger useful biological effects is in line with the concept of the hormesis theory discussed earlier. Interestingly, about 2/3 of patients describe a sense of wellness and physical energy throughout the ozone therapy, the euphoria may be due to improved oxygenation and/or enhanced secretion of growth hormone, ACTH-cortisol, and dehydroepiandrosterone. The hypothalamic area may benefit from release of serotonin and endorphins, as observed after intense dynamic exercise, thus modifying the stress and anxiety response. Ozone has been used as a Biological response modifier, with the following benefits: Increasing the levels of anti-oxidants of the most potent radical scavenger and cell wall protectors: glutathione peroxidase, catalase and superoxide dismutase, stimulating GSH regeneration via glutathione and thioredoxin reductase, increasing the levels of enzymes that detoxify oxidants and electrophils (catalase, SOD, GPx, NQ01, H0-1), increasing the levels of Phase 2 detox enzymes, inhibiting cytokine-mediated inflammation, reducing iron overload and subsequent oxidative stress, recognizing, repairing and removing damaged proteins, protecting from apoptosis induced via oxidative stress, increasing DNA repair activity. Ozone therapy as antimicrobials, works by disrupting the integrity of the bacterial cell envelope through oxidation of the phospholipids and lipoproteins, inhibiting fungi cell growth at certain stages, damaging the viral capsid and upsetting the reproductive cycle by disrupting the virus-to-cell contact with peroxidation. There is an increase in the red blood cell glycolysis rate, an increase in the amount of oxygen released to the tissues (implications in Coronavirus therapy?), activation of Krebs cycle by enhancing oxidative carboxylation of pyruvate, stimulating production of ATP (Energy). Ozone increases production of interferon and significant output of tumor necrosis factor and interleukin-2. The production of IL-2 launches an entire cascade of subsequent immunological reactions. (Activation of the immune system). It stimulates the neuroendocrine system and therefore produces a feeling of well-being and decreases inflammation through the activation of transcription factors, including nuclear respiratory factors (Nrf) Nrf2 and subsequently the suppression of NFkB (pro-inflammatory signaling pathway. Nrf2-dependent antioxidant response has been shown to protect against oxidative stress related diseases such as cancer, neurodegenerative diseases, cardiovascular disease, infections, lung emphysema, and inflammation. In short, Ozone therapy combats aging.

**Omega-3s**, essential fatty acids (EFAs) are fatty acids found primarily in cold water fish and algae, vital to flexibility and fluidity of all cells. EFAs are required for the normal growth and repair of the skin, blood vessels, and nerve tissues, and build, maintain, and repair cell membranes. Without healthy cell membranes, none of the other miraculous activities of cells would be possible. EFAs, in a dose dependent manner, may have a profound anti-aging effect, as they slow down the shortening of telomeres, thus protective against aging on a cellular level. Research subjects with the least amount of DHA and EPA experienced the most rapid rate of telomere shortening. However, those with the highest levels of the omega-3 fatty experienced the slowest rate of telomere shortening. "Levels of DHA+EPA were associated with less telomere
shortening and each 1-standard deviation increase in DHA+EPA levels was associated with a 32 percent reduction in the odds of telomere shortening," the authors wrote in their study, and "omega-3 fatty acids may protect against cellular aging in patients with coronary heart disease."

**Micro and Macro-Algae** have been studied extensively for nutrient potential. Algae, such as *Aphanizomenon flos aquae* (AFA) contain a high concentration of vitamins, especially of the B group. Vitamin B12 is essential for the synthesis of nucleic acids, erythrocytes, and for myelin formation. Thus, deficiency can result in nervous system-associated symptoms. Due to the volcanic origin of the lake, AFA contains a wide and complete spectrum of minerals and trace minerals. It is rich in pigments such as carotene, beta-carotene, and chlorophylls. Of particular relevance are its phycocyanins, with significant antioxidant, anti-inflammatory, and antiproliferative properties. As noted previously, AFA contains significant amounts of phenylethylamine (PEA), an endogenous molecule that is considered a general neuromodulator lacking in certain forms of depression and affective disturbances. It supplies EFAs in an all-natural form, with dynamic lubricating qualities that can actively increase the solubility of cholesterol deposits, thereby helping to maintain healthy blood cholesterol levels. The Total Lipid (fat) Content Averages c. 4.4% of dry weight with Total Saturated Fat c. 43% and Total Unsaturated Fat 57%, Total Omega-3 Essential Fatty Acids 38% comprised of Alpha-Linolenic Acid (ALA) 37%, Eicosapentanoic Acid (EPA) 0.4%, Docosapentaenoic Acid (DPA) <.1%, and Docosahexaenoic Acid (DHA) <.1%. Total Omega-6 Essential Fatty Acids are at c. 8% w/ Linoleic Acid (LA) 8% and Arachidonic Acid (AA) 0.1%. AFA is an ultimate photosynthesizer, contains fatty acids in an ideal balance (more ALA). Researchers at Massachusetts General Hospital who studied its fat content conclude that AFA is a good source of the most valuable fatty acids and “should be a valuable nutritional resource.” Interestingly, a study revealed that AFA raises the levels of the good fatty acids far more than would be expected based on its ALA content, which suggests that the range of micronutrients—was helping the study animals to utilize the fatty acids they were getting from other sources as well as those from the algae. The “good” fatty acid (ALA, EPA, DHA) levels increased, and the levels of the arachidonic acid decreased.

**Porphyra**, Red algae (Rhodophyta) are exclusively marine, found in deep waters attached to rocks. They are magnificent bioreactors, as they contain multitudes of bioactive compounds with antioxidant, antibacterial, antiviral, anticarcinogenic, and other properties, among which vitamin E (or α-tocopherol) and carotenoids are found within the fat-soluble fraction. The most powerful water-soluble antioxidants found are polyphenols, phycobiliproteins and vitamins (vitamin C). Phycoerythrin and phycocyanin. The red color of Porphyra results from the pigments which mask the other pigments, Chlorophyll a, beta-carotene and a number of unique xanthophylls. Phycocyanin is related to the human pigment bilirubin, required for healthy liver function and digestion of amino acids, and has an immune system boosting or anti-cancer effect. In one study, phycocyanin was given orally to mice with liver cancer. After five weeks, 90% of the phycocyanin group survived, but only 25% of the control group survived. After eight weeks, 25% of the phycocyanin group still survived, zero of the control group was alive. In another study, the white blood cell count (lymphocyte activity) of the phycocyanin group was higher than the control group. A research project found that seaweed extracts can boost the immune system by stimulating the body’s B cells formed in the lymph nodes, spleen, thymus, and tonsils. Phycocyanin affects bone marrow stem cells and stimulates hematopoiesis, emulating
erythropoietin (EPO), which is produced by healthy kidneys and regulates bone marrow stem cell production of red blood cells. Phycocyanin regulates white blood cell production, even when bone marrow stem cells are damaged by toxic chemicals or radiation. Seaweed is also high in soluble fiber that may have antioxidant, as well as immunological activity, and reduces the risk of colon cancer, constipation, obesity and diabetes. Polysaccharides in algae inhibit viruses. Porphyran, a sulphated polysaccharide, is anti-tumor and anti-oxidizing. This antioxidant activity may be helpful as an anti-aging strategy, given that aging is associated with a decrease in antioxidant status and increases in lipid peroxidation. The alginic acid found in sea vegetation acts as a chelating agent for heavy metals and the radioactive strontium 90 which is now found in our food chain. Algae help dissolve fat and mucus deposits where the body frequently stores environmental contaminants, and can also have an alkalizing effect, making it ideal for an often over acidic Western diet, which contributes metabolically, to cancer. Although seaweeds are not a conventional source of energy, their PUFA content can be as high as those of terrestrial vegetables, and lipids comprise 2-3% of dry weight of Porphyra, including linolenic acid, arachidonic acid and eicosapentaenoic acid. Furthermore, the ω 6/ω 3 ratio, was at most 1:32, and thus, could help to correct an imbalance. These ω3 fatty acids have demonstrated their effect on reducing coronary diseases, thrombosis and arteriosclerosis and certain antiviral activity. Sterols help to reduce cholesterol levels in blood, and have anti-inflammatory, antibacterial, antifungal, antiulcerative, and antitumoral activity. Porphyra and other sea algae, have a broad spectrum of vitamins and minerals with life sparing effects that contribute to longevity.

**Colostrum**, Regular use of bovine colostrum brings about a wide spectrum of anti-aging benefits, including: bone growth & density, muscle growth & support, anti-cancer, increased insulin sensitivity, anti-obesity, anti-inflammatory, cholesterol reduction, anti-hypertensive, antimicrobial, anti-viral, gastrointestinal tissue defense, improved cognitive function w/ delayed onset of Alzheimer’s symptoms. Chronic stress, discussed previously, hypothesized as a contributing factor for low brain serotonin, has been associated with poor memory performance. Alpha-lactalbumin significantly improved memory test performance in stress-compromised individuals and may be implicated in improvement of various age-related diseases, including neurocognitive disorders, d/t the ability of alpha-lactalbumin to boost glutathione (the master antioxidant) levels.

**Royal jelly (RJ)** is a functional food with a range of pharmacological activities: antioxidant, anti-inflammatory, antitumor, antimicrobial, anti-hypercholesterolemic, vasodilative, and hypotensive, and has been widely used to treat several health conditions such as diabetes mellitus, cardiovascular diseases, and cancer, amongst others. The anti-aging effect of RJ possibly originates from its antioxidant and anti-inflammatory properties, which improve glycemic status, lipid profiles, and oxidative stress—and hence can prevent the occurrence of various debilitating metabolic diseases.

**Fruits and Vegetables** are great sources of antioxidants that fight cell-damaging free radicals. Those with higher levels of antioxidants such as Vitamin C, E and selenium tend to have longer telomeres. Useful foods include carrots, sweet potatoes and yams, winter squash and green leafy vegetables, and tomatoes, citrus, cantaloupe and potatoes with skins provide plenty of Vitamin C. Soy, nuts, and seeds offer Vitamin E and whole grains provide selenium.
Berries
Emerging science supports therapeutic roles of strawberries, blueberries, and cranberries in metabolic syndrome, a prediabetic state characterized by several cardiovascular risk factors. Cranberries and blueberries have more antioxidants pound-for-pound than most foods on the planet, and support good health by eliminating free radicals from the bloodstream, where these unstable molecules wreak havoc on cellular functions, leading to diseases like heart disease, cancer, and dementia. A 2005 study on polyphenols found that these extracts can reduce age-related declines in learning, memory, motor performance, and nerve signaling. Strawberries lower total and LDL-cholesterol, but not triglycerides, and decrease biomarkers of atherosclerosis; blueberries lower systolic and diastolic blood pressure and lipid oxidation and improve insulin resistance; and low-calorie cranberry juice selectively increases HDL cholesterol, decreases biomarkers of lipid oxidation (oxidized LDL) and inflammation (adhesion molecules) in metabolic syndrome. These observations are due to up-regulation of endothelial nitric oxide synthase activity, reduction in renal oxidative damage, and inhibition of the activity of carbohydrate digestive enzymes or angiotensin-converting enzyme by these berries. Plant polyphenols are associated with several cardiometabolic health benefits, such as reduced postprandial hyperglycemia. Strawberry and cranberry polyphenols (SCP) effects on insulin sensitivity, glucose tolerance, insulin secretion, lipid profile, inflammation and oxidative stress markers was studied in insulin-resistant overweight or obese human subjects. Insulin sensitivity increased in the SCP group as compared with the Control group and had a lower first-phase insulin secretion response as measured by C-peptide levels.

Cranberry has some surprising benefits, as it turns out, and I would like to focus on it a bit here, because I had considered it primarily for urinary tract issues! Cranberries were found to have the highest antioxidant activity of other fruits studied, and contain considerable concentration of rare A-type PACs. Cranberry attenuates progression of NAFLD to NASH in high fat-fed obese mice. It improves blood flow and vascular function in subjects with coronary artery disease, with improved brachial artery flow and improvements in vascular stiffness. The red pigments have been shown to inhibit biofilm formation, which has body wide implications, given the prevalence of biofilms in chronic disease. These proanthocyanidins [PACs] have been reported to possess antimicrobial, anti-adhesion, antioxidant, and anti-inflammatory properties, and prevent the attachment of pathogens to host tissues, and can inhibit the formation of biofilms in the mouth and urinary tract. As noted previously, oral disease is a large contributor to chronic pathologies. Bacteria and inflammation play causal roles in most periodontal diseases. Enzymes called Matrix Metalloproteinases (MMPs) are secreted in a type of inflammatory-disaster response, and are responsible for oral tissue degradation, dental caries and cancers of the mouth. A-type cranberry proanthocyanidins may be useful in inhibiting the secretion of MMPs in patients with periodontitis, both in production of these enzymes and their catalytic activity and are useful for the prevention and treatment of tooth decay and periodontal disease. Cranberry PACs stopped the gum disease pathogen, Porphyromonas gingivitis, from adhering and forming biofilm, which markedly reduced its invasiveness, and prevented biofilm formation by Candida albicans, the causative agent of thrush and yeast infections. Cranberry juice also benefits urinary tract by increasing the alkalinity of urine. PACs have an inhibitory effect on bacterium responsible for causing urinary tract infections, Staphylococcus epidermidis, Staphylococcus aureus, clinical methicillin-resistant S. aureus (MRSA), Staphylococcus saprophyticus and Escherichia coli. and also inhibited biofilm production. Cranberry has a moderate antibacterial effect against
periodontal pathogens in biofilms, by affecting bacteria adhesion in the first 6 h of development of biofilms. This would suggest that daily dosing would be of value.

Flavonoids and their subset, bioflavonoids, possess a spectrum of antiviral activity against certain viruses, inhibiting infectivity and/or replication of the virus. Cranberry was tested against two strains of influenza virus and found that inhibitory effect was observed, particularly with repeated doses, against herpes infections by preventing adsorption of the virus by target cells. Type-A PACs targeted specific viral glycoproteins, resulting in loss of infectivity of HSV particles. A 2013 study, compared thirty-five varieties of blueberry with bilberry, black currant, and cranberry, rating their relative effectiveness against the influenza virus and bilberry, cranberry and blackcurrant have the greatest antiviral effects.

**Brain Health**

Glycation is associated with several neurodegenerative disorders, including Alzheimer's disease (AD), where it potentiates the aggregation and toxicity of proteins such as β-amyloid (Aβ). The anti-glycation and neuroprotective effects of several polyphenol-rich fruits, including berries, were studied, in regard to their free radical (DPPH) scavenging and reactive carbonyl species (methylglyoxal; MGO) trapping, anti-glycation, anti-Aβ aggregation and, murine microglia (BV-2) neuroprotective properties, and were shown to be superior at free radical scavenging, reactive carbonyl species trapping, and anti-glycation effects compared to their respective ACFs. For all the amazing benefits of cranberries, perhaps their most promising potential lies in the field of cancer prevention and treatment. This is covered more fully in the Cancer Lecture. There is an interaction of cranberry and other fruits, with dietary macronutrients in modulating life span. These many studies should provide insight for the design of effective interventions with cranberry and other botanicals for promoting healthy aging.

**Walnuts** Protect and Preserve Telomere Length. DNA information essentially writes the code for health or disease into every cell, making the length and integrity of telomeres vital to healthy cell replication. Leukocyte telomere length (LTL) is positively correlated with lifespan, and shorter LTL is associated with an increased risk of age-related disease, and therefore considered a reliable biomarker of aging.

Walnuts are an excellent source of PUFAs, known to have beneficial effects on the heart. Studies have been conducted on the effects of PUFA consumption on telomere length, primarily derived from fish oils, a source that is less sustainable than tree nuts, Walnuts contain high amount of alpha-linolenic acid and a rich matrix of antioxidants, namely polyphenols and vitamin E, which have also been related to maintenance of LTL.. Walnuts benefit the heart, brain, bones and more, and have been shown to reduce the risk of certain cancers, and can even help improve the stress response.

**Immunosenescence (Immune Effects of Aging) and Thymus**

A strong and vigorous immune system is critically important, and suboptimal nutritional intake, inadequate digestion and elimination combined with decreased liver function compound additive and cumulative detrimental effects on immune function, and many of the causes of compromised immunity are also involved in aging. The thymus gland (TG) is a small gland in the upper chest. After puberty, under the influence of many factors, including adrenal and sex hormones, the
active TG cells begin to die off, with much of the TG tissue being gradually replaced by fat and connective tissue. "The involution [shrinkage] of the thymus gland is one of the cardinal biomarkers of aging.". TG is the key regulator of immunity and thymic senescence precedes that of other organs, resulting in an altered development and exportation of naive T cells to the periphery. The primary hallmarks of immunosenescence are dampened immune responses to new infection or vaccination, and diminished anti-tumor immunosurveillance, including altered immune response phenotypes in activated T cells, increased memory T cell accumulation, and an inverted T lymphocyte subset ratio. T cells Immunosenescence is termed “cellular exhaustion,” with a loss of co-stimulatory surface molecule CD28 and other features of cellular senescence, and TG involution is a dynamic process that impacts overall T cell development and central T cell tolerance establishment throughout life. Immunosenescence and inflammaging describe two opposing arms of the aged immune system: immune insufficiency, with regard to infection, vaccination, and tumor surveillance, coupled with increased self-reactivity and chronic, systemic inflammation, and are dependent on an aging TG. Studies have shown a preservative and antiaging effect of embryonic and early fetal calf thymus which not only affect the immunological system, but also interfere with the process of organ aging. Thymus extracts has been associated with significantly increased longevity of treated mice and may be useful in preserving antioxidant activity, decrease the typical response to aging in the liver and possibly other organs, and may influence longevity in some animals. A study on TP5 (a synthetic thymopoietin) found that in treated animals significant changes were observed in T-lymphocyte, but not B-lymphocyte, populations, as well as in levels of bacteria with periodontopathic potential, which may explain its usefulness in feline stomatitis? TP5 enhances latex particle phagocytosis, with no apparent effect on chemotaxis. In patients with atopic dermatitis, TP5 significantly increased proportions of suppressor T-cells but had no effect on helper T-cells or B-cells. In three patients with primary T-cell defects, TP5 increased the proportions of helper T-cells from 12 to 13% initially to 44 to 50% during treatment. The thymus is also fundamental to the integration and proper interaction between the immune, endocrine and central nervous systems (CNS) and plays an indirect but considerable role within the neuroendocrine network. A number of homeostatic processes governed by the hypothalamopituitary axis are involved, including regulating tissue metabolism. In summary, decreased cellular immunity is directly associated with increased aging. Liquid thymus extracts have been shown to be beneficial in some clinical conditions affecting the elderly. They have been shown to have extra-immunological benefits on other organs and systems. The use of thymus extracts may be an important, but overlooked, option in treating the possibly preventing many clinical conditions of the aging person.

**TRIM (Thymus Regeneration, Immunorestoration and Insulin Mitigation)** was a trial which recruited nine white men aged between 51 and 65 years old and dosed them with the three-drug combo for a year: growth hormone for restoration, and DHEA and metformin to combat high blood sugar. (The latter two chosen for their promising anti-aging effects in animals). Regular blood samples analyzed immune cell counts, and medical imaging checked the composition of their thymus. At the end of the trial, not only were thymic cell changes reversed, the participants’ thymus also showed less signs of fat—they’d been replaced by healthy, regenerated tissue. The authors don’t know the mechanism of action but surmise that they’re acting on the same molecular pathways as restricting calories, which is also a strong de-aging intervention in animals.
Summary
In the dynamics of aging-related decrease of healthspan and lifespan, the production of free radicals along with exposure to various stresses (e.g., pollution, poor nutrition, and psychological stress) increases aging leading to oxidative stress and is associated with reduced production of antioxidant enzymes and activation of inflammatory pathways. Both oxidative stress and chronic inflammation lead to a trail of cellular and molecular alterations: telomere attrition, epigenetic alterations, genome reduced proteostasis, disturbed nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. Such age-related physiological alterations result in poor health and loss of function out of increased occurrence of various metabolic and neurodegenerative disorders. Age-related disorders are associated with increased mortality and premature death. The nutrients and supplements noted in this paper, suggest directions for improving the longevity and quality of life for our patients (and ourselves!)

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Cancer and Nutraceuticals - Emerging Therapies
PJ Broadfoot, DVM

Objectives
- To review some selected herbs, supplements, and nutraceuticals that have made their way into integrative practices.
- To review some practical approaches to adjunctive care will be shared in this lecture.

About Telomeres
Cancer is a scourge of modern-day medicine. There is an overwhelming abundance of ongoing research and the subject is too broad to address in a single lecture. One of the intriguing directions in cancer studies is the role of telomeres and therapeutic approaches that may affect the genetic code and replication of neoplastic cells. Tissues are made of cells that perform specific functions. Cells are made up of smaller components called organelles, one of which is the nucleus, containing the chromosomes holding all the genetic information, comprised of the bases: Adenine (A), Guanine (G), Cytosine (C), and Thymine (T), that make up the sequences needed to form and duplicate their cells via mitosis. All cells have a programmed lifespan by which they are synthesized, multiply, and eventually undergo apoptosis (cell death) when they are no longer functional. Each time a cell divides, the double-stranded DNA separates in order for the genetic information to be copied. When the copy is complete and mitosis begins, the place where the cell is snipped apart is at the telomere, and the DNA coding is duplicated but not the telomere. To ensure that information is passed correctly from one generation to the next daughter cells, each chromosome has a special protective cap at the end of its “arms” likened to the ends of shoelaces, called a telomere, made up of repeating DNA sequence (for example, TTAGGG) at the end of the chromosomes, and can reach a length of 15,000 base pairs. These function by preventing chromosomes from losing base pair sequences at their ends, and prevent chromosomes from unraveling, sticking to each other, or fusing into a ring. Each time a cell divides, some of the telomere is lost (usually 25-200 base pairs per division), and when the telomere becomes too short, the chromosome reaches a “critical length” can no longer replicate, making the cell malfunction, become cancerous or die via apoptosis. A good analogy is to consider cellular replication as an old-fashioned photocopy machine: the more a cell copies itself, the more blurry and misaligned the image becomes, until, finally, the genetic material of the cell (DNA) begins to fracture and the cell itself becomes a pale copy of the original.

Successive mitoses progressively degrade the genetic material, specifically the telomere. A well-known "molecular clock" is telomere shortening, as the number of times a cell can divide is bounded by a phenomenon known as the Hayflick limit which dictates that the average cell will divide between 50 to 70 times before apoptosis, depending on the length of the telomeres, which shorten just before the cell divides. Scientists can use the length of a telomere to determine the age of a cell and how many more replications it has left. As cellular division slows, it undergoes a progressive deterioration known as senescence, which we commonly refer to as aging. Cellular senescence explains why our organs and tissues begin to change as we grow older. In the end, cells are "mortal" and subject to senescence. All, that is, but one. Cancers cells are the one cell type that can truly be considered "immortal," because they do not undergo apoptosis, but can continue to multiply without end. Shortened telomeres are associated with many types of cancer, including pancreatic, bone, prostate, bladder, lung, kidney, and head and neck. Shortened
Telomeres and reduced telomerase activity have been identified in prostate carcinogenesis, ovarian cancer, genomic instability, and breast cancer pathogenesis. Research is showing more and more evidence that loss of telomere function, either by altering telomere binding proteins or by loss of telomeric sequences, is associated with the deterioration of cells leading to increased aging and disease. Shorter telomeres are associated with, and often predict co-morbid conditions including cardiovascular disease, type 2 diabetes, dementia, cancer, and increased mortality, independent of chronological age.

**Telomerase**
Cancer cells are malignant cells which multiply until they form a tumor that grows uncontrollably. Assuming that spontaneous mutations can occur with approximately each 20 cell divisions (about 1 million cells), and assuming that mutations provide a premalignant cell with a slight growth advantage, then after 60 to 100 doublings (at least in cell culture conditions) the cells would contain some very short telomeres that are uncapped and initiate DNA-damage signaling, which presents a potential anticancer senescence “brick wall” that protects large long-lived species, such as humans, from the early onset of cancer. 8 to 15 key oncogenic changes are probably required for a normal cell to become a cancer cell, but senescence can be bypassed, leading to telomerase activation and cancer progression. Telomere activity is controlled by two mechanisms: erosion and addition. Erosion occurs each time a cell divides, while addition is determined by the activity of telomerase, a.k.a. telomere terminal transferase, which is an enzyme made of protein and RNA subunits. Transfection with the telomerase gene is sufficient to greatly extend the replicative life span of normal somatic cells. In telomerase-negative cells, telomere length can be viewed as a cumulative history of preceding cell division as well as a predictor of future capacity to divide. Telomere shortening activates the senescence program by triggering the cell-cycle control/tumor suppressor proteins Rb, p16, p21, and p53. When tumor suppressor protein function is deficient, due either to mutation or corruption by viral oncoproteins (e.g. human papillomavirus proteins E6 or E7), cells lose their senescence signaling machinery. Without such growth-braking machinery, cells may continue to proliferate despite critically shortened telomeres. A genomic crisis ensues, characterized by genetic instability with chromosomal fusions and rearrangements. Cellular survivors may establish mechanisms to repair critically shortened telomeres and maintain telomere length, allowing growth to resume.

Telomere maintenance in such cells is performed by telomerase- a ribonucleoprotein reverse transcriptase (hTERT) that replaces telomeric DNA otherwise lost during standard Watson-Crick chromosome replication. Although the telomerase gene is inactive in most adult somatic cells, the gene can be reactivated during crisis. Telomerase preferentially lengthens the shortest telomeres, preventing mutations, rearrangements, and/or fusions. Thus, cells that survive crisis, acquire telomerase activity, or other telomere lengthening tools necessary for long-term genomic stability. Since the majority of human tumors show telomerase activity, crisis survival with reactivation of the telomerase gene is thought to be a common event in malignant transformation. Telomerase is inappropriately expressed in roughly 85% of cancers, and the level of its activity is higher in advanced and metastatic tumors. Telomerase confers cellular immortality through the addition of TTAGGG tandem repeats to the end of the telomere, thereby maintaining stable telomere length, allowing continued proliferation of neoplastic cells. It is comprised of two main components: hTERT, the catalytic subunit of telomerase which catalyzes the addition of nucleotides; and hTR, an RNA template which acts as a primer, in addition to telomerase-associated proteins. Limiting the growth potential of tumors has been the focus of
chemotherapeutic intervention for decades, and because of their selective expression in neoplastic growths, telomerase and telomeres have become attractive and novel targets for the development of anticancer therapeutics. While germ line cells, stem cells, and select others including cardiovascular cells do express detectable levels of telomerase, it is mostly quiescent, and most normal cells have minimal or no detectable telomerase activity. The specificity of the promoter for the telomerase catalytic gene and the antigenicity of the protein product, hTERT, provide additional strategies for killing telomerase-positive tumor cells. Unfortunately, the strong link between telomerase and cancer has led some to confuse telomerase activation with cancer. A nice review clarified the difference between telomerase, which does not cause growth deregulation, and oncogenes, which do. It also addressed the concept of telomerase repression as a tumor suppressor mechanism early in life, with detrimental tissue degeneration and tumor-promoting consequences late in life. Thus, telomerase inhibition can be therapeutic in cancer patients, while controlled telomerase activation for degenerative diseases may reduce, rather than increase, the frequency of age-related tumorigenesis.

Telomerase in cancer cells is found to be 10-20 times more active than in normal body cells and provides a selective growth advantage to many types of tumors. If telomerase activity was to be turned off, then telomeres in cancer cells would shorten, just like they do in normal body cells, and would prevent cancer cells from uncontrolled division in the early stages. In later stages, the cancer should be removed, then anti-telomerase therapy could be administered to prevent relapse. Telomerase research could reveal valuable information to combat aging, fight cancer, and even improve the quality of medical treatment in other areas such as skin grafts for burn victims, bone marrow transplants, and heart disease. Multiple mechanisms have been proposed for engaging telomerase activity, involving TERT, which may autoregulate itself because it is located very close to the telomere end of chromosome 5 in long lived species. Telomerase is active during early human fetal development, then becomes silenced in most tissues at approximately 3 to 4 months gestation. When telomeres reach a certain initial length (~15–20 kb) during human development, three-dimensional chromatin structures involving telomere position effects over long distances may silence the TERT gene. In cancer, as telomeres shorten, the chromatin-silencing effects may become relaxed, resulting in a permissive environment for telomerase promoter mutations and telomerase reactivation, which is consistent with the observation that almost 70% of all cancers are in the aged. Although telomerase expression is a hallmark of malignant transformation, telomerase activity itself is not inherently oncogenic. In fact, normal human fibroblasts transfected with the human telomerase gene grow indefinitely while maintaining a normal phenotype. Thus, in cells that have a normal complement of tumor suppressors, telomerase can be used safely to prevent senescence. This finding has encouraged attempts to use telomerase to promote cell growth for tissue engineering: involving vascular, skin, pancreatic, and muscle cells. Telomerase may also be useful as a therapy for age-related degenerative diseases that involve irreversible losses of cells from tissues. In principal, telomerase may allow growth of sufficient numbers of cells to repopulate such hypocellular tissues.

**Holistic Approaches**

An inadequate lifestyle and aging are both closely related to chronic inflammation, increased oxidative stress and decrease in telomerase activity. Several studies have linked **chronic stress** to shorter telomeres. A study compared healthy women who were mothers of healthy children (the
control moms) and those who cared for chronically ill children (caregiving mothers). On average, the caregiving mothers had telomeres that were 10 years shorter than the control moms. Another study that examined African American boys found that those who came from stressful environments had telomeres that were about 40 percent shorter than peers from stable homes. A recent study found that those who **exercise** were about 3 percent less likely to have super short telomeres than a person who didn’t exercise, and response is proportional to the amount of exercise. This correlation is strongest among those in middle age, and intense runners had telomere lengths that were, on average, 75% longer than their sedentary counterparts. Thus, factors like exercise may lead to an attenuated telomere attrition and aging via maintenance of good body composition, which likely helps to maintain a good metabolic balance, as well as healthy states of oxidative stress and inflammatory status.

Altered telomere length has been also associated with **night shift work**, in which molecular alterations are potentially related to a higher carcinogenic risk. DNA methylation of estrogen receptor genes and the tumor suppressor genes TP53, CDKN2A, BRCA1, BRCA2 are relevant in key cellular processes such as cell growth, apoptosis, and DNA repair and have been associated with increased breast cancer risk, methylation of repetitive elements and telomere length. Shift work which causes circadian disruption has been classified as “probably carcinogenic to humans” (Group 2A) by the International Agency for Research on Cancer (IARC). The best evidence comes from two prospective cohort studies that showed an increased risk in a subgroup of female nurses after over 20–30 years of rotating night shift work. The mechanisms hypothesized for the association between circadian disruption and the induction and/or promotion of malignant tumors are multifactorial and consequent defects in circadian cell-cycle regulation may favor uncontrolled cell growth; melatonin suppression may lead to an up-regulation of the effects of estrogen upon the breast epithelial cell; sleep deprivation is known to suppress immune surveillance, thus potentially allowing the formation and/or growth of malignant clones.

**Hormesis - Stress to the Rescue**
Data on mice indicate that caloric restriction (specifically short-term starvation) used as an activator of hormesis, increases the stress resistance of normal but not glioma or neuroblastoma cells *in vivo* to high doses of etoposide, a chemotherapy drug. A clinical trial studied alternate day dieting to improve normal cell and tissue survival in cancer patients scheduled to be treated with oxidative damage-producing chemotherapy drugs. An even more novel idea for employing hormesis to improve human health is based, on the observation that cancer incidence is lower in countries where there is a high infectious disease burden, leading to the mimotope-hormesis hypothesis, that the lower incidence of cancer is due to an increased auto-immune response triggered by epitopes (antigens) associated with the infection that mimic the epitopes found on tumor cells.

**Foods with Vitamin and Antioxidant Benefits** are believed to protect cells and their telomeres from oxidative damage. Foods like berries and artichokes can slow down aging and help prevent or reduce cell damage. Foods high in antioxidants **Vitamins C and E** are positively associated with longer telomeres in a dose-dependent manner in women. The addition of physiological concentrations of vitamin C or vitamin E to the culture medium slows down the age-dependent shortening of telomeres as well as decrease in telomerase activity in cell cultures, hence
increasing the life span. Oranges, peppers, berries such as cranberry, Porphyra algae, and kale are among the top vitamin C foods. **Vitamin E** is linked to reduction of DNA damage; slowing of skin aging; upregulation of telomerase; and muscle maintenance. Exposure of cells to tocotrienols enabled them to extend the length of their telomeres, and rejuvenated the telomerase enzyme, while simultaneously preventing damage to DNA. For vitamin E, consider almonds, spinach and sweet potatoes. **Vitamin D3** is crucial for boosting the immune system and activates telomerase activity by as much as 19.2%. D3 is found in cod liver oil, herring, catfish, cooked mackerel or salmon and sardines or tuna canned in oil, and a precursor to Vitamin D is found in deer antler. **Folic Acid** stimulates the activation of telomerase, and is found in lentils, spinach, asparagus, lettuce, avocado, broccoli, and tropical fruits. A useful nutrient is **Acetyl L-Carnitine** found in beef steak, ground beef, pork and bacon.

**Omega-3** fatty acids and fiber help reduce chronic inflammation, which induces cell division, prematurely wearing down telomeres. EFAs, in a dose dependent manner, have a profound anti-aging effect, as they slow down the shortening of telomeres. Research subjects with the least amount of DHA and EPA experienced the most rapid rate of telomere shortening, and those with the highest levels experienced the slowest rate of telomere shortening. Each 1-standard deviation increase in DHA+EPA levels was associated with a 32 percent reduction in the odds of telomere shortening and may protect against cellular aging in patients with coronary heart disease. n PUFAs inhibit telomerase activity in tumor cells, and the inhibitory potency is elevated with an increase in the number of double bonds. PUFAs, EPA and DHA were the most potent telomerase inhibitors, suggesting that PUFAs directly inhibit the enzymatic activity of telomerase as well as modulate the telomerase at the transcriptional level. Omega 3’s can be ingested as extracts, e.g. fish oil capsules, et.al., or can be obtained from whole foods. The author’s personal experience has been with **Aphanizomenon Flos Aquae (AFA)**, which has been a practice mainstay since 1995. It supplies EFAs in an all-natural form, with dynamic lubricating qualities that can actively increase the solubility of cholesterol deposits, and the Total Lipid (fat) Content Averages c. 4.4% of dry weight with Total Saturated Fat c. 43% and Total Unsaturated Fat 57%, Total Omega-3 Essential Fatty Acids 38% comprised of Alpha-Linolenic Acid (ALA) 37%, Eicosapentanoic Acid (EPA) 0.4%, Docosapentanoic Acid (DPA) <.1%, and Docosahexaenoic Acid (DHA) <.1%. Total Omega-6 Essential Fatty Acids are at c. 8% w/ Linoleic Acid (LA) 8% and Arachidonic Acid (AA) 0.1%. AFA is an ultimate photosynthesizer, contains fatty acids in an ideal balance (more ALA). Interestingly, a study revealed that AFA raises the levels of the good fatty acids far more than would be expected based on its ALA content, which suggests that the range of micronutrients improve utilization of fatty acids from other food sources. The “good” fatty acid (ALA, EPA, DHA) levels increased, and the levels of the arachidonic acid decreased. **Cyanobacteria**, such as Spirulina, and Aphanizomenon Flos Aquae (AFA) and Chlorophyta, such as Chlorella, amongst others, are known to produce intracellular and extracellular metabolites with potential biological activities, such as antibacterial, antifungal, antiviral, antitumor, anti-HIV, anti-inflammatory, antioxidant, antimalarial, and other effects. **Phycocyanins**, e.g. Phycocyanobilin (PCB) are functional compounds that can prevent free radical-derived damage to biomolecules.” It is present in AFA Algae, and Porphyra, and acts in tumor cell growth inhibition and free radical scavenger activity. The AFA PCB reduces the colony formation capacity of specific prostate cancer cells and thyroid cancer cells confirming the possibility of PCB to modulate cancer cell proliferation. It inhibits in a dose-dependent manner, a cytosolic enzyme involved both in tumor progression and in phytochemical...
bioavailability. This molecule that provides the blue color can amount to up to 15% of the dry weight of the AFA algae, has antioxidant and anti-inflammatory effects, and was evaluated for its ability to protect normal human erythrocytes and blood plasma samples against oxidative damage in vitro. A water-based extract of AFA containing high concentrations of phycocyanin inhibited in vitro growth of one out of four tumor cell lines, indicating that at least some tumor cell types may be directly sensitive to killing by phycocyanin. Phycocyanin also stimulates the migration of immune cells in the body especially stem cells and it’s the only natural compound known to do so. Consumption of AFA results in an immediate change in the trafficking of immune cells. The effect is transient and cell-type specific, and long-term consumption does not lead to hyper-stimulation of the immune system. AFA makes natural killer cells "patrol" better throughout the body, when using a low oral dose of algae (1.5 gram). Other research describes the identification of three new high molecular weight polysaccharide preparations isolated from AFA that are effective activators of human monocytes/macrophages, that are one hundred to one thousand times more active for in vitro monocyte activation than polysaccharide preparations that currently used for cancer immunotherapy.

Another substance, distributed in plants and seaweeds, was studied for its inhibitory effect on human telomerase in a cell-free system. Termed sulfoquinovosyldiacylglycerol (SQDG), it inhibited telomerase activity dose-dependently with 50% inhibition at 22 μM, and eicosapentaenoic acid, one of the fatty acid components of SQDG, is a potent telomerase inhibitor with 50% inhibition at 19 μM. It’s speculated that the structure of the sulfate group and fatty acid of SQDG is important for the potent telomerase-inhibitory effect and has potential use as a therapeutic dietary compound for telomerase inhibition.

**Fruits and Berries** Consumption of fruits and vegetables has been associated with reduced risk of chronic diseases such as cardiovascular disease and cancer. Phytochemicals, especially phenolics, in fruits and vegetables are suggested to be the major bioactive compounds for the health benefits. A study investigated the profiles of total phenolics in common fruits. **Cranberry** (Vaccinium macrocarpon) had the highest total phenolic content and corresponding antioxidant and antiproliferative capability, followed by apple, red grape, strawberry, pineapple, banana, peach, lemon, orange, pear, and grapefruit. For all the amazing benefits of cranberries, perhaps their most promising potential lies in the field of cancer prevention and treatment. The polyphenols derived from cranberries have been shown to inhibit the growth and development of cancers of the breast, colon, prostate, lung, and other tumors. The unique combination of phytochemicals in cranberries may be what contributes to chemoprotective mechanisms. Cranberry flavonoids were tested for their effect in vitro against ovarian cancer cells, and found induced cancer cell death, as well as decreased enzymatic activity, deactivating pathways of progression and arresting development of new cancer cells. Patients diagnosed with prostate cancer were found to have a significant decrease in serum PSA—22.5%, in the group consuming cranberry powder, and whole fruit contains constituents that may regulate cancer-gene expression. Studies performed utilizing a variety of in vitro techniques, demonstrated “positive effects against 17 different cancers,” and in vivo studies “supported the inhibitory action of cranberries toward cancers of the esophagus, stomach, colon, bladder, prostate, glioblastoma and lymphoma.”, via induced cancer cell death, by apoptosis, necrosis, and autophagy. Cranberries and cranberry-derived extracts reduced cancer cell proliferation, modified cell signaling away from new cancer cell production, and decreased markers of oxidative stress. Studies strongly
support the potential of cranberries as a possible adjunct in the prevention and treatment of a multitude of cancer types. The red pigments have been shown to inhibit biofilm formation, which has body wide implications, given the prevalence of biofilms in chronic disease, including many cancers. The health-promoting bioactivities of botanicals can be attributed to their high content of phytochemicals including proanthocyanidins (PACs) and flavonoids. PACs induce apoptosis and down-regulate telomerase activity in hepatocellular carcinoma. Tumor inhibition by cranberry may involve synergistic activities between the cranberry phytochemicals discussed above, including the flavonols (quercetin being the major flavonol), PACs, and ursolic acid. Some possible mechanisms of action supported by in vitro evidence include induction of apoptosis in cancer cells, decreased invasion and metastasis as a result of inhibition of MMPs, inhibition of ornithine decarboxylase expression and activity, and inhibition of inflammatory processes including cyclooxygenase (COX) activity. Recent studies also suggest a potential role for cranberry as a dietary chemopreventive.

Colostrum has a wide spectrum of anti-aging benefits, including anti-cancer defense, and helps to regulate multiple metabolic pathways that are implicated in cancer generation. PRPs in bovine colostrum have the ability to regulate activity of the immune system, in conjunction with hormones of the thymus gland.

IGF-1 is the main biomarker for HGH (Human Growth Hormone), which is present or produced by precursors in colostrum. Supplementation with colostrum has resulted in a statistically significant rise in IGF-1 levels of 17 percent. (IGF and HGH, covered in more detail, in other sections.) Glutathione, described as the “Ultimate Antioxidant,” has demonstrated an ability to regulate telomerase in fibroblasts which produce collagen, and it can recharge other antioxidants, like Vitamin C. Cells produce Glutathione, but this capacity diminishes with age, and the concentration parallels telomerase activity. It is very well documented that glutathione and its precursors are present in colostrum in relatively high levels. Colostrum’s alpha-lactalbumin boosts glutathione levels, which functions in not only detoxification of toxins but of also neutralizing carcinogens. Another way to increase glutathione levels in the body is to take a non-denatured whey protein powder, which is a glutathione precursor. When you combine whey protein powder with colostrum, it can have a powerful impact on balancing the immune system. Porphyra and other algae, can contain very high levels of antioxidants particularly during the summer, with levels of glutathione reductase, catalase, and carotenoids being higher during times of emersion relative to immersion. Dimethylglycine (DMG), one of the first supplements in the author’s arsenal, supports the production of glutathione. N-acetylcysteine (NAC) – found to reduce influenza episodes and boost glutathione production. Vitamin C also boosts production of glutathione. Another primary anti-cancer combination in colostrum, which also helps to regenerate the Thymus, are the three components, Thymosin alpha and beta, and IGF-1, covered in more depth in the next section.

Deer Antler contains IGF-I, which has been implicated in the pathogenesis of human cancer. Telomerase activity was assayed in prostate cancer cell lines treated with and without IGF-I/IGF-I analogs. Relative expression of human telomerase reverse transcriptase (hTERT) mRNA and protein was determined. IGF-1 stimulated baseline telomerase activity in all three cell lines and clearly stimulates telomerase activity in prostate cancer cells through a dual mode of action. European researchers have shown that growth hormone and IGF-1 do what antioxidants cannot do. IGF-I initiates the transport of nucleic acids into the nucleus of the cell where the DNA resides, and provides raw material needed to repair damage to the DNA and initiate cell division.
Thus, IGF -1 repairs the blueprint of life and helps to retard the aging process. When the DNA is repaired it can better resist carcinogens and protect us from cancer. The question arises, does antler reduce the incidence of cancer or does it promote cancer? While there is no specific evidence to date showing that VA cures cancer, VA has been shown to slow tumor growth and demonstrate antitumor activity and increased the survival rate of mice that have tumors, from 25-40%, and, in some cases, inhibits metastases. Antlers contain telomerase, which is critical in cell regulation. Mice that received a combination of VA and anti-cancer drugs survived longer and had fewer side effects than those given anti-cancer drugs alone. VA can be described as regulatory rather than stimulatory, as it tends to balance the immune response. VA may prevent stress-stimulated hypertrophy of the adrenal glands and involution of the thymus. The nutrigenomic potential of deer velvet products is rather remarkable, and the burgeoning data from past and ongoing research make it a nutrient powerhouse to watch in the future. Reports of immune enhancement from velvet antler demonstrate significant immune stimulatory activity, as well as enhancement of phagocytes and immunoglobulin levels in mice. An increase in monocytes in rats, necessary to the immune function of lymph, spleen, bone marrow, and loose connective tissue also has been reported.

Collagen
In concert with this, as antler and Perna support mesenchymal tissues, it has been found that the invasive metastasis of cancer is etiologically secondary to a degenerative change in the connective tissues, notably the condensed connective tissue of the “basement membrane” underlying the epithelium of the dermal and mucosal tissues. This, in turn, could be secondary to a deficiency of Vitamin C. A deficiency could involve the collagenous intercellular cement substance that normally holds the epithelial cells together in orderly arrangement, thus contributing to faulty healing and metastasis of precancerous lesions, in which there is a constant loss of connective tissue—usually hyaline changes in the collagen and fraying at the edges of epithelial cells, with a complete disappearance of yellow elastic tissue. It is in this de-elasticized area that the first epithelial down-growths occur. The ground substance (collagen), an intercellular cement substance capable of holding epithelial cells together assumes a watery consistency in scurvy. This liquefaction is due to a depolymerization of glycoprotein—the major constituent of the normal ground substance, and the glycoprotein thus liquefied is released into the bloodstream, resulting in an increased serum level. Administration of ascorbic acid (vitamin C) in scurvy rapidly restores the normal consistency of collagen. A pronounced deficiency of vitamin C is found in cancer cases. The degree of malignancy is determined inversely by the degree of connective-tissue resistance, dependent upon the adequacy of vitamin C status. As an example, the scirrhous, or hard, cancer of the breast is slow to metastasize and may remain inactive, or “in situ,” for many years, whereas the medullary, or soft, cancer of the breast is extremely invasive. Cancer cells become “amoeboid,” and perhaps they have lost their connective-tissue anchorage as a direct result of vitamin C deficiency. Effort should be directed toward prevention of the cause of the cellular disarrangement—collagenous breakdown of poorly healing epithelial and subepithelial tissues, since such lesions may readily become precancerous. Smoking neutralizes or destroys to a great extent what little vitamin C is taken in food, as one cigarette tends to neutralize in the body about 25 mg of vitamin C, or the content of an average-sized orange. This effect is due to the pronounced chemical action of ascorbic acid as a reducing agent. Physical and chemical carcinogens may act indirectly by bringing about or exaggerating a latent deficiency of vitamin C resulting in cancer due to a collagen disease of nutritional
etiology! Collagen studies: Explanted lungs were collected from transplant surgeries to capture the regional heterogeneity ranging from mild to severe disease. Healthy donor lungs were collected as “healthy” controls and structural changes related to disease severity, relative telomere length and quantitative histology of chromosomal damage and extracellular matrix (elastin, total collagen, collagen 1, and collagen 3) were measured. The study found shorter telomere length and increased chromosomal damage in diseased lungs compared to controls, in which telomere length was associated with total collagen. This would suggest a role for collagen containing compounds, such as Perna and Deer Antler. The landmark study of cartilage therapy for cancer began with Dr. John Prudden in 1974 when he was granted a study protocol by the U.S. Food and Drug Administration. All patients enrolled had failed with chemotherapy, radiation, and surgery. Multiple cancers were studied: breast, cervix, ovary, prostate, lung, liver, bone, stomach, pancreas, brain, thyroid, and Hodgkin’s Disease (lymph). Ninety percent of the patients had a positive response and some of the cures were achieved fastest when chemotherapy was combined with cartilage. In fact, cartilage protected the patients from the severe side effects of chemotherapy.

**Propolis** is a sticky resinous substance collected by honeybees, that may affect telomerase. In the study, leukemic cell cultures were exposed to varying amounts of propolis and analyzed at different time points. The researchers found that the highest concentration of propolis -- 60ng/mL -- significantly decreased telomerase expression levels in comparison to a control cell culture.

**Ashwagandha** a.k.a. Indian ginseng or Withania somnifera, the foremost adaptogen in Ayurvedic medicine has some possible uses in cancer. An attribute of some cancer cells is their ability to maintain telomere length, by a different mechanism, known as ALT (Alternative Mechanism of Lengthening of Telomeres). This will induce DNA damage signally, leading to senescence or apoptosis. Telomerase inhibitors are potential anticancer drugs, but they are ineffective for ALT cancers (c.15% of all cancers.) The ALT pathway is thought to be the primary pathway for telomere maintenance in human osteosarcomas. Withaferin-A from Ashwagandha, has anti-tumor effects, and has cytotoxicity for ALT cells. Ashwagandha root extract has also showed promise towards maintaining telomere structure, as in an in-vitro cell culture model, it was shown to enhance telomerase activity by 45%. TA-65, the telomerase activator obtained from the Chinese medicine, can elongate short telomeres and increase health span of mice without increasing cancer incidence. Ashwagandha root extract powder, at a concentration of 10 µg - 50 µg/ml increased telomerase activity by ~45%, in the Human HeLa cell line upon 72 hrs. exposure.

**Astragalus membranaceus** extracts were assessed for the effects on telomere shortening rate and DNA repair ability in 2BS cells. The telomere shortening rates of the cells cultured with HDTIC-1 or HDTIC-2 were much less than that of the control cells, with a significant reduction in DNA damage, and that damage was significantly repaired after cells were continually cultured with HDTIC for 1 h. Thus, the slowdown of telomere shortening rate, the reduction of DNA damage, and the improvement of DNA repair ability induced by HDTIC may be responsible for their delay of replicative senescence.
**Thymus Function and Cancer**

There has been some speculation that rejuvenating thymus function might also help to prevent cancer, because declining immune systems fail to detect and destroy cancerous and precancerous cells. Immunotherapy is one of the more promising forms of anticancer therapy, as the approach involves stimulating the patient’s immune system to better fight cancer. Restoring thymus activity may restore immune system function and guard against cancer. Trials in mice show that growth hormones, e.g. GH and IGF-1 can regrow the thymus, with continuous use. Dr. Fahy developed a clinical trial using hormones to regrow the thymus, a cocktail primarily consisting of Human Growth Hormone (HGH), Metformin and DHEA. HGH has also been shown to restore thymus function in AIDS patients. Dubbed the TRIIM (Thymus Regeneration, Immunorestoration, and Insulin Mitigation Trial) study, which consisted of a 12-month treatment for nine men ranging from 50 to 65 years old, an age range in which most human immune systems start to collapse. The team used MRI scans to evaluate the density of the thymus before and after treating the participants, and monitored many factors, including those related to general health and immune system function, such as T-cell population, lymphocyte telomere length and telomerase activity, and biological age based on an epigenetic clock. All showed significant regression of epigenetic age. Preliminary analyses indicate that there was a consistent and substantial increase in thymic density, which indicates replacement of thymic fat with more water-rich material, and in previous studies on human immunodeficiency patients, this coincided with improved thymic function. Improvements occurred in 8 out of 9 men, without side effects.

**Melatonin**

The heterogeneous nature of breast cancer makes it challenging to treat. Anti-estrogenic agents like melatonin have found their way into breast cancer treatment, and studies confirmed an inverse correlation between nocturnal melatonin levels and the development of mammary cancer. In a review of 480 studies, 80 eligible articles about melatonin molecular mechanism in breast cancer were selected. Interestingly, this hormone can induce apoptosis through the suppression or induction of a wide range of signaling pathways, and it is useful with concomitant administration of conventional chemotherapy agents, by alleviating unfavorable effects of those agents and enhancing their efficacy. Melatonin mechanisms involved include antiproliferative effects via modulation of cell cycle, ability to induce apoptosis in cancer cells, anti-angiogenic and antimetastatic effects, anti-estrogenic activity, the capacity to decrease telomerase activity, immune modulation, and direct and indirect antioxidant effects. Numerous studies have shown that melatonin has remarkable oncostatic properties and can reduce the promotion and/or progression of tumors. Its antiproliferative properties have been demonstrated in tumors including breast, endometrial, prostate, colon, ovarian, choriocarcinoma, melanoma, neuroblastoma, osteosarcoma, and leukemia, with efficacy in lymphoproliferative tumors. In normal cells, melatonin increases telomerase activity, but in cancer cells, it attenuates telomerase activity both in vivo and in vitro. Melatonin inhibits telomerase activity and the expression of the TERT mRNA subunit. Some findings suggest an interaction between the membrane and nuclear melatonin signaling pathways to modulate telomerase activity. In one study, eight nude mice received an MCF-7 xenograft and then were treated for 5 weeks with 0.1 mg/mL of melatonin in the drinking water, resulting in a significant reduction in the weight of tumors and reduced metastases when compared with the control group. As indicated by the Telomerase Repeats Amplification Protocol (TRAP) assay, a significant decrease in telomerase activity was observed in the group treated with melatonin. In conclusion, melatonin influences telomerase both in vivo.
and in vitro. Besides these oncostatic properties, melatonin deserves to be considered in the treatment of cancer for two other reasons. First, because its hypnotic-chronobiotic properties, melatonin use that can address sleep disturbances, a major co-morbidity in cancer. Second, because melatonin’s anxiolytic and antidepressant effects, it has a possible application in two other major co-morbidities seen in cancer patients, i.e., depression and anxiety.

**Mitochondrial support is critical as dysfunction plays key role in oxidative stress** and accumulating reactive oxygen species (ROS) lead to an increased rate of telomere shortening due to a less efficient repair of single strand breaks in telomeres themselves. Ultimately, mitochondrial dysfunction can accelerate telomere shortening, and improvements in mitochondrial function lowers the production of ROS and lessens telomere attrition.

Supplementation with nutrients necessary for efficient mitochondrial energy include vitamin C, vitamin E (mixed tocopherols and tocotrienols), thiamin, riboflavin, magnesium, creatine, N-acetyl cysteine, lipoic acid, acetyl-L-carnitine, and coenzyme Q10.

**Alpha Lipoic Acid**
Alpha Lipoic Acid is one of the most powerful antioxidants. Known as the “Universal Antioxidant,” Alpha Lipoic Acid is both water- and fat-soluble, so it can neutralize free radicals in basically every tissue in the body. Alpha Lipoic Acid stimulates telomerase activity in mice, leading to health improvements in the subjects. Alpha lipoic acid (ALA) stimulated expression of PGC-1α and TERT and reversed DNA damage, vascular senescence, and atherosclerosis. Further investigation is needed to identify whether ALA induces TERT in human cells, which cell types are susceptible, and whether such changes have clinical significance.

**Homotox**
The homotoxicological catalysts need to be considered in cancer, as ultimately, there is damage to mitochondrial function that must be addressed for repair. Coenzyme compositum, Ubichinon compositum, and Glyoxal are critical in this regard. Glyoxal and methylglyoxal, catalysts, act as photoamplifiers resulting in increased production of light and re-establishment of coherence. Methyglyoxal D6&D9 have a wavelength of 300 nm.

**Mistletoe**
The exact tumor-inhibiting action of the extract of Viscum is controversial. The mechanism of action on tumor cells by mistletoe may be due to enhanced cytokine release IL-1, IL-6, and Tumor Necrosis Factor alpha), which affect fibroblastic activity in the matrix, amongst other actions. Its effect may be due to the lectins, as Mistletoe lectin has been reported to induce apoptosis in different cancer cell lines in vitro and has shown antitumor activity against a variety of tumors in animal models by inhibiting telomerase activity and inducing apoptosis that resulted from dephosphorylation of Akt in the survival signaling pathways. Viscum album triggers molecular changes that inhibit cell growth and induce apoptotic cell death of cancer cells. A recent PubMed search under this agent resulted in more than 400 hits, indicating the quantity of work currently under way. Viscum has been found to reduce ascites accumulation in advanced cancer patients in humans. Viscum album is a key ingredient in Aesculus compositum, Ginseng compositum, Thalamus compositum, and Thyroidea compositum. The main indications are Impregnation Phases, precancerous states, and neoplastic phases. The varieties available, have
specific indications. The most common mistletoe host trees are ash (fraxini), apple (mali), oak (quercus), pine (pini), and spruce (abietis), maple (aceris), birch (betulae), elm (ulmi), willow (salcis), almond (amygdali), poplar (populi), hawthorn (cratagi), and linden (tiliae). Apple tree mistletoe is frequently used for breast and abdominal cancer. Viscum pini is used for skin, testicular, nerve, and nasopharyngeal cancers, sarcomas, and sometimes for post-menopausal breast cancer. Use in lymphatic cancers such as B-cell lymphoma and CLL. P type is the most potent for stimulating the bone marrow.

Drugs that selectively kill senescent, aging cells, are termed ‘senolytics.’ Oubain (Strophanthus), a cardiac glycoside, is a senolytic agent with broad activity. Cardiac glycosides synergize with anti-cancer drugs to kill tumor cells. Ouabain also eliminates senescent pre-cancerous cells. One study suggested that cardiac glycosides may be effective anti-cancer drugs via multiple mechanisms, and senescent cells targeted by cardiac glycosides suggest a potential to be used against age-related diseases! Research into the mechanism of action of Strophanthus has shown that Strophanthus extracts have opposite effects whether the substance is given in concentrated or very diluted (potentized) form. At very low levels Strophanthus stimulates the so-called sodium/potassium pump which enables more potassium to enter the cells. Senescence is a cellular stress response that results in the stable arrest of old, damaged or pre-neoplastic cells. Oncogene induced senescence is tumor suppressive but can also exacerbate tumorigenesis through the secretion of proinflammatory factors from senescent cells. Given the broad range of senescent cells targeted by cardiac glycosides, their use against age-related diseases warrants further exploration.

**Procaine** was presented as a possible cancer adjunctive therapy, at a Heel meeting in Germany, decades ago. Our practice uses Procainum compositum injections from Heel. Gerovital H3 (GH3), a buffered procaine drug was developed to treat depression in an aged population and was found to be a mono-amine oxidiaze inhibitor (MAOI). Experiments were carried out in tissue culture settings using a mouse embryo fibroblast (MEF) to which GH3 was added. The MEF had a normal life span, grew from seven to nine generations. Next, a culture of MEF was treated with a cancer inducing RNA type C virus, the MEF developed normally until the fifth generation, when suddenly the cells started multiplying chaotically, and soon forming a continuous line of cancerous cells. In a further study expansion, the cancerous cells were treated with a solution of procaine, the cell multiplications stopped after 2-4 hours, they became vacuolated and after 24-48 hours and underwent apoptosis. When normal MEF cells were treated first with a procaine solution and next with a cancer inducing RNA type C Virus, nothing happened, the MEF cell developed normally and died at the ninth generation, suggesting that procaine had protected the MEF cells. Procaine HCL is a telomerase activator, and when added to cultures of chick embryos, it extended the life span of these cells to 12-14 multiplications, almost doubling the original life span. Procaine is the first telomerase activator, where an "old drug" is involved. One study demonstrated that PCA acts as an inhibitor of DNA methylation in cancer cells, causing global genomic DNA hypomethylation and demethylation and reactivation of tumor suppressor genes. Procaine inhibits DNA methyltranferase. It exhibits growth-inhibitory effects in cancer cells, causing mitotic arrest. It may be an anti-senescence, anti-aging and anti-cancer-agent as confirmed at the cellular/telomerase level.
Summary
Could telomerase activity represent the Achilles heel of cancer cells? The lack of telomerase in most normal cells suggests minimal side effects, fueling enthusiasm for the therapeutic use of telomerase inhibitors. Some scientists fear that enhancing telomerase may also lead to cancer. While animal and test tube experiments are not conclusive, experiments show that this fear is unfounded for the most part. While telomere therapy with telomerase offers tremendous promise in clinical medicine, it is hampered by remaining questions of safety, e.g. how likely is this therapy to trigger abnormal tissue growth over the long term? A Duke University study suggests that telomerase by itself is not capable of inducing cancer. In research carried out on cells in test tubes, the scientists noticed that overexpression of telomerase failed to produce malignant changes, and researchers could not find evidence of tumor formation of either the hTERT cells or the control cells. A team of scientists at the UT Southwestern Medical Center immortalized human fibroblast cells with telomerase. The UT researchers reported that, over the long term, these telomerase-treated cells did not show the changes associated with cancer. The UT scientists also noted that the age-related changes to cells did not reverse, even after the transplantation of telomerase modified cells. In fact, the researchers noticed that collagen synthesis decreased and reduced the strength of the engineered tissue. While cell therapy with hTERT holds tremendous promise, researchers are still unsure about the long-term risks. For example, might hTERT-modified cells be more dangerous if the mutational changes activate cancer genes? Doctors need to balance the potential risk of hTERT gene therapy with its ability to save lives.

The telomere trail is a fascinating glimpse into possibilities for future therapies. Hopefully, this series of studies and theoretical approaches will give us rational ways to regulate and eradicate this dreaded pathological path.

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Promoting Longevity - on the Telomere Trail  
PJ Broadfoot, DVM

Objectives

- To understand the basic science behind telomeres and their contribution to health.
- To explore some of the nutrients and supplements that have been purported to improve telomere health, and thus contribute to wellness and longevity.

The anti-aging industry has seen tremendous growth over the last 20 years. The newest science behind anti-aging is focusing on the speed of chromosome shortening and the effect of critical hormones. Certain lifestyles, behaviors and nutrients influence key hormones and genetic components that allow for aging with maintained vitality. There are 75 trillion cells within the human body. Each cell contains a nucleus with 2 chromosomes that contain the DNA. Each chromosome possesses about 100 million protein bases, and the cap of each end of the chromosome is the telomere. Telomeres may be the key to aging and cancer by maintaining the structural integrity of chromosomes (DNA). Telomere length determines the number of times that a cell can divide, so as DNA strands become shorter with aging, they eventually become too badly damaged to replicate new cells. This senescence is associated with aging, cancer, and shorter lifespan. The average telomere is about 15,000 bases long at conception. In utero, the process of cellular division begins, and as the cells divide, the telomeres begin to shorten. During a 9-month gestation period, humans lose 5,000 bases and by the time of birth are already down to 10,000 bases. According to cutting edge new theory on aging, telomere length will dictate the aging process and eventual death. Once the telomeres reduce down to about 5,000 bases, DNA can no longer support life. Based on normal cellular division, the human lifespan should be approximately 120 years. But if the cells divide at an accelerated rate, the telomere shortening process accelerates and results in aging faster. Several factors play a significant role in cell division and telomere shortening. This process is about 30% related to genetics and 70% is based upon lifestyle and factors that increase free radicals accelerate the aging process, as the oxidative stress results in cleaving of bases off of the telomeres, which accelerates the telomere shortening process. Telomeres are important for chromosome integrity and are maintained by an enzyme called telomerase, which adds bases to the ends of telomeres and keeps them from weakening and fraying, thus preventing DNA strands from shortening, and allowing identical, undamaged cells to replicate over and over. Geneticists have found that aged people with shorter telomeres were three times more likely to die from heart disease and eight times more likely to die from an infectious disease than people with longer telomeres. Shortened telomeres have also been identified in patients with cancers of the pancreas, bone, prostate, bladder, lung, kidney, head, and neck. As noted, telomere length is not necessarily determined by genes, but also by lifestyle, diet and exercise, and longer telomeres have been positively associated with healthy life and longevity. Telomere length has been shown to be associated with nutritional status in human and animal studies. Individuals with longer telomeres have an overall improved health profile and better cognitive functions and lipid profiles as compared to controls. Researchers have found that you can actually lengthen your telomeres.

Many toxins create massive amounts of oxidative stress resulting in a chronic inflammation cycle that damages cells, DNA, proteins and lipids. Bodies can be highly deficient in using resources and strategies that enhance antioxidant defenses that fend off the free radicals. Our
modern culture is inundated with lifestyle toxins that create massive amounts of oxidative stress, and we are highly deficient in using resources and strategies that enhance our antioxidant defenses. Therapies, such as repetitive ozone treatments have been reported to act as a potent antioxidant to boost telomerase activity, protect the mitochondria from damage of free radicals and therefore prevent DNA deterioration.

**Stress and Anxiety Reduction**

A variety of lifestyle and environmental factors can increase stress in the body, including poor diet, EMFs, chemicals, heavy metals, pharmaceuticals, pollution, ad infinitum. Stress not only affects mental and emotional states, it can contribute to the eventual shortening of telomeres associated with cellular aging, or senescence, and many serious chronic and deadly health conditions. Scientists have discovered that the multiple biochemical pathways of chronic stress dampen telomerase activity and accelerate telomere-shortening. Stress causes the release of cortisol, which is linked to lower levels of telomerase, that prevents telomere shortening. A direct connection has been termed psychoneuroimmunology: recent studies have revealed that chronic stress may have a profound effect by shortening of DNA telomeres, predisposing to chronic diseases and cancer. Anxiety disorders increase the risk of onset of several age-related somatic conditions, which might be the consequence of accelerated cellular ageing. Patients with anxiety had significantly shorter LTL (Leukocyte Telomere Length) compared with a control, in analyses adjusted for socio-demographics, health and lifestyle. Patients with current anxiety disorder had shorter telomere length, suggesting accelerated cellular aging, which in part may be reversible after remission. In addition to reducing stress and anxiety, gentle seasonal detoxification can provide profound cellular health and anti-aging benefits.

Antioxidative nutraceuticals can be used to reduce free radicals and reactive oxygen species, by decreasing the level of ROS (Reactive Oxygen species) and free radicals. Something as simple as sleep can have an influence, as a study in China looked at the immune systems of people with sleep apnea compared to people who slept normally. The ratio of white blood cells with longer telomeres was significantly higher in healthy people than for people with sleep apnea. Changes in diet and lifestyle can also control telomerase activity in peripheral blood mononuclear cells. Night shift workers have shown clear changes in telomere health, in nurses with at least 12 years of night shifts. Genomic instability following telomere shortening is a well-established mechanism of tumor development and some studies documented an increased cancer risk among subjects with reduced telomere length.

**Insulin and growth hormone** are two key hormones that are associated with the aging process. Growth hormone (HGH) enhances the cellular repair processes. It regulates metabolism to burn fat, build muscle, and reduce the negative effects of stress. It enhances collagen production and repair, resulting in improved skin texture, supporting aging joints, and improving resistance to cancer. Telomeres appear to shorten faster for people with rheumatoid arthritis. Longer telomeres are associated with lower risk for the immune disease. Elevated insulin levels increase cellular division and telomere shortening. Researchers have estimated that over 80% of the US population has some level of insulin resistance, and thus are prediabetic or clinically diabetic, and forces the pancreas to secrete more insulin in order to lower blood sugar. A recent study found that obese children have telomeres that are 24% shorter than non-obese children, which is frightening, considering the rate at which obesity is climbing. Another recent study called the
TRIM (Thymus Regeneration, Immunorestoration and Insulin Mitigation) trial recruited men between 51 and 65 years old and dosed them with a three-drug combo for a year: growth hormone for restoration, and DHEA and metformin to combat high blood sugar. The latter two were also partly chosen for their promising anti-aging effects in animals. Blood samples were used to analyze immune cells, and medical imaging was employed to check the composition of their thymus. Normally with age, the number of different immune cell type changes, with potentially detrimental effects, but with this trial, not only were the cell changes reversed, but the participants’ thymus also showed less signs of fat—they’d been replaced by healthy, regenerated tissue. It should be noted that the authors don’t know how the drugs are working, but they theorize that they’re acting on the same molecular pathways as restricting calories.

Minerals Vitamins and Nutrients
Magnesium is necessary for many enzymes involved with DNA replication and repair, and an animal study showed that magnesium deficiency is associated with shorter telomeres, while a human cell study shows that magnesium deprivation causes rapid loss of telomeres and inhibits cell replication. Zinc is involved with binding signals to DNA, and DNA repair, and a deficiency can result in an excessive amount of DNA strand breakage. A lack of zinc in the elderly is associated with excessive numbers of short telomeres. A novel antioxidant that contains zinc is carnosine, which slows the rate of telomere depletion in human fibroblast cells, while extending their longevity. Carnosine is also a major brain antioxidant, making it a great stress management nutrient. Antioxidant properties of vitamin C and E are positively associated with longer telomeres in a dose-dependent manner in women. The addition of physiological concentrations of vitamin C or vitamin E to culture medium slows down the age-dependent shortening of telomeres as well as decrease in telomerase activity in cell cultures, hence increasing the life span. In cells treated with vitamin E (6-O-phosphorylated form of α-tocopherol), there was a reduction in the ROS due to scavenging by the vitamin. Thus, these nutrients may serve to limit oxidative damage to telomeric DNA that would otherwise cause shortening of telomere length. Vitamin E is linked to reduction of DNA damage; slowing of skin aging; upregulation of telomerase; and muscle maintenance Exposure of cells to tocotrienols enabled them to extend the length of their telomeres, and rejuvenated the telomerase enzyme, while simultaneously preventing damage to DNA. Vitamin D3 supplementation modulates peripheral blood mononuclear cell (PBMC) telomerase activity in overweight African Americans (@ 2000 IU per day). PBMC telomerase activity was measured and Vitamin D supplementation significantly increased PBMC telomerase activity, which suggests that vitamin D may improve telomere maintenance and prevent cell senescence and counteract obesity-induced acceleration of cellular aging. This is especially pertinent, given that Vitamin D is protective in viruses such as CoVid-19, which has clearly been shown to have a higher risk factor in the obese. The amino acid, homocysteine when elevated, can threaten heart health, and triples the speed at which telomeres shorten. Nutrients associated with lowering of this marker in humans include: Vitamin B12 – 500 mcg, Folic acid – 800 mcg, Vitamin B6 – 25 mg, Riboflavin (B2) – 25 mg, and Trimethylglycine (TMG) – 500 mg, given daily.

Foods, Nutraceuticals
Aging is the process of accumulation of various health hazardous chemicals in the body, such as free radical and reactive oxygen species, resulting in an increase in the risk of diseases and eventually leads to death. Several nutrient based therapies have been shown to have telomere
sparing effects. Healthy function of telomeres requires adequate methylation, in which a methyl group is donated to the genetic material of the telomere, epigenetically marking the telomeres for proper function. An adequate supply of methyl donors is needed for telomeres to work properly and a primary methyl donor is SAMe, which uses nutrients like methionine, MSM sulfur, choline, and trimethylglycine as building blocks. Forming SAMe from these building blocks requires vitamin B12, folic acid, and vitamin B6. Folic acid and B12 actually play multiple roles in supporting telomere genomic stability. Adequate dietary protein is required, particularly those rich in sulfur, e.g. those in whey protein, eggs, cottage cheese, dairy, red meat, chicken, legumes, duck, nuts, and seeds. Eggs contain the highest source of choline in the diet, with others such as red meat, chicken, dairy, nuts, and seeds containing moderate amounts.

**Honey and Bee Products**

A study in Malaysia found that beekeepers have significantly longer telomere length as compared to non-beekeepers, proportional to the longer periods of consumption of bee products. Bee products such as honey, royal jelly and propolis are widely known for their great antioxidant capacity. Honey consists of up to 95 % carbohydrates and includes an extensive selection of proteins, enzymes, amino acids, minerals, trace elements, vitamins and polyphenolic compounds. Antioxidant capacity of honey and propolis is thought to be mainly contributed by the phenolic compounds and flavonoids in them. A study conducted showed that honey exhibited protective effect in endothelial cells against oxidative stress. Although the main mechanisms on how bee products protect telomere length in beekeepers are unknown, we presume that bee products provide protective effects on telomere length against oxidative stress.

**Ashwagandha** a.k.a. Indian ginseng or Withania somnifera, is considered the foremost adaptogen in Ayurvedic medicine. Ashwagandha root extract has showed promise towards maintaining telomere structure, as in an in-vitro cell culture model, it was shown to enhance telomerase activity by 45%.

**Astragalus** Two isomers extracted from Astragalus membranaceus induced delay of replicative senescence. A study assessed the effects of these two compounds on telomere shortening rate and DNA repair ability. The telomere shortening rates of the cells cultured with Astragalus isomers were much less than that of the control cells and exhibited a significant reduction in DNA damage after exposure to 200 microM H(2)O(2) for 5 min., and induced DNA damage was significantly repaired after the damaged cells were continually cultured with one isomer. These results suggest that these compounds slow down the telomere shortening rate, which is mainly due to the biological properties of the compounds including the reduction of DNA damage and the improvement of DNA repair ability. In addition, the reduction of telomere shortening rate and DNA damage, and the improvement of DNA repair ability may be responsible for their delay of replicative senescence.

**Ginkgo biloba** extract increases endothelial progenitor-cell (EPC) numbers and functional activity. Recent studies have demonstrated that increased EPC numbers and activity are associated with the inhibition of EPC senescence, which involves activation of telomerase. Ginkgo biloba extract dose-dependently prevented the onset of EPC senescence in culture and increased proliferation of EPCs. The inhibition of EPC senescence by Ginkgo biloba extract in
vitro may improve the functional activity of EPCs in a way that is important for potential cell therapy.

**Silymarin Rapamycin**, an antiproliferative agent used on drug-eluting stents, induces endothelial progenitor cells (EPCs) senescence through telomerase inactivation and may impair the reendothelization of an injured arterial wall, leading to thrombosis. A study examined whether silymarin, a complex of flavonolignans with hepatoprotective and antioxidative properties, can protect EPCs against rapamycin-induced senescence. Mononuclear cells were isolated from peripheral blood of healthy volunteers. EPCs were cultured in endothelial cell growth medium-2 in the presence or absence of rapamycin (0.1 ng/mL) and/or silymarin (12.5–50 μg/mL). Silymarin increased telomerase activity 3-fold, reduced the number of senescent cells, and increased EPC proliferative activity (up to 64%) in comparison with cells cultured with rapamycin alone. Moreover, silymarin partially prevented impairment of tubular-like structure formation in Matrigel by rapamycin. These findings suggest that silymarin counteracts the inhibitory effects of rapamycin in EPCs. Silymarin may protect EPCs against the antiproliferative effects of rapamycin and restore their reconstructive ability.

**Turmeric (curcumin)** The “one-stop shop” herb for longevity! Curcumin prevents telomere shortening and may promote elongation by increasing telomerase expression; preserves brain health by preventing age-related brain damage; reduces oxidative stress; promotes mitochondrial homeostasis; and increases AMPK activity.

**Other Nutrients:** quercetin, green tea catechins, grape seed extract, and resveratrol all show specific ability to help preserve telomeres, with grape seed extract and curcumin showing the ability to generate longer telomeres. Antioxidants like glutathione have been shown to slow down telomere loss.

**Bovine Colostrum** contains telomerase and brings about a range of anti-aging benefits, including bone growth & density, muscle growth & support, anti-cancer defense, increased insulin sensitivity, anti-inflammatory activity, immune modulation, and many others.

**Omega-3s**, the fatty acids found primarily in cold water fish and algae, may have a profound anti-aging effect, as they slow down the shortening of telomeres. The triad of inflammation, oxidative stress, and immune cell aging are important pre-disease mechanisms that can be modified by nutritional interventions. Telomerase levels are linked to exposure to proinflammatory cytokines and oxidative stress. In a recent trial, omega-3 (n-3) polyunsaturated fatty acid (PUFA) supplementation lowered the concentration of serum proinflammatory cytokines, and also assessed whether n-3 PUFA supplementation affected leukocyte telomere length, telomerase, and oxidative stress. The double-blind four-month trial included 106 healthy sedentary overweight middle-aged and older adults who received (1) 2.5g/day n-3 PUFAs, (2) 1.25g/day n-3 PUFAs, or (3) placebo capsules that mirrored the proportions of fatty acids in the typical American diet, and it was found that supplementation significantly lowered oxidative stress, measured by F2-isoprostanes, which were 15% lower in the two supplemented groups compared to placebo, and telomere length increased with decreasing n-6:n-3 ratios, and data suggests that lower n-6:n-3 PUFA ratios can impact cell aging. In another study, on coronary disease patients, research subjects with the highest levels of omega-3 fats experienced the
slowest rate of telomere shortening. Individuals with the least amount of DHA and EPA experienced the most rapid rate of telomere shortening, while those with the highest levels of the omega-3 fatty experienced the slowest rate of telomere shortening. "Levels of DHA+EPA were associated with less telomere shortening before and after sequential adjustment for established risk factors and potential confounders. Each 1-standard deviation increase in DHA+EPA levels was associated with a 32 percent reduction in the odds of telomere shortening, raising the possibility that omega-3 fatty acids may protect against cellular aging in patients with coronary heart disease.

Micro- and Macro-Algae have been studied extensively for nutrient potential. A study which screened a total of 304 marine algae samples collected from various Japan coasts was undertaken, and several extracts from those algal samples showed telomerase inhibiting activity. In particular, an extract from a green alga, Caulerpa perturbarioides strongly inhibited telomerase activity, suggesting that it may be possible to develop novel anti-cancer agent in view of its specific anti-telomeric property.

Porphyra A red Rhodophyta, exclusively marine, found in deep waters attached to rocksand was used in a study which investigated the inhibitory effect of sulfoquinovosyldiacylglycerol (SQDG), distributed in plants and seaweeds, on human telomerase in a cell-free system. SQDG inhibited telomerase activity dose-dependently and it was found that eicosapentaenoic acid, one of the fatty acid components of SQDG, is a potent telomerase inhibitor with 50% inhibition. The structure of the sulfate group and fatty acid of SQDG is likely important for the potent telomerase-inhibitory effect. Fatty acids in algae, including polyunsaturated fatty acid content, can be as high as those of terrestrial vegetables. Lipids comprise 2-3% of dry weight of Porphyra, including the essential fatty acids linolenic acid, arachidonic acid and eicosapentaenoic acid – EPA. Furthermore, the ω 6/ ω 3 ratio, is c. 1:32 in Porphyra, and thus, could help to correct an imbalance.

Aphanizomenon flos-aquae (AFA) contains alpha-linolenic acid (ALA) and the long-chain omega-3 fatty acid known as docosahexanoic acid (DHA). Nearly 50% of AFA’s lipid content is the essential fatty acid alpha-linolenic acid (omega-3), the precursor to EPA and DHA. Researchers at Massachusetts General Hospital who studied its fat content revealed that AFA raises the levels of the good fatty acids far more than would be expected based on its ALA content alone. It was concluded that something about the algae—probably its range of micronutrients—was helping the animals to utilize the fatty acids they were getting from other sources as well as those from the algae. The “good” fatty acid (ALA, EPA, DHA) levels increased, and the levels of the arachidonic acid decreased.

Collagen, Glucosamine and Chondroitin Some analyses showed that telomerase expression has a significant positive correlation with chondroitin sulfate and type II collagen expression: The lower expression of telomerase paralleled the lower expression of chondroitin sulfate and type II collagen, suggesting that telomerase may be involved in the proliferation and apoptosis processes of nucleus pulposus cells, ultimately leading to intervertebral disc degeneration. Another study reported the effect of ROS/ DNA damage on telomere length and telomerase activity and discussed potential glucosamine and AGEs effects on telomere length.
**Green Lipped Mussel (Perna Canaliculus)**, a shellfish from New Zealand, obtains nutrients directly from the phyto-plankton and minerals in sea water. In all, there have been identified at least 50 nutrients in the GLM, and in particular, it contains all 9 classes of glycosaminoglycans: Chondroitin-4-Sulfate, Chondroitin-6-Sulfate, Chondroitin-Poly Sulfate, Dermatan Sulfate, Heparan Sulfate, Heparin, Keratan Sulfate, Hyaluronic Acid, and Proteoglycan, some of which have been studied individually for telomere support, as evidence above. In addition, it contains fifty-three lipids and the unsaturated fatty acids (UFA) have been fully identified, of which 37 were PUFA, and a further 21 UFA were detected; a remarkable diversity! The major fatty acids are DHA, EPA and palmitic acid. GLM has been shown to contain a unique $\omega$-3 fatty acid, eicosatetraenoic acid (ETA), and these fatty acids have been associated with healthier telomeres. Diets with a high ratio of $\omega$ 6 fatty acids to $\omega$ 3 fatty acids are associated with cardiovascular disease, cancer and inflammatory and autoimmune diseases.

**Deer Velvet Antler (VA):** antlers are a natural source of glucosamine, chondroitin and collagen, and has been used for 2000 years as a healing substance and is beneficial for general body support, besides stimulating HGH production and containing IGF-1. A study demonstrated that IGF-1 gene silencing decreased telomerase activity in deer antler cells and provided evidence that IGF-1 gene expression is correlated with telomerase activity during rapid growth of the antlers. Velvet promotes telomere lengthening, which allows for greater cellular replication. A Chinese study reported that nutrients in VA allowed the human cell to live 300% to 400% longer! Telomeres appear to shorten faster for people with rheumatoid arthritis. Longer telomeres are associated with lower risk for this immune disease.

**Thymus Extracts (TE)** A strong and vigorous immune system is especially important in the health of the elderly. In the past 40 years, science has discovered that the Thymus Gland is a key regulator of immunity. "The involution [shrinkage] of the thymus gland is one of the cardinal bio-markers of aging." The thymus is a primary lymphoid organ responsible for T-lymphocyte differentiation and maturation. Thymocytes differentiate into mature T cells that are essential for the immune response against infection, which may be associated with telomerase activity, allowing T cells to acquire telomere sequences that are long enough to undergo several rounds of replication. Telomerase activity has been demonstrated at low levels in peripheral blood lymphocytes but at high levels in germinal centre B cells and thymocyte subpopulations and is activated in the normal human thymus at different times of life. Telomerase activity was detected in thymic protein extracts from two newborn babies, a 12-year-old boy, and from two of six adult patients, aged 54 and 66 years. This suggests that the thymus can remain functional despite involution in elderly patients. It has also been suggested that intra-thymic maturation and selection of T cells are associated with telomerase activity, which allows T cells to acquire telomere sequences that are long enough to undergo several rounds of replication. Studies have indicated that the telomere length varies considerably with hypoxia levels and cell types, and telomere length in lymphocytes may indicate the extent to which hypoxia affects the immune system. The active substances produced by embryonal thymus and early fetal thymus not only affect the immunological system, but also interfere with the process of organ aging, and liquid thymus extracts have been associated with improved health and increased longevity and may be useful in preserving antioxidant activity. The thymus is also fundamental to the integration and proper interaction between the immune, endocrine and central nervous systems (CNS). There is recent evidence that indicates the thymus plays an indirect but considerable role within the
neuroendocrine network. The use of thymus extracts may be an important, but overlooked, option in treating and possibly preventing many clinical conditions of the aging person.

**Hyperthermia**

Hyperthermia is a potent sensitizer of cell killing by ionizing radiation (IR); however, hyperthermia also induces heat shock protein 70 (HSP70) synthesis and HSP70 expression which is associated with radio-resistance. Because HSP70 interacts with the telomerase complex, and the telomerase catalytic unit (hTERT) extends the life span of the human cells, a study was done to determine if heat shock influences telomerase activity and whether telomerase inhibition enhances heat-mediated IR-induced cell killing. It was demonstrated that moderate hyperthermia (43 degrees C) enhances telomerase activity. The results suggested that inactivation of telomerase before combined hyperthermia and radiotherapy could improve tumor killing. Another study looked at the whole effects of Repetitive Hyperthermia (RHT) in Dahl hypertensive rats. It found not only a slight BP-lowering effect but also a preventive effect of increasing BP probably due to increased eNOS, by increased shear stress and HSP, and prevented cardiac hypertrophy. In conclusion, RHT attenuates the development of cardiac hypertrophy and fibrosis and preserves telomerase, and the length of telomere DNA in salt-induced hypertensive rats through activation of eNOS and induction of HSPs.

Another important aspect of this topic is telomere quality, as different from telomere length. In some ways, telomeres are the weak link in DNA. They are readily damaged and must be repaired, yet they lack the repair efficiency of other DNA. This results in an accumulation of partially damaged and poorly functioning telomeres of lower quality, regardless of length. One way to view our potential to influence the aging process is simply to slow down the rate. In the context of telomeres, this means utilizing strategies to slow down the rate at which they shorten, while helping to protect and repair them to maintain their quality. An emerging body of nutritional science says that this is now possible. Another intriguing possibility is that we may be able to lengthen telomeres while maintaining their quality, actually turning back the biological clock. This can be done by improving the activity of the telomerase enzyme which can add length back to telomeres, while simultaneously protecting the longer telomeres to ensure quality. Fortunately, we now have the ability to influence the length of these tiny genetic clocks. The field of Nutrigenomics/ Epigenetics give us the tools to encourage younger acting cells and help avoid age-related problems by maintaining telomere length. The science of telomere biology is always moving forward, and we can move with it!

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Natural Immunity vs. Vaccine Immunity
Todd Cooney, DVM, MS, CVH

Objectives
• To gain understanding of how vaccines harm immunity.
• To learn how natural immunity is superior and how homeopathy helps achieve this protection.

Introduction
Vaccines are generally accepted today as the best way to stimulate immunity and seen by most veterinarians (and the public) as “safe and sure.” Yet naturally acquired immunity is superior to vaccine immunity in every way. Vaccines harm the immune system, creating new problems. The focus here will be on topics of immune dysfunction, herd immunity, titers, antibody-mediated suppression, and the paradox of vaccination. I’ll conclude by looking at homeopathy as a helpful way to help the body’s natural response to disease, and a solid alternative to vaccination.

Homeopathy and Natural Immunity
Homeopathy is a very useful way to augment the body’s natural response to disease, is accessible to the masses, and offers a solid alternative to vaccines. Homeopaths have always believed the best way to boost health is to give the most similar remedy as treatment or prevention and avoid the harmful effects of vaccination altogether. Dr. Dorothy Shepherd, a British homeopath in the early 1900s, says this in her book, Homoeopathy and Epidemic Disease:

“My own personal opinion is that inoculation with any type of serum in any of these infectious diseases is harmful and can easily and safely be replaced by a remedy, or remedies, according to our law of similars that ‘like cures like’ in healthy individuals.”

I tell my clients this - rabies is the only legally required vaccine, and should only be given to healthy animals, according to the vaccine label insert. The others are not useful, necessary, or required (except by some self-appointed vaccine police). It is typical for me to see several cases each week in my general practice involving animals with chronic disease who are still getting vaccinated because they were overdue, or it’s clinic policy. This makes me crazy.

Therefore, I spend time explaining to clients a much better way to build immunity instead of vaccination, as it keeps the immune system intact and well regulated, not confused, and dysregulated (think autoimmunity!). Along with excellent nutrition, homeoprophylaxis involves using specific remedies or nosodes (Greek nosos = disease). Nosodes are made from natural products of disease and help with immunity. I use nosodes in practice instead of all vaccines except rabies. For example, I recommend pups get Parvo nosode 200c weekly until at least 6 months old, as this age group is most susceptible to Parvo, and has constant potential exposure. This protocol has eliminated Parvo from my practice over the past 12 years.

Immunity - Measles/Distemper as Review
The process of contracting and recovering from infectious disease is a powerful and elegant response of the entire immune system, which vaccines try to replace. It’s easy to skim over this truth in the heat of debate about vaccines. Take measles as an example, which is very similar to
canine distemper. Measles has a near 100% attack rate, and most exposed individuals become ill with very clear symptoms. Most parents of previous generations diagnosed measles before the doctor ever saw the patient. Both viruses have affinity for upper respiratory tract mucous membranes, are dispersed by droplets (coughing, sneezing), and ingested or inhaled by others. During the 10-14-day incubation, virus multiplies in tonsils, adenoids and nasopharyngeal lymphoid tissues, then moving to regional lymph nodes of head, neck, and finally to spleen, liver thymus, and bone marrow, the major organs of immunity. During this phase, the patient feels well and usually has no symptoms.²

When symptoms first appear, virus-specific antibodies are already found in blood, and the peak of symptomatology matches that of antibody response.³ The illness we label measles/distemper is really the mighty effort of the entire immune system to expel the virus from the blood, a complex mechanism with many parts working in concert. The first lines of natural defense are the epithelial cells lining the oral, nasal, and pharyngeal cavities. They are first to contact the virus, and best designed to expel it, usually by sneezing, coughing and producing discharges.⁴ Monocytes and macrophages are also activated, and step up their policing of blood, endothelial cells, and connective tissue to detect, engulf and destroy invading viruses.⁵ Other phagocytic white cells (neutrophils, basophils, and eosinophils) may also respond to bacteria, allergens and toxins. The complement system, interferons, interleukins, and other cytokines enhance phagocytosis. Taken together, this cellular immunity provides the first line of defense against foreign microbes, while coordinating and regulating the whole process.

As this is happening, lymphocytes from thymus and bone marrow produce specific antibody against the microbe, which helps the removal process. This is called humoral immunity, and includes opsonins, which trigger phagocytosis of microbes; agglutinins, to aid clumping of microbes and antigens, and precipitins, which render them insoluble. All these help the cellular mechanisms in their tasks. The peak of this process is a permanent memory of the infection in the genetic material of the immune cells, enabling a prompt, efficient response in future encounters.⁶

**Long term benefits of Natural Immunity**

This massive outpouring of immune response is deeply health-giving in two ways:

1. *Specific* - the recovered individual will never again be susceptible, no matter how many re-exposures or outbreaks occur.
2. *Non-specific* - equally important, the entire immune system is now primed for a strong, rapid concerted response to any other future infections. This natural immunity is a huge benefit for the general health of individuals and their descendants, and the entire population of the species.

As we rush to develop new vaccines and force them on population, it is easy to forget that a healthy immune system develops by mounting an acute, vigorous response to infection, and the challenges of exposure and recovery from illness are fundamental in achieving and maintaining good health throughout life.
Natural Immunity and Cancer
A great deal of evidence shows that humans recovered from childhood illness (measles, mumps, chicken pox, influenza) have significant protection from chronic problems later, such as autoimmune disease and cancer of various types. One British study found 53% lower incidence of ovarian cancer in women with a history of childhood measles. Another study looked at over 600 melanoma patients in Europe and Israel, and found those who previously experienced influenza, pneumonia, or almost any febrile infection earlier in life were much less likely to develop melanoma than those who had not. Other studies with glioma tumors of the brain and leukemia/lymphoma showed similar correlations.

Herd Immunity
Public health officials tell us large scale outbreaks no longer occur once 80% of the population contracts and recovers from a disease. This works by protecting susceptible individuals from minor exposures. However, we currently have vaccination rates up to 95% for measles and still have ongoing outbreaks, adding to the illusion of looming, imminent threats to public health.

Vaccine advocates love to remind us measles was once a killer disease, and still has a 20% fatality rate in populations exposed for the first time (like Africa). Measles decimated native tribes in the New World on first exposure, but within a few centuries evolved into a normal disease of childhood. This “herd immunity” became widespread before the first measles vaccine appeared in 1964. At that time in the United States, almost all school children acquired and recovered from measles completely (400,00 - 800,000 cases per year), without complications or sequelae, a ‘graduation ceremony’ for a developing immune system.

Titers - False Proof of Immunity?
Vaccines with modified live or killed virus usually do not contain adjuvant; it’s not needed to trigger antibody production to the wild virus. Detection of virus-specific antibody in the blood is seen as “proof” of immunity. However, this is misleading. A positive serological titer is proof of immunity only in the absence of vaccination. In absence of vaccination, a positive titer means natural exposure occurred, with likely lifelong immunity the result. Why isn’t a positive titer a guarantee of immunity?

Research with vesicular stomatitis virus (VSV) in immunized mice showed - virus neutralizing antibodies against live VSV were produced for much shorter time than virus specific antibodies. Detection of virus specific antibodies does not mean protection against wild virus; serology only measures virus specific antibodies antibodies, and does not tell when virus neutralizing antibody disappears, and real immunity wanes. Vaccines postpone susceptibility but don’t eliminate it completely.

Antibody - Mediated Suppression
If pre-existing antibody binds to a protein, more antibody to that protein is produced; this is called antibody-mediated enhancement. This is the basis of immunologic memory, on which the whole theory of vaccination is based. If pre-existing antibody binds to a complex particle (virus or bacteria), it prevents the immune response to that particle, and is called antibody-mediated suppression. This prevents unneeded excesses of antibody production once levels are sufficient. But this can also result in a problem called original antigenic sin. Pre-existing neutralizing
antibody cross reacts but doesn’t match perfectly the pathogen. This lets the antibody suppress the response against the pathogen but is unable to clear it from the body. This allows the infection to progress unhindered and worsens the pathology.

This happened in 2009 with H1N1 influenza in humans, noted for the extreme severity and high mortality rates among healthy adults, especially those vaccinated for flu in 2008.14 Yearly flu shots are only 30% effective in people over two years old, and same as placebo in those less than two years old.15 A flu shot might help create a state of antigenic sin to a new virus strain, so getting vaccinated is similar to playing Russian roulette, doing little for disease prevention.16 Might we be creating similar conditions with the plethora of animal vaccines used today?

**Paradox of Vaccination**

Vaccines manipulate the immune system to gain temporary protection, if any, from disease. How does natural immunity work in populations, and how does vaccinating eliminate natural immunity, and interfere with maternal immune protection of offspring?

Naturally immune mothers protect offspring by passive transfer of immunity via placenta and breast milk. Passive transfer depends on virus-neutralizing antibody in the serum and breast milk of immune mothers (Interestingly, females produce much higher antibody levels than males). Offspring exposed to a virus while nursing a naturally immune mother will usually have asymptomatic infection, and life-long immunity to the virus. Unlike natural exposure via mucosal surfaces, most vaccine exposure is via bloodstream, inducing serum antibodies, not mucosal antibodies. Only mucosal exposure leads to antibody production in the mammary gland, so vaccinated mothers lack ability to transfer vaccine-induced antibody by lactation. Vaccinated mothers also have lower levels of virus-specific antibody in serum compared to naturally immune mothers. So, vaccinated mothers transfer few, if any, protective antibodies to the fetus via placenta, compared to naturally immune mothers. Therefore, there is increased risk of measles in infants born to vaccinated mothers compared to naturally immune mothers from the early 1990s, compared to previous decades, when measles was still endemic in the United States.17

This lack of maternal immune protection in the early 1990s, resulted in a 75 X increase in subacute sclerosing pan encephalitis (SSPE) in the United States. SSPE follows measles acquired in infancy, when immunity is low. The lack of maternal protection is attributed to vaccination of these mothers in their childhood (routine childhood vaccination for measles in the US began in early 1960s). This eliminated the chance for many mothers-to-be to develop natural immunity that would protect their babies someday.

Could a similar pattern be happening in our dog world? As prevalence of natural immunity decreases, and mothers pass less real immunity to offspring, could this explain the apparent rise in neurologic and behavior issues in dogs, especially? Hmm…

Disrupting natural immunity is a dangerous and irreversible result of prolonged vaccination campaigns. It pushes the risk from young to adult, leaving vulnerable youth without viable maternal protection at all. Not to mention the chronic immune disruption or autoimmunity triggered by vaccination 100% of the time.18 The vaccine paradox is reduction of overall acute
diseases, but increased danger of illness in the next generation, along with higher rates of chronic
disease. We are told this is for the greater good, but is it really?

As an early veterinarian said after discovering the wonder of using nosodes to prevent canine
distemper in 1929, “Of course the subject of bringing about immunity by any other means than
the use of a hypodermic syringe is going to stick in the crop of a good many.”

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Homeopathy and Epidemic Disease
Todd Cooney, DVM, CVH

Objectives
- To understand the history of homeopathy and epidemic diseases
- To learn how to apply homeopathy to veterinary epidemic diseases

Introduction
The Smithsonian Natural History Museum exhibit, *Outbreaks Epidemics in a Connected World*, opened in May 2018 in Washington DC. We have a strong curiosity about disease epidemics, and a latent dread as well. As I write this in April 2020, the world is on lockdown due to the corona virus, COVID-19, which everyone is only too familiar with by this time.

Epidemics are always big news - past, present and future - especially future. Scientists try to predict the next big outbreak and how to deal with it. Recently we’ve had Zika, Ebola, Yellow Fever, Dengue Fever, Measles, to just name a few. From its earliest days, homeopathy treated epidemic diseases with great success compared to conventional or allopathic methods. This successful record fixed homeopathic medicine firmly in the consciousness of people worldwide, even resulting in a large monument to homeopathy’s founder, Dr. Samuel Hahnemann, in our nation’s capital.

Patients suffering from Typhus, Cholera, Malaria, Yellow Fever, and Influenza, among others, all enjoyed much higher survival rates under homeopathic care, compared to those receiving allopathic treatment. The same homeopathic treatment principles apply to infectious diseases of animals, though these successes are not widely known. We will cover a few key examples in the medical literature, human and veterinary, and discuss what can be done today to help with epidemic diseases.

Early Epidemics and Homeopathy
The scientific literature contains over 28,000 volumes, 9000 references, and over 500 books/pamphlets on homeopathy and epidemic diseases. The clear consistent finding is a much lower death rate with homeopathy compared to allopathic treatment. This holds true even today, comparing such common diseases like pneumonia.

The earliest example of homeopathic medicine and epidemic disease is Belladonna and Scarlet Fever (Scarlatina), which Dr. Samuel Hahnemann was first to recommend and use successfully, both to prevent and cure this awful disease of children in 1801. Hahnemann noticed a child already receiving homeopathic belladonna for other complaints resisted Scarlet Fever while three siblings in the same house became ill. As a trial, he began giving the remedy belladonna to children in other families when the first child became ill, and found it to be protective, despite a 90% attack rate. His success of using this remedy caused regular physicians to adopt it, and by 1838 the Prussian government made its use mandatory.

Another early example is Typhus Fever in 1813 Germany. After Napoleon’s army attacked Russia, they returned through Germany, and spread lice-born Typhus to the town of Leipzig. Hahnemann happened to be in the area at the time and treated 180 cases with only two deaths (1.1%).
Conventional mortality rate for Typhus then was about 20% (536 deaths of 2742 cases in Vienna, Austria between 1850-52, about 40 years after Hahnemann’s success in Leipzig).  

In 1830, a Cholera epidemic was reported to be coming from east of Europe. Hahnemann read newspaper accounts of the disease, considered the symptoms, and published an article on certain homeopathic medicines which might help, without seeing a case. When cholera struck Europe in 1831, there was 40%-80% mortality with allopathic treatments, while homeopathic treatment saw just 9% mortality. For example, in 21 hospitals in Europe, there were 63 deaths per 100 patients (63%). In Vienna, Austria alone 1360 of 4500 patients (30%) treated allopathically died. However, three homeopaths in Vienna reported treating 309 cases with only 18 deaths (6%). 

The Great Influenza Pandemic of 1918-19 was the most severe epidemic in recent times. Twenty percent of the world was infected, and nearly 50 million died. The epidemic so devastated the United States that the average lifespan decreased by 10 years. Homeopathy helped widely with prevention and treatment. Cases treated with allopathy approached 30% mortality, while homeopathy had a death rate around 1% or less. One example is Dr TA McCann of Dayton, Ohio, who reported mortality rates of 28.2% for 24,000 cases treated with allopathy, and only 1.05% for 26,000 cases treated with homeopathy. Dr. Herbert Roberts from Derby, Connecticut surveyed 30 physicians, who reported 6602 cases with 55 deaths (0.8%).

Recent Epidemics and Homeopathy
An example relevant to veterinary medicine occurred in Cuba in 2007 during an epidemic of Leptospirosis, a major zoonosis during rainy seasons in the tropics. Symptoms are variable, and potentially fatal, including meningitis, pneumonia, hepatitis, nephritis, mastitis, myocarditis, hemorrhagic crises, and multi-organ failure. Mortality rates vary from 4% to 50%. Conventional vaccine programs exist but have not improved the morbidity and mortality of this illness.

During the 2007 outbreak of Lepto, the government tried homeopathic prevention, or homoeoprophylaxis, in three high risk provinces. 2.1 million people (88% of population) received two doses of a Lepto nosode (Nosolep) 200c potency, spaced 7-9 days apart. One year later, 2.3 million people (96% of the population) in the same three provinces received two doses of Lepto nosode 1m potency, 7-9 days apart. Regions receiving the nosode had 84% fewer cases of Lepto as a result, even though these provinces were highest risk for the disease. Areas not getting nosode had a 22% increase in cases, despite vaccination, and being considered lower risk. The cost of homoeoprophylaxis (nosodes) was 98% less than conventional vaccines, even though the only commercially available Lepto vaccine for humans was made in Cuba at that time. 

An epidemic of meningococcal meningitis (Neisseria sp.) in Brazil occurred in 1974-5, affecting 250,000 people with 18,000 deaths, resulting in 75,000 permanent brain damage or disability cases. Mortality rate in children treated without antibiotics is over 80%. During this outbreak, in the city of Guarantingueta in San Paolo state (pop. 78,000), 18,000 children received one drop of homeopathic Meningococcinum A+C orally as prophylaxis. Within the first three months, only five children (of 18,000) contracted meningitis, compared to 10 children in the control group of 6464. This extrapolates to a drop from 15,000 to 2100 in the entire population, which is significant.
India experienced recurrent epidemics of Japanese Encephalitis (JE) since 1970, with mortality rates of 30%. Between 1987-89, 5175 of 16,871 cases died (31%). In 1991, 322,812 people received a single dose of homeopathic Belladonna 200c potency, in 96 villages of three districts. Follow up indicated no cases in the sampled population. Another Indian state had positive results after a program of giving three different homeopathic remedies over several days in 1999. Results following were 343 cases in 2000, with 72 deaths; 30 cases in 2001, with 4 deaths; 18 cases and no deaths in 2002; then in 2003 and 2004, no cases reported at all.9

Veterinary Epidemic Examples
Canine distemper is an ancient disease of dogs, and the most extensive reference to using homeopathy is by Dr. Horace BF Jervis in an AVMA monograph on Distemperinum (nosode of distemper) in 1929. He described his daily struggle with this disease in practice, and the disappointing results with conventional treatments. He decided to try homeopathy, which he was learning at the time. A homeopathic pharmacy in Chicago prepared a nosode in two potencies, 30c and 200c, to use for prevention and treatment. He noticed the nosode could abort clinical canine distemper if given in the early stages; otherwise he had to use other homeopathic remedies. He noticed the death rate in his ‘distemper ward’ drop drastically, and ‘felt a load lift off his shoulders.’ He regretted not taking it up years before, and was sorry other vets were not interested to try homeopathy (I know the feeling!). I love this quote, towards the end of the monograph - “Of course the subject of bringing about immunity by any other means than the use of hypodermic syringe is going to stick in the crop of a great many.”10

Kennel cough is ever present in contemporary veterinary practice, and almost everyone requires the vaccine, thinking it gives protection against this mild self-limiting upper respiratory disease of dogs. Christopher Day, a British homeopathic veterinarian, proved superior results with kennel cough nosode in the face of an outbreak in a dog shelter situation during the 1980s. The kennel experienced high numbers of this contagious tracheobronchitis despite conventional vaccination, with most dogs affected. Day suggested adding a kennel cough nosode to the drinking water of all dogs, and new cases dropped to zero within a very short time and remained at that level.11

Parvo virus is still considered epidemic in dog populations, after suddenly appearing in the late 1970s out of nowhere. For over 20 years of conventional practice, I followed regular guidelines of puppy vaccination, but still saw frequent cases of Parvo, and attributed it to vaccine “failure.” About 12 years ago, I began to question vaccination, as I learned more about homeopathy, and gradually converted to using no vaccines in practice, except rabies. As time went on, I adopted a protocol using nosodes for puppies, to assist with natural immunity. I began to compare statistics on these pups, out of curiosity. I found that pups receiving nosodes might still contract Parvo and have symptoms, but had much higher survival rates, compared to 76% death rate for vaccinated pups which developed Parvo. I also found about 40% of vaccinated pups still became ill with Parvo, which surprised me at first. These findings gave me confidence to recommend this protocol to all puppy owners, which I still do today. I’ll go into more depth about Parvo and homeopathy specifically in the last hour.12
Genus Epidemicus

“Since every case of disease in a given epidemic has the same origin, the disease puts all those who have fallen ill into the same kind of disease process.” - Hahnemann, aphorism 73, Organon

The term *genus epidemicus* refers to the combined symptoms of a large group of individuals afflicted with the same disease. This idea also originated with Hahnemann, as stated in the Organon,

> “Each epidemic has its own selfsame character which is common to all of the individuals who are taken ill. If the character of the epidemic disease is discovered (**the genus epidemicus**), this will point to the homeopathically fitting (specific) remedy for the totality of the cases.”

Finding the genus epidemicus helps narrow down remedy choices to a very small number likely to help most cases of the epidemic, by combining symptoms of large numbers of patients into one totality, then using this to select remedies. Epidemic diseases by nature are acute diseases, with a rapid onset and quick tempo or pace. There is very little prodrome, then comes crisis, followed by resolution in a short time (recovery or death). Treating acute disease in an epidemic is similar to being attacked by a drunken person with fists and knives - there’s little time to analyze options, or you’ll be dead! Here are some practical examples from the veterinary world.

Canine influenza began to make headlines in 2015, with outbreaks in Chicago and Florida, involving small numbers of dogs and low mortality. Media attention generated great concern and fear among people for the health of their dogs, leading to increased sales of the canine influenza vaccine in many veterinary practices. Veterinary homeopath Dr. Will Falconer proposed the use of certain homeopathic remedies as the most useful for treatment of dogs exhibiting characteristic influenza signs. He listed two homeopathic remedies as being most similar to the current influenza “epidemic” in U.S. dogs - *Phosphorus* and *Nux vomica*. Using the principles of genus epidemicus prescribing, these two remedies would likely treat or prevent the disease in exposed dogs showing similar signs.

Parvo, again. Many Parvo cases present with characteristic symptoms, giving us a high index of suspicion without any lab work or test. How many have ever said, or heard a technician say “Phew, that smells like Parvo!”? Many cases present with nausea, vomiting, restlessness, extremely foul-smelling diarrhea (the repertory calls the odor ‘cadaveric’), and often a desire for small sips of cold water, or ‘hovering’ over the water dish without drinking. These symptoms match *Arsenicum album*, which happens to be a very good remedy for treating Parvo. This could be considered the genus epidemicus for Parvo, in my opinion, though some cases will require other remedies. The patient’s state can shift rapidly, sometimes requiring a different remedy every few hours.

Since I began using homeopathy in 2008, I’ve treated hundreds of pups with parvoviral disease this way, using only homeopathy and fluid therapy. I’m convinced the response and recovery time is much better than I saw with conventional medicines in the past.

**Conclusion**
Anyone practicing genuine homeopathy is always ready to face any new epidemic disease, because the Law of Similars applies to any given patient at any given time. Homeopathy does not need years, months, weeks, or even days to develop new remedies and prophylactics in the face of newly emerging epidemics - the potential matching remedy, or genus epidemicus, already exists in our Materia Medica of proven medicines.

Homeopathy is safe, cost-effective and a very consistent and strong therapeutic with prophylactic effects against real world epidemic diseases, human and animal, well proven over the past 200+ years. Fortunately, facts are more stubborn than prejudice, as the dominant world medical system still exhibits a plausibility bias against homeopathy (“it doesn’t work because it can’t work”).

And in closing, consider the strong words of British homeopath, Dr. Dorothy Shepherd, “As homeopaths we should not be backward in pressing our claim of being able to cure, really CURE acute epidemic diseases.”

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Parvo in Dogs: Successful Prevention and Treatment with Homeopathy
Todd Cooney, DVM, CVH

Objectives
- Review epidemic diseases in animals, focusing on Canine Parvo.
- To learn the homeopathic approach to Canine Parvo cases.

Introduction
Canine Parvovirus (CPV) is the most common viral disease of pups in the United States and strikes fear into the heart of many new puppy owners. The virus appeared suddenly in the late 1970s, and is related to Feline Panleukopenia, also a parvovirus. This talk will cover the use of homeopathic methods to prevent and treat CPV, concluding with case data from my practice, covering 10 years in all, and the results of this information. Over-vaccination is a huge problem today in veterinary medicine (the worst thing we do, in my humble opinion). This talk will give you an alternative, and increase your confidence to walk away from over-vaccination, and improve the overall health of your patients, whatever species they happen to be.

Sudden Emergence of Parvo
Canine Parvovirus (CPV) is considered a highly contagious disease of dogs and can cause acute gastrointestinal illness in pups between 6 - 20 weeks old, although older dogs are sometimes affected. Rarely, a myocarditis occurs in neonatal pups due to CPV. The virus named CPV type 2 causes the disease, and first appeared in Europe in 1976. By 1978, the virus was found worldwide, causing a pandemic of myocarditis and gastroenteritis. The virus is not limited to dogs, but occurs in wild species such as coyotes, wolves, foxes and skunks. CPV is closely related to Feline Panleukopenia Virus (FPV), discovered in the 1920s and affects cats, minks and other species. CPV likely arose from 2 or 3 genetic mutations in FPV, allowing it to expand to the canine host range.

Cornell’s Baker Institute for Animal Health scientists, Drs Leland Carmichael and Max Appel, first isolated CPV in late 1978, and by 1979 developed the first vaccine for Parvo. By 1981, they created an improved attenuated vaccine for the disease. The Baker Institute says CPV strikes pups with deadly disease less frequently now due to decades of vaccination, but outbreaks still occur, and they say, “vaccinating your dog is of the utmost importance.” But is it really? Cornell also states, “dogs that recover from CPV infection retain lifelong protective immunity against the strain that infected them.”

No Parvo Vaccines Needed?
The conventional world tells you to vaccinate early and often to stay ahead of Parvo, but is this really the best option? My experience as a homeopathic veterinarian clearly says otherwise. I stopped vaccinating pups (and adult dogs) for CPV completely in 2010 and can say Parvo is less a concern now than it was then.

I recently talked to a client on the phone who said, “Dr. Todd – I just found out my pup was exposed to Parvo, and I talked to the rescue group leader where I adopted him, and she said to get him in for a “shot vaccine” ASAP, because that homeopathic stuff doesn’t work!” After discussing the realities of vaccination and immunity (which aren’t the same), and our experience
here with pups developing strong immunity aside from ‘shot vaccines,’ he felt much better. His pup received a nosode (Greek *noses* = disease) for Parvo at our clinic the week before, and continued to do well, with no symptoms of Parvo disease, and his confidence in homeopathy grew, while his fear of Parvo shrank.

I began to question the wisdom of injectable vaccines several years ago, especially when the fibrosarcoma issue in cats surfaced and was linked to vaccination, then the Purdue study with dogs appeared, linking vaccination to autoantibody production and autoimmune disease. After completing Dr. Richard Pitcairn’s Professional Homeopathy course for veterinarians, I began to adjust my approach to vaccination in practice, as my mind began to think like a homeopath. I started to give pups only two doses of injectable DHPP (distemper, hepatitis, Parvo, parainfluenza), then later reduced it to one, followed by a homeopathic nosode. Then in 2010, I began using nosodes exclusively, no longer using injectable DHPP at all, nor any other conventional vaccine except rabies.

For one thing, I no longer saw anaphylactic reactions after vaccines administration, such as hives, facial swelling, vomiting, diarrhea - and the occasional death. And the little pups certainly appreciated not being “jabbed” on their first visit to the clinic. But, as I began to really look at the data from my practice, other less obvious truths emerged.

Our practice offers a wellness package for puppies, where they receive homeopathic nosodes instead of injectable vaccines, except for legally required rabies vaccine. Nosodes are homeopathic medicines made from the products of disease and have a long history of providing great protection against various diseases, especially if given close to the time of exposure. Christopher Day, a British homeopathic veterinarian, previously reported on nosodes in kennel cough outbreaks in dogs, as well as use in other species. I currently use nosodes prepared by Hahnemann Laboratory in California, dissolved in solution (ethanol and water), and given orally in small amount (2-3 drops per dose). I use 200c potency mostly but have also used 30c. Our goal is to give nosodes at ages where susceptibility and exposure are likely. I reviewed case records from our practice over an 18-month period to look at the incidence of Parvo in our puppy population. The findings are similar to those reported in a previous Dogs Naturally article (November 2011), which stated 28% of vaccinated pups still get Parvo disease, and Parvo kills more vaccinated pups than unvaccinated.

During this time, we saw 275 pups for wellness packages, and 12 of these became ill and tested Parvo positive; 10 of the 12 survived. In addition, 35 other pups, not part of wellness packages, tested positive; 20 survived and 15 died.

Of the total 30 survivor pups, only 6 were vaccinated (20%), whereas 13 of 17 pups which died were vaccinated (76%). Fifteen of the 30 survivor pups received nosodes only (50%), and no vaccines, whereas none of the pups who died received nosodes only (0 %). A small number of pups received vaccines first, then nosodes later (1/30 survivors, or 3%; 5/17 dead pups, or 29%). All pups received only homeopathic medicines for treatment, which are well known historically for treating acute epidemic disease in humans, such as typhus and cholera. Nonvaccinated pups usually respond much more quickly to a homeopathic remedy, and are more likely to survive, compared to vaccinated.
A total 19 of 47 pups were vaccinated and still got parvo disease (40%). Pups receiving nosodes only had 0% mortality, compared to vaccinated pups with 76% mortality. This agrees with the results reported previously in Dogs Naturally magazine (November 2011). These findings confirmed the impression I had for years that vaccinated pups still get sick with Parvo, and when they do, are much less likely to survive the ordeal.

I continue to inform my clients of these facts, and this encourages them with positive news as they choose the no vaccine route for their pup and focus instead on optimizing the pup’s immune system with nosodes, excellent nutrition and dietary supplementation. This allows the pup to develop a robust immune defense against the many challenges it may face, be it Parvo, or other pathogens and parasites. The pups who survive Parvo disease grow into some of the healthiest animals I’ve seen in almost 30 years of practice.

**More Proof of Natural Immunity to Parvo**

To put this in perspective, our practice started in February 2012, and presently has 10,203 total clients, with 21,923 total patients. Over the six-year period under study here, we saw 54,322 appointments, which equates to 9,039 per year, or 174 per week. This is a one doctor practice, with a relief vet coming two days per week if I’m out. So, we are a busy place.

A retrospective view of our clinic records gives more support for non-vaccination (except rabies) and using natural methods to boost immunity to Parvo. Over the last six years (January 1, 2014 to January 1, 2020) we had a total of 651 puppy wellness packages and sent home an additional 918 Parvo nosodes (for those not wanting the entire package), for a total of 1569 pups. During this same time, we had 133 pups test positive for CPV, while 104 tested negative. Of the 133 positive, 51 received nosodes (43 survived / 8 died), and 82 had no nosodes (66 lived / 16 died).

An interesting note is that after 2015, we began to give the Parvo nosode weekly until at least six months old; prior to that, we only gave 3 doses, spaced one month apart. All eight of the deaths in nosode-treated pups occurred prior to this change. Since going to weekly nosode dosing, we’ve seen only 5 cases of Parvo, and four of those were in 2016, so only one case in the last three years (of those receiving nosode). And all five cases survived, with only homeopathic treatment and possibly fluid therapy. Prior to making the change to weekly nosode dosing, we saw 46 Parvo positive pups, with 8 deaths (out of 686 total pups). This amounts to 6.7% of pups testing positive, and 17.4% of the positive pups dying. Beginning in 2016 with weekly nosode dosing, only 5 of 883 tested positive (0.6%), with zero deaths. I will continue to track this trend over the next several years to see if any changes occur. Speaking to my conventional veterinary colleagues in the area, Parvo is still a very common problem in their practices; in fact, they blamed me at first for what they felt was an increased incidence of the disease. Hmm…I look forward to sharing these figures with them. So, let’s look at how to treat Parvo with homeopathy, if it does occur.
Homeopathic Remedies for Parvo
I tend to use a small group of polychrest remedies to treat pups sick with Parvo. A polychrest is a remedy deemed exceptionally useful from over 200 years of clinical experience. Hahnemann says:

“There are a few medicines, the majority of whose symptoms correspond in similarity with the symptoms of the commonest and most frequent of human diseases and hence very often find an efficacious homeopathic employment...they may be termed polychrests.”

By choosing rubrics (or symptoms) corresponding to the most characteristic symptoms of Parvo, we find a list of remedies range in order, according to their similarity. Here is a graph using MacRepertory software, listing just four symptoms:

This is just a portion of the analysis, listing the first eight remedies, and choosing from all possible remedies. Arsenicum album is highest ranking, followed by Ipecacuanha, Phosphorus and Veratrum album, all tied for second.
Here’s a second analysis, using a larger number of rubrics/symptoms:

Arsenicum album is still in highest position, followed by Ipecacuanha, so the first two didn’t change, but the longer list of symptoms does bring other remedies up to consider. One remedy I use often is Nux vomica, especially in the early stages of the disease, if vomiting and nausea are the only symptoms. This remedy will often abort the clinical progression within 12 hours without any other treatment.

If we limit the selection to only antipsoric, or chronic disease remedies, the list changes slightly: So Arsenicum and Phosphorus are the two highest ranking chronic remedies for this group of symptoms; both remedies are also very useful in acute situations. Using the longer list of symptoms again results in a different list of remedies to consider:
Arsenicum album is the highest ranking, with Sulphur, Mercurius and Silicea following. It’s helpful to consider the chronic remedies as possible constitutional treatments for the Parvo case, toward the end of the illness, or if they seem to be ‘stuck’ and not making good progress. Most pups with Parvo will respond very well within 24 - 48 hours, especially if never vaccinated. Let’s finish up with a few actual cases.

**Some Case Examples**
The first is Mia, a 5-month female Pit Bull. She presented with vomiting and diarrhea of 2 days duration, lethargy and no appetite. Hydration was normal, gums pink, and abdomen seemed slightly tender on palpation. Parvo test was positive (Idexx SNAP Elisa). Due to financial constraints, I gave one dose of Nux vomica 10M in exam room, and sent the same remedy home in solution, to give repeated doses as needed. The client reported the next day that Mia improved after the first dose and began eating/drinking a few hours later with no further vomiting or diarrhea. This is not unusual in my experience.

Next is Pudgey, a 5-month male Beagle mix. He came in with history of vomiting and diarrhea; stool was very foul smelling with blood (cadaverous odor), restlessness in cage, up and down and changing positions often. Parvo test was strong positive. He was moderately dehydrated, so I gave Arsenicum 10M and began IV fluid therapy (lactated Ringer’s with 5% dextrose and vitamins B and C) over the next 24 hours. Next day, the restlessness and foul diarrhea were improved, but he now seemed more nauseous (vomiting and heavy drooling) and was becoming more irritable. I gave Nux vomica 10M, and these symptoms resolved over the next 6-8 hours. The next morning, he was barking in the cage, ate and drank without vomiting, and went home that afternoon.
Lastly is a pair of cases – two sibling pups from the same household, Pepper and Precious, both 4-month female Chihuahuas. Both began Puppy Wellness Packages at our clinic on the same day in August 2014. Pepper became ill and came in first, tested positive for parvo on October 29, and received one dose of Arsenicum 10M, as this seemed to match her symptom picture best. She began eating and drinking that afternoon and went back home without any further treatment. Her sister, Precious, came in and tested positive November 3rd, with slightly different symptoms, mostly nausea and vomiting. I gave her Nux vomica 10M and began IV fluids, as she was in worse shape than Pepper had been on presentation. The next day, her symptoms shifted to more of an Arsenicum state (restless, foul smelling diarrhea with blood), so I gave Arsenicum 10M; a total of 3 doses over the next 3 days, as she stayed in this state, without really deteriorating further or changing symptoms. The last day, she improved quickly and went home. Four cases of Parvo, all managed slightly differently, depending on the individual’s symptom picture.

Conclusion
In my three talks today, we’ve covered natural immunity compared to vaccine immunity, the nature of epidemic diseases and the outstanding role of homeopathy over the last 200+ years, and end by showing in a real life example what a difference homeopathy makes in dealing with an everyday epidemic such as Canine Parvovirus. Homeopathy focuses on establishing a high state of health, with natural resistance to disease. In such populations, there will be few susceptible individuals, as the existing level of chronic disease will be lower. Combine this higher level of resistance with alternative ways of building immunity, and the overall health picture of our animal friends will be much brighter.

References
4. Pitcairn Institute of Veterinary Homeopathy. www.pivh.org
Clinical Animal Nutrition Can Be Profitable
Ava Frick, DVM, CVC, FAIS

Objective

- To provide some tools and ideas (based on 22 years of experience) on how to create a profitable nutrition practice

Is nutrition really that important? It is important enough to Purina that in 2018 they established The Purina Institute, “to elevate the topic of pet nutrition with veterinarians to help drive conversations with clients about its role in a pet’s overall health.” Veterinary Practice News, December 2019. To me, this says that after all these years, veterinarians are still graduating without a deep-seated understanding and appreciation of nutrients and tissue function. And, even with all the food companies out there pushing food value, veterinarians remain in a state of confusion about vitamins, minerals, nutrients. What exactly is this one or that one needed for? There is plenty of room for more productivity and income surrounding nutrition.

The article went on to say that based on a poll, veterinarians believe nutrition is critical to pet health. But, when it comes to talking with the client about it, less than 1 in 4 veterinarians have that conversation. They recognized the reason as “time.” But that is an easily fallen upon excuse. If one had the answers and knew how to use nutrition to help that animal get over the illness and become healthier, then the doctor would talk about it and charge for their time. I believe it is a lack of confidence and tools in that area of science and knowledge. I will introduce to you a system where the doctor and any interested staff can have the tools and the confidence to know the right answer or where to go find it easily. Then the exam room scene will change.

Making Money with Nutrition

The degree that one will become successful in a field of interest will be determined by the amount of time spent learning and practicing that art. There is a balance required between the book reading and the direct application. Too much of one or the other in study will result in confusion, lack of understanding, disappointment, and inevitably the decision that one is not capable of doing it. Maybe this scenario has happened to you somewhere in your past when it came to nutrition. You can be able to recommend specific vitamins, minerals, fatty acids, amino acids, and herbs with confidence and certainty. And, that is what will make you money! That, plus charging for your time and expertise, I do. Clients are looking for these answers. When you provide them orthomolecular nutritional guidance that changes chronic problems, you will find more owners asking for the same help.

Here are my steps:

1. Initial assessment, history, clinical signs, diet, seasonal or chronic issues. You may need to restructure your time as traditional practices often only allow for 10- to 15-minute visits. My valuation is $145 for a 30-minute visit, $265 for an hour.
2. Next, the clients fill out a Clinical Animal Nutrition (CAN) Survey™. It is scored, then I review with them the answers, what they mean, and how each relate to the history and clinical signs. This can be a part of the visit fee or you can list it out separately and charge a rate for your time, added to what your current office fees are.
3. Start with some dietary improvements and prescribe a base supplement support per CAN survey results.
4. Submit a laboratory test to further evaluate mineral, vitamin, enzyme, protein, essential fatty acids, and probiotic needs. It is called Hair or Fur Tissue Mineral Analysis (TMA). The laboratory I use is Analytical Research Labs in Phoenix, AZ. The cost at that lab is $45 and I charge $140 for the first test, less on follow up tests.
5. Recheck visit is scheduled for 4 weeks after the TMA was submitted to review the test results and further customize the nutrition program. This is called nutritional balancing. I allow at least 30 minutes for this visit. New supplements will be prescribed to better address the changes on the TMA test. Then tract with follow-up tests every 3 to 6 months with another CAN Survey and TMA. Additional recheck visits may be monthly pending your practice style and the animal’s conditions being addressed.

Evaluation and Discussion
Listening and looking for what part of each of the story has an organ-system-nutrition aspect. What is going on that could have a nutritional component? The bottom-line answer is everything! There is nothing that happens biochemically or physiologically that does not have something to do with a nutrient; vitamin, mineral, fatty acid, amino acid, etc.1,2

Optional Blood Tests
Often the animals I see for nutrition consulting have already had blood tests or are very young and just getting started so do not have organ system dysfunction. The parents in this situation want to start their new youngster out right with customized nutritional recommendations hoping to avoid early illnesses and have a longer healthier life. We can compare blood tests with the results from the CAN Survey. Often, they will match, further supporting the need for specific vitamins, minerals, or other many nutrients.

Diet Improvements
There are many philosophies circulating about what a diet should and should not be and the scope of this lecture does not include delving into that discussion. But I will insert a few ideas to improve what they are eating to maximize nutrient assimilation and other creative ways to make money with a nutrition-based practice. My opinion is that the more we reach to give the animal what their species and breed was designed to eat, what their innate computer is familiar with, and similar to what they would have consumed where they originally came from, the better their health will be.

- Less processing. Less processing, more “real” food (as I call anything other than kibble), some raw, dehydrated, freeze or air dried, and even balanced home cooking recipes can be created as a start to providing a more digestible, sustainable, nutrient dense meal. You can learn to create balanced home cooked recipes, and charge for that service, with www.Balance-IT.com.

- If it must be kibble. Busy life styles make feeding dry kibble easier. And, to my clients who feel the need to do that, I show them the research done at Kansas State University comparing extruded to baked kibble. There is a unique phenomenon that occurs with the
cooking or processing of starch that makes it potentially indigestible and it is called
Amylose-Lipid Complexation (A-LC). The A-LC is a function of heat, moisture, content,
type of starch, type of lipid, and degree of gelatinization. In processing, amylase traps
lipids. Starch gelatinization traps lipids to amylase, reducing free fat availability. This
can be good for the product, as it lowers rancidity and extends the shelf life, but not good
for the body. When fresh meat versus meat meal is used in the food there is a much lower
A-LC score. Fresh meat will produce only 0-20% A-LC. Unrendered fresh meat may be
protected from thermal and mechanical conditioning, thereby preventing A-LC
formation. The extrusion process of making kibble raises the A-LC 90-100%, while
baked kibble tested was less than 60%.³

As of this date there are currently only six companies that make a baked kibble. All of the other
dry foods are processed via extrusion. The first four on this list use meat and meat meal, the last
two use only meat meal. Lotus – lotuspetfoods.com, Stella & Chewys – stellaandchewys.com,
Oven Baked Tradition – ovenbakedtradition.com, Bake to Nature – threedog.com, Well Made –
cloudstar.com, Pinto Canyon – pintocanyon.com.

- **Don’t feed cats like dogs.** The natural feline diet is a meat-based of rodents, birds, and
rabbits that contain little carbohydrate (CHO). Metabolically they have adapted to use
proteins and fats as energy sources. Cats continue to use protein for maintenance of blood
glucose even when dietary protein is limited. Therefore, it is not good to reduce dietary
protein even in the face of renal disease. Cats have a limited ability to adjust protein
utilization to the amount of protein in their diets. Protein oxidation does not decrease in
cats fed reduced amounts of protein. They will continue to use protein for production of
energy and in other metabolic pathways even in the face of low availability of proteins,
leading to malnutrition.

Carnivores require 2 to 3 times more dietary protein than omnivores. Specifically, amino acids
taurine, arginine, methionine, cysteine, tyrosine, and carnitine. Diets high in fiber increase the
need for taurine. Heat processing reduces taurine availability. Cats lack amylase in the saliva.
Further, they have low activities of intestinal and pancreatic amylase, supporting the lack of need
of and ability to digest and utilize CHOs. Any dietary CHO not used for energy is converted and
stored as fat. This is common in the high-starch, energy-dense extruded kibble, which lead to
obesity and hepatic lipidosis. Many of these diets contain high concentrations of insoluble fiber,
which increases fecal bulk and volume, and detrimental effects on protein digestibility. Canned
(and raw or dehydrated) foods are generally best to provide a more optimal dietary combination.
Carnitine supplementation is recommended for obese cats on a weight loss program.⁴

- **Consider food components:** type of food, food energetics, archetype, and individual
supplementation needed for unique qualities of the patient.

**Evaluate the CAN Survey and Initiate Supplement Program**
Using the CAN Survey allows your clients to have input, based on home lifestyle and behavior,
in helping to determine what are the primary, secondary, and tertiary struggling body
components or systems. The survey gives you needed information to make nutritional
recommendations with greater confidence. Discuss the items they checked and how the numbers
and groupings give clues to what is really going on from a nutritional perspective. Organ systems are then categorized as *Primary, Secondary,* and *Tertiary* based on the greatest percentages. The categories or systems that are analyzed are:

1. Sympathetic division of the autonomic nervous system
2. Parasympathetic division of the autonomic nervous system
3. Carbohydrate Metabolism
4. Cardio – Pulmonary
5. Hepato-Biliary (liver, gall bladder)
6. Digestive (parotid glands to colon) or Enteric division of the autonomic nervous system
7. Endocrine: Thyroid, Pituitary, Adrenal Glands
8. Musculoskeletal System
9. Renal (kidney, urinary bladder)
10. Immune System
11. Pain (chronic pain and vitamin deficiencies go hand in hand)

The questions are to be answered by the pet owner. Because of that, they were designed in a manner that a pet owner would see the signs and describe them. When they score each applicable question, they should enter as a (1) = mild severity or not very often, (2) = moderate severity or with some frequency, or (3) = severe or present almost all the time. In that way, the percentage can be calculated for each system and the top three noted for targeting nutritional support. Each category has a list of key recommendations. Here is what one category looks like. There is not enough space to have the entire survey here, but I will bring them with me to the conference or you can go to this website and download them for free. www.LifeExtendMethod.com.

<table>
<thead>
<tr>
<th>GROUP ONE – SYMPATHETIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth, eyes, nose</td>
</tr>
<tr>
<td>Keyed up, fails to calm</td>
</tr>
<tr>
<td>Nervous</td>
</tr>
<tr>
<td>Unable to relax, startles easily</td>
</tr>
</tbody>
</table>

SCORE GROUP ONE: Number marked = Number divided by 36 X 100 = %

GROUP 1: SYMPATHETIC – Supplement recommendations could include: Calcium, magnesium, zinc, inositol, choline, kelp, endocrine support focusing on adrenal and pituitary, St. John’s Wort.¹,²

In initiating a supplement program, you will need to have selected a company, or two or three, that you are comfortable working with to provide the products needed. That decision might consider at least some of these points:⁵

- Time the company has been in existence
- Quality of products
- Number of products available
- Customer service
- Education available to guide you in product knowledge
• Palatability
• Cost and profit margin
• Level of detail and depth you are interested in pursuing clinical animal nutrition and nutritional counseling
• Current good manufacturing practice (CGMP)
• Third party purity testing
• National animal supplement council (NASC) membership

Submit Hair Tissue Mineral Analysis (TMA)
Individual customized nutritional balancing can be further augmented based on the results of a TMA report. A 564-dog case study research published in 2017 substantiates the most typical mineral state in dogs based on tissue calcium, magnesium, sodium, and potassium levels. This test yields information regarding patterns, trends, and function, as opposed to organ disease, as well as toxic metals and ratios that indicate the animal’s oxidation rate.6

Recheck, Review TMA Results with Client, Start the Next Step Toward A Nutrient Balancing Program
The next two presentations will go into how to utilize and interpret this profit-making avenue.

There are simple steps that can be taken to build your confidence in having a nutrition practice and generating money via laboratory supported nutrient recommendations. Yes, initially it will take some time, like any new adventure. But in the end, the means are greatly justified.

References
Objective

- To gain an appreciation of how easy and affordable it is to submit a fur sample for mineral and toxic metal analysis and how the information it provides could help to understand underlying situations that affect body function and create conditions that can be treated with nutrient recommendations.

Fur (hair) tissue mineral analysis (TMA) is a technique using soft tissue mineral biopsy that provides a reading of the mineral deposition in the cells and interstitial spaces of the hair over a 2 to 3-month period. Hair and fur are chemically indistinguishable, having the same chemical composition, and are made of keratin. The primary difference between hair and fur is the word usage. Because hair in the growth phase is exposed to the internal metabolic environment (circulating blood, lymph, and extracellular fluids) and retains the metabolic products presented to it as it hardens, it becomes a perfect tissue sample for testing body function, metabolic trends, and toxic metals. This form of testing allows for measurement capabilities of nutritional alterations and improved recommendations for vitamin and mineral supplementation or nutrient augmentation. Hair analysis offers a perspective for studying both “disease” trends and for studying “stress” and physiological coping mechanisms.¹

TMA is a non-invasive and a cost-efficient screening test (medical professional cost usually under $50). It has been used throughout the world to assess individual or herd nutritional status, providing a sensitive indicator of the long-term metabolic trends from the effects of diet, stress, and toxic metal exposure. Most deficiencies in animals are brought about by altered relationships of minerals within the body. It has become evident that both the retention and loss of minerals by the animal are equally as important as the nutrients consumed from the feed or diet itself.

The fur is collected via clipping or cutting, primarily from the ventrum so that there is no visible bald spot. It should be no longer than 1.25 cm in length (cut off excess) and taken close to the skin. Samples are weighed on a small scale provided by the laboratory to at least 100 mg (less than 100 mg would produce insufficient sampling), placed in a paper envelope, and submitted to the lab. Hair that has not been washed for more than four or five days is more prone to environmental contamination. Therefore, a bath given within two days is preferred. If a salt-based water softener is used in the home, hair sodium levels may be affected. Dogs that swim in the ocean regularly will need to be kept out of it for several days and washed 1-2 days prior to collection. Hair should be dry when it is sampled; otherwise, it cannot be weighed correctly. The sample should be taken between four and twenty hours after washing. This allows the hair to re-equilibrate after washing.

For animals treated with topical insecticides and pesticides, it is recommended to collect the sample during the last week of the treatment cycle (i.e., 1 week before the next application for most products). The animal can be bathed and then clipped 4 hours later. Alternately, the ventrum, where the sample will be collected, can be lightly sprayed with alcohol, wiped clean, and then clipped, avoiding the topical application zone. While the laboratory is responsible for the technical aspects of the test, the results will only be as good as the raw material or sample
that is received. For this reason, the more care that is exercised by the person sampling the hair, the better the results will be.

Hair is 10-15% porous, and washing agents used in the laboratory process can remove not only the exogenous elements but also penetrate inside the shaft and wash out some of the loosely bound minerals, like potassium, sodium, calcium and magnesium. Washing a sample during test preparation removes quantities of water-soluble macro-minerals. When hair samples are not washed by the laboratory prior to assessment, the analysis can accurately measure macro-minerals. Therefore, it is important to select a laboratory that does not wash the submitted specimen prior to the mass spectrometer analysis.²³ For that reason, I prefer Analytical Research Laboratory (ARL) in Phoenix, Arizona.

Computer-controlled mass spectrometers and induction coupled plasma instruments are used today at hair testing laboratories in the U.S. All commercial hair testing laboratories in the U.S. are licensed and inspected annually by the federal government as part of the Clinical Laboratory Improvement Amendments (CLIA) act.

There are thousands of biochemical reactions that ultimately control metabolism, digestion, and the regeneration of body tissues. The vast majority of these reactions depend on minute amounts of trace minerals for their activity. If these essential minerals are not present to fuel the processes, then the body’s ability to regenerate, metabolize, or break down noxious substances is compromised.

Mineral levels and ratios, as reported on the test, can be affected in the body by the presence of toxic metals, nutritional deficiencies, infections, illness, or stress from a myriad of sources, including mental. Assessment of an individual’s stage of stress and oxidation rate (how fast the body metabolizes the food in exchange for energy) can be determined by this test. Changes in body chemistry are reflected in the cellular metabolism as measured by the hair tissue mineral levels and inter-relationships. These can indicate metabolic dysfunction before clinical signs occur. While blood values reflect what is in the blood at that moment, hair analysis provides a record of how the body stores and disposes of elements. The choice of hair as a testing medium is because blood chemistries change dynamically from day to day, while hair values give a more stable view of the overall mineral nutrition.⁴

In a recent publication, tissue mineral levels and electrolyte patterns of calcium (Ca), magnesium (Mg), sodium (Na) and potassium (K) were analyzed in 564 dogs (300 male, 264 female; 99% neutered or spayed) of variable breeds. The health conditions or clinical signs of the dogs ranged from apparently healthy to dermatitis, anxiety, nervousness, aggression, gastrointestinal conditions, metabolic conditions, neuromuscular, pain, and degenerative joint disease. Ninety-four percent (94%) of the 564 dogs were found to have high Na to K ratios with low Ca and Mg. Ca, Mg, Na, and K are prevalent minerals in the body, regulate osmotic balance, and are involved in most body functions. According to mineral analysis research, both results (levels and ratios) are indicative of inflammation.⁵
Determining the tissue level of key macro and micro minerals can help to explain and better treat many conditions. Both a deficiency and excess of Ca and Mg have been shown to be of pathogenic value in the development of endocrine disorders and thyroid disease. A tissue Ca deficiency can exhibit as a sympathetic dominant state (alarm or fright-flight reactions), anxiety, bruising, high blood pressure, “fast” oxidation/metabolic state, insomnia, irritability, muscle cramps and spasms, nervousness, hyperactivity, osteoporosis, weakened ligaments and tendons. When the extracellular fluid level of Ca ions drops below normal, the nervous system becomes progressively more excitable due to an increase permeability of the neuronal membrane to Na.

A deficiency of tissue Mg affects the autonomic nervous system, behavior, muscle tone and function. Clinical signs include poor appetite, irritability, weakness, muscle tremors, tetany, twitching, numbness, tingling, confusion, disorientation, personality changes, apathy, memory loss, skin lesions, tissue calcification, elevated cholesterol, cardiovascular changes, tachycardia, elevated parathyroid hormone, pancreatitis, and stress. Magnesium deficiency increases catecholamine secretion, which raises sensitivity to stress and is also a factor in urinary loss of Mg.
High tissue Na levels are indicative of excessive adrenal gland activity and excitability. Excess Na combined with too much phosphorus, low tissue levels of Ca, Mg, K, and zinc result in adrenal insufficiency. Na, when elevated in the tissue, is a stress that is associated with anger and fear, the emotions of the “fight or flight” response, and an indication of body inflammation. With the activation of the stress response, the adrenal glands increase their secretion of the hormone aldosterone, which increases the retention of Na in the cells and tissues.

A TMA also addresses key mineral ratios. For example; the Calcium/phosphorus (Ca/P) ratio on a hair mineral analysis is an indicator of an individual's autonomic state. The autonomic state is important as it is closely related to the activity of the adrenal, thyroid, and pituitary glands. A low Ca/P ratio in dogs and cats, indicates a sympathetic state, while a high ratio indicates a parasympathetic state. Ca/P ratio reflects the endocrine gland activity of the anterior and posterior pituitary. Causes of autonomic imbalance include a poor diet, mental stress, fearful thinking, structural imbalances, physical or emotional traumas, and exposure to toxic metals and chemicals. All these can affect the hypothalamus and pituitary gland.

The body’s oxidation rate (fast, slow, mixed) can be determined by comparing the Na/Mg and Ca/K ratios. Oxidation is affected by stress and ways that the body responds to stress. The stress may be from within, such as nutrient deficiencies, fatigue, disease, or environmental sources. Stress may also arise from a mental perspective and how the individual perceives life events. Many factors can influence tissue mineral levels and ratios. The goal is to reach a balanced state, neither too fast nor too slow. It is an optimum condition in which the metabolism can speed up or slow down at will and not get stuck or held up.

Toxic metals are fixed in the protein structure of the hair tissue as the hair grows. Hair gives a record of exposure over time and the metals are easy to detect and measure accurately in the hair tissue. However, hair testing only reveals what is in the hair, not the entire body load. Each toxic metal has target organs. For example, lead deposits mainly in the bones and brain. Cadmium deposits in the kidneys and periosteum, mercury in the kidneys and brain, and so forth. These metals become part of the actual structure of the tissue or enzyme. Damage from toxic metals may occur due to their physical properties, their chemical properties or even electromagnetic interference. They often interfere with the absorption and metabolism of essential minerals and they displace vital minerals in enzyme binding sites. This can inhibit or completely disable the affected enzymes. Hair is not a target tissue for toxic metals, but it is a tissue used by the body to eliminate toxic metals.7

I have utilized TMA testing for 15 years and with the information therein have helped to accurately identify reasons for clinical signs in patients that were not responding to traditional medical approach. It is beneficial in isolating allergies, protein losing diseases, reason for cruciate ligament tears, rear leg tremors, anxiety, chronic conditions, and many idiopathic "diseases". We like to believe that a new baby is perfect, but far from it. They are born with whatever the mother has or doesn’t have. Starting TMA testing on early examinations can serve to prevent future conditions by addressing the issues and introducing correct nutrient balancing. Macrominerals are essential in metabolism in that they activate catalytic and enzyme functions. Hair analysis is used not only for measuring those minerals but also to monitor the nutritional state of animals.
Disease trends and metabolic changes can be documented and supported by using hair TMA. Helping or treating stress with specific minerals can improve the overall health status. Malabsorption or bio-unavailability of specific minerals can occur due to gut interference; improper form; lack of other needed vitamins, minerals, or amino acids; and ligand interruption, to name a few. When performed to standards and correctly interpreted, a TMA can be used as a screening tool in animal wellness programs; and for those in suboptimal health, for monitoring mineral deficiencies, mineral excesses, biochemical characteristics, system imbalances, supporting behavior, endocrine indices and is a key tool for making well planned, laboratory supported, nutritional supplementation recommendations.

References

8. Grogan J. Hair mineral analysis provides a unique perspective on a horse’s biochemical individuality. Integrative Veterinary Care. Fall 2013;38-42.
Interpretation and Nutritional Balancing with Tissue Mineral Analysis
Ava Frick, DVM, CVC, FAIS

Objective
- To learn how to break down the information presented on a Hair Tissue Mineral Analysis (TMA) test and support the body with nutrient specific recommendations.

When I assess a TMA report, I take these steps:
1. Look across the chart to see which minerals are generally low or high. The first four are the electrolytes; calcium, magnesium, sodium, potassium. Other minerals include iron, copper, manganese, zinc, chromium, phosphorus.
2. How close they are to the optimal line - the dark line across the bar graph is the optimal level, within a small deviation above or below.
3. Assess for any minerals that are excessively low or excessively high. This will reflect the level of distress for those minerals. There are times when a low mineral may need to be supplemented (calcium, magnesium). But, where manganese is low in presence of high sodium, it should not be directly supplemented. It is very important for joint stability but will rise in the tissue as the adrenals are balanced and the sodium and aldosterone levels drop.
4. Next, I review the mineral ratios; note the optimal mean ratio and patient ratio. These were reviewed in the prior lecture as to their meaning. Key ones being; Ca/Mg, Ca/K, Na/Mg, Na/K, Ca/P.
5. Then determine the oxidation rate. Based on the Ca/K and Na/Mg ratios it will be fast, slow, or mixed.
6. Lastly, I look at the toxic metals; lead, mercury, cadmium, aluminum, arsenic.

Reasons that minerals may be low or high in the body can include:
- Carbohydrate overload
- Inadequate mineral levels in food
- Chemicals
- Heavy metals
- Herbicide exposures binding or pulling minerals out of tissue
- Interference with uptake or use
- Processing of food
- Breed idiosyncrasy
- Other mineral/vitamin deficiency or elevations
- Neutering and cytokine elevation causing a rise in inflammatory processes
- Drug interactions
- Other disease or present conditions
Ratios
The body functions based on not only a single mineral (is it low or high) but also the ratios. Mineral ratios are indicators of the status of body function, including inflammation, stress, autonomic state, metabolic system predictors, and behavior. The ratios are reported in the bottom right corner of the page. Mean Ratio is optimal. Pt Ratio is the patient.

How to Address an Imbalanced Ca/Mg Ratio
1. Begin by reducing dietary carbohydrates. A high-carbohydrate diet depletes zinc, vitamin B6, and often lacks taurine, which is found only in meats. Deficiencies of these nutrients may cause a magnesium loss or bio-unavailability.
2. Correct the diet in accordance with the oxidation type.
3. Improve digestion with enzymes and probiotics.
4. Supplement with enough zinc, magnesium, vitamin B6, and taurine is helpful, along with supplements indicated by other hair analysis patterns.
5. Reduce stress. Severe stress can inhibit or even override any dietary or supplement program.

**How to Address an Imbalanced Ca/K Ratio**

1. Fast Ratio = K>Ca or the Pt Ratio is too low
   - When the potassium level greatly exceeds calcium, the thyroid is running very fast. A hyperthyroid cat needs 250 times more calcium than a euthyroid cat. Therefore, calcium supplementation is key.
   - Zinc helps to rebalance potassium
   - Support other organs that are stressed; liver, kidney, digestion
   - AVOID supplements or joint supports of any kind that have added vitamin C as it further depletes calcium

2. Slow Ratio = Ca>K or the Pt Ratio is too high
   - When the calcium level is greatly exceeding optimal, the body is trying to take a rest. Pushing the body into a faster state by treating with thyroid replacement may not be optimal. An older body physiologically cannot run like a young one. 70-year-old people function differently than a 25-year-old. Giving replacement hormonal therapy at a high dose can be like driving a car at high speeds; the motor and engine will wear out sooner and can cause an old vehicle to burn up.
   - Allow the body some rest, support the endocrine system with appropriate vitamins, minerals, and herbs.
   - Vitamin C to reduce an extremely high calcium - whole food source is preferred over ascorbic acid as that is only the antioxidant part of vitamin C.

**How to Address a High Na/Mg Ratio**

1. Zinc supplementation: Zinc lowers high sodium. This mineral deficiency is widespread in dogs. Test results may have zinc at close to optimal, but there is not adequate available zinc to deal with the consistent stress, elevated sodium, and day-to-day needs. Zinc is required in over 200 enzyme reactions in the body alone. Additionally, the immune system, liver, and skin need zinc for optimal function.
2. Magnesium supplementation: Magnesium also has a lowering effect upon sodium and is helpful in correcting the ratio.
3. Other nutrients that help to reduce elevated sodium:
   - Taurine
   - Vitamins A & D. This can be provided with fish oils if the thyroid ratio is not slow. If it is, use other whole food sources.
   - Choline
   - Inositol (Vitamin B8)
4. Many people assume that high sodium indicates an excessive salt intake. The test is measuring sodium, not sodium chloride. I have found in many hundreds of dogs with a high sodium level, the addition of KCl helps address the adrenal state and bring the aldosterone into a better level, helping to lower sodium.
How to Address High Na/K Ratio
1. A high Na/K ratio often indicates a zinc deficiency. Zinc lowers sodium and raises the potassium level. Zinc deficiency is prevalent in dogs. Test results may have zinc close to optimal, but there is not adequate available zinc to deal with consistent stress and elevated sodium. More zinc is needed if the ratio is very high.
2. Magnesium also has a lowering effect upon sodium and is helpful in correcting the ratio. The zinc or magnesium levels on the hair analysis may appear normal or even elevated.
3. Support the kidneys. A very high Na/K ratio may indicate kidney stress.
4. Support the immune system. While a low Na/K ratio is associated with a weak immune system, a high ratio may indicate autoimmune tendencies or an overactive immune system.

How to Address Low Na/K Ratio
1. Improve nutrition quality
2. Support digestion
3. Reduce stress and get a routine that permits rest
4. B vitamin complex
5. Support thyroid and adrenal glands
6. Immune system support with zinc, vitamin A, herbs, whole food vitamin C (if Ca levels are not low), copper

How to Address Imbalanced Ca/P Ratio
1. Enzymes to improve protein assimilation and digestion
2. Support glandular activity and cellular respiration
3. Replenish minerals
4. Eliminate toxic metals and chemical exposure. Get into a routine of cleaning paws nightly and bathing more often
5. Improve diet based on the oxidation rate

Oxidation
Oxidation is the amount of time it takes for a body to convert the food eaten (fats, carbohydrates, protein) into energy or fuel for that body. Energy is formed and released at different stages during two cycles – glycolysis and the Citric acid cycle. To get the most power out of foods, both periods need to work at the right rate. If carbohydrates and amino acids are oxidized too slowly (“slow oxidation”) in one cycle or too quickly in another cycle (“fast oxidation”), energy production is reduced. Both fast and slow oxidizers suffer from inefficient energy production, but for opposite biochemical reasons. Fast oxidizers burn their food quickly, and slow oxidizers are the opposite.

Fast Oxidizers (Both Thyroid Ratio and Adrenal Ratio are Fast)
These bodies have higher caloric needs. Fats provide more calories and longer-lasting energy. In contrast, sugars burn too fast, offer fewer calories, and often further enhance the oxidation rate. For this reason, fast oxidizers should avoid starches and carbohydrates as they convert to sugars. Even complex carbohydrates are recommended only in small amounts.
**Slow Oxidizers** (Both Thyroid Ratio and Adrenal Ratio are Slow)
These bodies require more protein and less fat in their diets. Protein with every meal is most important to maintain their blood sugar level and support adequate adrenal and thyroid gland activity. Animal protein is essential because it provides nutrients such as zinc, alpha-lipoic acid, sulfur-containing amino acids, and L-carnitine. Meats also provide other less-known nutrients that the slow oxidizer requires. Digestive enzymes are often helpful in helping to obtain all the nutrition from their food. Keep in mind that processed meats (extruded, dry food diets) are no longer the “real” meat.

**Mixed Oxidizers** (One of Either the Thyroid or Adrenal Ratio is High and the Other is Slow)
These bodies can be fed a blend of the recommendations for a fast or slow oxidizer. As this animal is in transition, it will find one of the other rates soon. Hedge toward the stronger of the two based on TMA ratios, the animal’s appearance, digestion, and any other symptomatology that is pertinent. Trying a little bit of each until you find out right where the animal does the best would also be an excellent way to determine what to feed.

**Toxic Metals**
Specific nutrients are needed for the body to release toxic metals. The dietary and supplement program provides toxic metal antagonists, chelating agents, and enhances the activities of the organs of elimination. Toxic metals are revealed on hair analysis tests as they are being eliminated. Even with these measures, toxic metals stored deep within the tissues can take years before the body is able to eliminate them. Toxic metals can only be eliminated as fast as the body is able to do it safely. Months to even years may be required. Progress can be traced by repeat hair mineral tests.

The first step to begin eliminating heavy metals is to enlist an effective nutrient balancing program:
1. Replace missing minerals and vitamins
2. Support the organs of elimination such as the skin, liver, kidneys and colon
3. Enhance energy production as energy is required to eliminate toxic metals

Balanced body chemistry will support the metabolism to facilitate the elimination of toxic metals. Once the organs are better equipped, the detoxification can begin.

Mineral therapy can help remove toxic metals. Each toxic metal has specific mineral antagonists that inhibit its absorption or metabolism. For instance, cadmium antagonists include calcium and zinc. Mercury antagonists include selenium. The antagonists include the physiological minerals needed to replace the toxic metals. As step #1 above is implemented, the body will begin to let loose of toxic metals in exchange for the optimal mineral.

The use of natural chelating agents or antagonists, can help remove toxic metals but this option should only be used after steps 1-3 have been well established and several TMA tests have been followed.

This is a brief introduction to interpreting a TMA and how, with this information, you can begin to make some calculated nutrient recommendations. There is 70 years of study and research that
has gone in to developing this science. Once you understand it, the puzzle becomes easier to solve and the changes seen in the patients are traceable.

References
Photobiomodulation - De-Myth-stifying Light Therapy Devices
Janet Gordon Palm, DVM, CVCP

Objectives
- To differentiate between heat and non-heat producing light therapy devices is essential to an awareness of safe treatment applications.
- To understand how power, wavelength, and frequencies impact the treatment success of animal response at a quantum level.

Introduction
Photobiomodulation is described as “a form of light therapy that utilizes non-ionizing forms of light sources, including LASERs, LEDs, and broadband light in the visible and infrared spectrum. It is a non-thermal process involving endogenous chromophores eliciting photophysical and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain and inflammation, immunomodulation, and promotion of wound healing and tissue regeneration.” (NAALT)

Distinguishing Laser and Light Therapy Devices
A brief review of Lasers reminds us that Light Amplification by Stimulated Emission of Radiation (LASER), is characterized by monochromatic (one wavelength), traveling coherently (in sync), in a focused direction. The resulting beam is thus crisp and sharp as energy is focused into a smaller surface area.

LED is Light Emitting Diode and is characterized by non-monochromatic wavelength, non-coherent, and multidirectional. The familiar glow visualized upon viewing the beam demonstrates the energy being dispersed in a wider surface area. LEDs are not as likely to cause deep thermal burns as a result of this energy dispersion. Laser classification is determined by risk of thermal damage and potential damage to the retina. These Classifications range from Class 1-Class 4. Thermal changes begin to occur with Class 3 and 4 lasers due to the increase in power as well as wavelengths beyond the visible light spectrum.

- Low power lasers (Class 2, 3a) are defined to have power up to but not including 500mW (0.5Watts).
- High power lasers (Class 4) have 500mW and above.

The blink response is triggered when eyes are exposed to light wavelengths between 400nm and 660nm. Wavelengths below or above this range can be damaging. The near infrared wavelengths over 800nm are characteristic of strong Class 3b and Class 4 lasers.

Specialized eye protection is required for operator, patient, and anyone within 20 feet of the device in operation. OSHA guidelines require not only approved specialized eye protection, but also a specialized dedicated laser room where opening the door would cause the laser to stop operation. Also advised is removal of jewelry in order to minimize potential of damage from spectral radiation.
Strict adherence to these guidelines will help to ensure that litigations can be prevented that would obstruct the future of this promising technology.

Differentiation of the different lasers and capabilities can be determined by the
- Wavelength (405nm, 635nm, 830nm, 904nm, 1064nm)
- Power (High >500mW; Low <500mW)
- Pulsations/ frequencies (continuous wave vs pulsed)

There has been an equal amount of growing interest in LLLT, as there has been confusion, misinformation, and sometimes less than stellar results. Laser devices vary in power, wavelength, frequencies, and whether they are in fact a true laser, or an LED. There is a lack of clarity in what should be required knowledge of vital information regarding the device specifications prior to purchase. Current studies can be a source of confusion as there is a lack of clarity in reporting the dosimetry parameters. Variations in wavelength, power density, irradiation time, application specifics, and repetition regimens can result in ineffective treatments, tissue damage and negative results. Often, a positive result is extrapolated to a device that has completely different wavelength and power output. This generalization can be a recipe for disappointment at best, or disaster in the event of thermal injury.

Knowledge of the benefits and limitations of the device allows appropriate and safe use as well as optimum results. Although there can be no question that high power Class 3b and 4 units can have beneficial results in areas of joint and muscular rehabilitation, they have potential to cause thermal injury either due to improper handling of the device, or to fragile endocrine and gonadal tissues intolerant of this temperature variation. Proper training can undoubtedly minimize this risk, however, it is this author’s opinion, validated by colleague reported consequences such as the “smell of burning feathers”, singed guinea pig hair, third degree burns on an equine spine, and other evidence of thermal injuries, that this is an unacceptable risk when non-invasive options are available.¹ Sensitive endocrine tissue (adrenals, pancreas) as well as gonads exposed to the deeper penetrating wavelengths of a Class 4 laser may be at risk of developing future pathology. These organs are known contraindications for elective treatment using high power lasers.

A non-heat producing Class 2 non-thermal Low-Level Laser (5mW and 7.5mW) with visible light wavelengths of 635nm (red) and 405nm (violet) is a safer option that exists. At one hundredth of the power of Class 4 lasers, these Class 2 lasers cause vasodilation and photobiomodulation without generating heat. The case responses will demonstrate that in a living organism, a therapeutic response can occur well before a calculated therapeutic dose is achieved. Examples include expediting major wound healing, neurologic conditions, musculoskeletal issues, arthritis, abscesses, infections, immune stimulation, and endocrine balance. Also included is the ability to affect the sympathetic and parasympathetic nervous system to calm animals, increase appetite, and improve gut motility.

**Therapeutic Dose vs Therapeutic Response**
The now outdated concept that more power and longer wavelengths are essential to affect deep tissues is challenged by obvious patient response. While this may be true to deliver a calculated therapeutic "dose" to a measured distance in a mathematic calculation or cadaver leg, that
argument doesn’t take into consideration the unique characteristics of a living biological system with the properties of bio-photons, biologic water, electromagnetic fields, and the intercellular Integrin system of signal transduction. **Therapeutic response** can occur to deeper structures (6cm) within a treatment time of 6 minutes, as measured by MRI. This is in direct contradiction to the 4 hours of treatment time that many established laser experts have claimed with the insistence that the therapeutic dose must be achieved. Tuner and Hode have since discussed that the idea of therapeutic dose needs to be re-evaluated.

In order to understand this cascade effect of cell-to-cell response to affect deeper tissues, one needs to turn to Albert Einstein who proposed the **stimulated emission of radiation** phenomenon. Absorption of the light energy results in the photons exciting the electrons orbiting the nucleus of the atom to a higher orbit. When these electrons decay back to the ground state, they emit a photon to the neighboring atom, whose electrons excite, also emitting a photon as they retreat to ground state, and the process continues in a 3-dimensional cascade effect eventually affecting the entire organism. Lending credence to this continuing cascade effect, Mester has shown that laser effects are systemic. Studies on burn victims, when only one affected limb was treated, have shown the laser treated area healed faster than the control group, however the opposite non-treated area also healed faster than the controls. Incisions on rats behaved similarly.

**Importance of Communication and Case Selection for Optimum Results**

Rehabilitation at the cellular level works best when considered as an adjunct to healing along with rehabilitation at the spinal and connective tissue levels with some form of neuronal modulation such as acupuncture, osteopathy, chiropractic, VOM and myofascial release techniques. Other building blocks for healing include adequate nutrition, hydration, exercise for lymphatic drainage and circulation, as well as mental enrichment to aid in managing the deleterious effects of stress. The author feels that managing the animal’s emotional state and their primary need that day, is of equal importance to any healing modality performed beyond that initial interaction.

Having performed thousands of laser therapies over 10 years on multiple species including birds, dogs, cats, pocket pets, horses, cattle, tigers, lions, raptors, and other wildlife, the author is familiar with a myriad of responses. This can range from the "wow" response (horse able to bend his neck immediately) seen typically with managing acute pain and inflammation; to gradual improvement noticed after several treatments as tendons and ligaments heal.

In the event of slight to no response within 6 laser treatments, the rationale includes several possibilities. 1) Either the cells have rehabilitated to the extent they can, (prompting a review of nutrition, hydration, nutraceutical status) as healthy cells do not respond to biostimulation as pathologic tissues do; 2) There may be an underlying condition yet to be diagnosed; 3) the wrong diagnosis has been made; 4) the treatment protocol needs to be tweaked and thus the need for close follow up and progress exams.

Communicating these factors to owners is paramount to compliance and expectations. It is not practical to imply a prediction of who will receive a “wow” response, and who may offer a previously non-existent left lead canter in 1-2 weeks. That is why close follow up calling is imperative within 1-3 days and medical progress exams initiated when appropriate. In seven plus
years of performing LLLT, this author has yet to have an owner regret their investment, as realistic expectations were explained.

**Roll of Frequency LLLT in Healing**
There is controversy concerning the validity and importance of frequency (oscillations or pulsations) of the laser light in the overall effects of healing response. Previous pioneers in the study of varying frequencies of micro-electric current energy (Tesla, Rife) support this concept. Light in various energy forms has been extrapolated with exciting results.

**Treatment Intervals and Protocols**
It MUST be noted that the protocols used with this laser system cannot translate to other lasers. These unique specifications are found to be tissue friendly, non-heat generating, and thus have more tissue versatility than many other laser devices.

The treatment protocols vary on a case-by-case basis, which is where the true "Art" of medicine comes in. Determining factors are as follows:

- **Physical exam / Supporting Diagnostics**
- **Diagnosis- or list of differentials**
- **Chronicity of Condition or Symptoms**
- **Owner Compliance to Schedule and Costs**
- **Response to Treatment**, and thus follow up is imperative!

A) **Accelerated Plan: Severe trauma, pain**
- 2 treatments 90 + min apart; 3 days in week 1; 1 treatment / day for 3 days in week 2, then 1 treatment/day for 2 days per week; Total 8-13 treatments
- 60-120 seconds for each module
- 70-90 min between Treatments allows physiologic changes to occur in order to receive optimal benefit as a second treatment. LLLT is cumulative and the benefits will be seen sooner with the accelerated plan. Noticeable benefits may be witnessed within hours with acute injuries, or several days if healing connective tissues and fractures.

B) **Chronic Plan: Long Term, Low Grade Pain**
- 2 treatments on day one; 2 treatments once weekly for 2 weeks, then 1-2 treatments/week

C) "**Try and See" Plan: Diagnosis Open**, or owner has financial limitations.
- This would involve 2 treatments day one, then; then 1 treatment/ week.

**Autonomic Nervous System Applications for Calming**
The autonomic nervous system controls all life functions and is always in a state of balance. When the sympathetic tone is high (fright or flight) the parasympathetic tone is low (homeostasis, digestion, appetite).

The sympathetic ganglion reside along the paralumbar muscles between T1-L3. The line-generated beams of the laser device can access this entire area. As photonic energy is absorbed using Rife inspired frequencies for sympathetic nervous system, electrons are stimulated to higher orbits, subsequent photonic emissions to neighboring atoms occur in a cell-to-cell cascade.
while the sympathetic tone is continually stimulated. When the pre-programmed light stops in 120-180 sec, the sympathetic tone plummets, allowing the parasympathetic tone to increase. Within minutes, a fractious, painful, or emotional animal can be calmed to a more harmonious state. Appetite, peristalsis, and focus are restored. Blood pressure has been documented to decrease.6

Similarly, the parasympathetic tone can be further enhanced. After the sympathetic protocol, the calming can be even more stimulated. The areas to receive the laser light input would be cervical and sacral, where the parasympathetic ganglion reside.

It is important to note that the sympathetic stimulation should NOT be used in shock, anesthetic emergencies, or near-death cases. In these cases, the Parasympathetic stimulation ALONE is indicated. Further stimulation of a sympathetic tone in these fragile patients could be detrimental and send them over the edge.

It is advised to prepare the staff to have the laser available, set for parasympathetic settings to have at hand for any shock, severe trauma, anesthetic emergency, collapse, or fragile state. This will save time in the event of an emergency. If there can be a fraction of a second plateau in an otherwise downward spiral that can make the difference between life and death, it is well worth it.

**Immune System:** Borrowing on the concept of varying the frequencies for specific tissues, allows for access to enhancing the immune system.10

**Wounds, soft tissue, tendon, ligament injury, Post-op Applications:** The proposal that laser energy merely promotes cellular energy rather than changing cell function explains why injured tissue cells respond to laser therapy whereas there is little effect on non-injured cells.

Laser energy is more effective in treating pathological states, therefore, when healthy subjects are used, the outcomes may be subdued. Although tissue healing is accelerated, no hyperplastic effects have been reported. During wound healing, laser wounds had more collagen and a higher tensile strength than the controls, until healing was complete, at which time both lasered and control groups were similar. Laser energy catalyzes normalization rather than creating a super normal effect. Thus, proud flesh (in the case of a horse) would not be accelerated beyond that of non-lasered individuals.11

LLLT is used for pre and post-op surgical applications in soft tissue as well as orthopedics. Studies have shown that when using the bactericidal Violet 405nm 5mW on osteoblasts in cell culture when studying infected arthroplasties, over 15mW altered osteoblast function. It was concluded that 5mW was the maximum power recommended to stimulate osteoblast function.12 As a reminder, popular Class 3b units are generally over 60mW and Class 4 are 500mW, and the heat produced can be felt and found to be uncomfortable.1 Use of the violet/red low power laser in orthopedics for fracture repair and infection control is exciting.

**Colic, Obstipation, Decreased Gut Motility**

Neuronal adjustment and myofascial release is very helpful in restoring nerve communication to
the end organ system including peristalsis to the gut. The light energy absorption and eventual response to the thymus, spleen and lymphatics is intended to speed the production of macrophages and killer T cells.

**Arthritis, DJD, Fractures**
Sympathetic/parasympathetic calming balance should be performed if appropriate. Nervous system settings for the nerve root that innervates the area of involvement, as well as pain/inflammation settings for the area of involvement would be suggested. These can be accessed simultaneously with some Class 2 lasers that offer two probes, or sequentially as with single probes. The line-generated beam allows for entire spine, leg, or multiple legs laser at the same time.

**Endocrine Disease**
Endocrine diseases can also be treated, as there exists no contraindication due to the non-heat producing qualities of this laser. Although a cure is not suggested, there have been cases of reversal of early onset diabetes when pancreatic inflammation has been decreased, and islet cells stimulated to regenerate their insulin producing abilities.

**Cancer**
Palliative care for cancer patients is indicated, as the benefits of improved circulation, lymphatic drainage and decreased pain and inflammation in a non-heat producing effect has been demonstrated.

**Conclusions**
True Photobiomodulation is a non-thermal process. Although light therapy devices have become a mainstay in cutting edge human and veterinary practices for pain management and advanced healing, benefits must outweigh risks. This is to ensure confidence that our integrative healing intentions abide by our oath to “Do No Harm.”

There is little doubt that heat has been beneficial in vasodilation, it is not however, well tolerated by sensitive tissues such as the endocrine organs and gonads. Care must be given to ensure safe guidelines are strictly adhered to. LED therapy has been helpful in healing. Although LEDs lack the focused energy of a true laser, LEDs placed over wounded tissue or acupuncture points has been beneficial. The abilities of the non-thermal low-level laser with its line generated beam, low power and visible light wavelengths, allow safe treatment of a myriad of infectious, inflammatory, and degenerative diseases. The ability to affect the Autonomic Nervous System to calm and stimulate appetite and gut motility, treat endocrine, gonads, laminitis and sensitive tissues not amenable to heat, shows promise. Managing arthritis and joint disease, as well as expediting wound and fracture healing effectively without the additional risks of higher power units, has been proven. The safe use and lack of need for eye protection allows for confident staff use and client and handler safety. In addition, the ability to treat from a safe distance without sedating the animal, with no risk of retinal damage, is invaluable.

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Frequency Specific LLLT - It “Hertz” So Good
Janet Gordon Palm, DVM, CVCP

Objective
- To demonstrate that the role that frequency plays in conducting the orchestra of the symphony involved in healing.
- To demonstrate that incorporating frequencies into energy medicine can aid in the management of chronic disease conditions.

Introduction
There is controversy regarding the benefit of frequency specificity in treating patients with low power laser therapy. This presentation will draw from previous works performed by Nikola Tesla, Albert Einstein, Royal Raymond Rife and other pioneers in their studies of varying pulsations in electric current as well as the existence of biophotons. Varying the frequency of different forms of energy has been shown to affect specific tissues and organisms. Feline species are equipped with a self-healing series of vibrations that we know of as the act of purring. These vibrations have been measured in a range of 20-150 Hz, correlating with known healing frequencies of different tissues. Case responses of the use of varying frequencies of low power laser light in multiple species will allow for a vibrant conversation intended to stimulate further investigation, as well as inspire participants to open their minds to the quantum physics involved in frequencies incorporated into LLLT. To quote Nikola Tesla, “If you want to know the secrets of the Universe, think in terms of energy, frequency, and vibration.”

Roll of Frequency in Healing
There is a continuing conversation concerning the validity and importance of frequency (oscillations or pulsations) of the laser light in the overall effects of healing response. In this author’s experience, as well as other operators of laser devices with similar specifications and capabilities, the answer is clear. Frequency does make a difference. It is worth pursuing in an evidence based medicine research setting.

Dr. Richard Gerber surmises in the book Vibrational Medicine that the human organism is a series of interacting multidimensional subtle energy systems. If these systems become imbalanced, there may be resulting pathological symptoms, which manifest on the physical, emotional, mental and spiritual planes. He suggests that these imbalances can thus be healed, by rebalancing subtle energy templates with the right frequency of vibrational medicine. He also states “our tissues which compose our physical form are fed not only by oxygen, glucose and chemical nutrients, but also by higher vibrational energies which endow the physical form with the properties of life and creative expression. Further, health is a total balance of our subtle energetic systems with the forces of our physical vehicle, and with the forces of Mother Nature.”

Considering that the String Theory of Quantum Physics suggests that the physical universe consists of a series of vibrations, James Oschman PhD’s book Energy Medicine, The Scientific Basis, denotes that all tissues have a vibrational state unique to it. Royal Raymond Rife discovered in the 1930s that by varying the frequencies of micro electric current, different microorganisms are affected. Laser light, another form of electromagnetic energy, can be pulsed...
in varying frequencies, which is measured in Hertz.

When varying the laser frequencies, combined with the tissue compatible (non-heat producing) low power, visible light wavelength, different tissues can be affected more specifically. This allows the practitioner to practice the “Art” of veterinary medicine as individualized treatment protocols can be prescribed. Some of the early pioneers and their contributions to this form of energy medicine deserve mention.

**Nikola Tesla**

Tesla’s contribution in the 1890s was life altering for many. He hypothesized that electronic waves produced by lightening discharges could have significant benefits for human health. He invented the Tesla Coil, and a magnifying transmitter to excite the atmosphere into producing a natural form of lightning. A veritable showman, he couldn’t help but engage in personal demonstrations. An early paper entitled “High Frequency Oscillators for Electro-Therapeutic and Other Purposes” was presented in 1898 at the annual meeting of the American Electro-Therapeutic Association in Buffalo N.Y. The paper surmised that when a person was subjected to the action of such a magnifying coil, luminous blue light streams are seen in the dark emanating from all parts of the body. Tesla maintained that these blue light streams and radiofrequency (RF) electronic wave therapies in general could make it possible to minimize aging and disease.

At the turn of the century, a Russian physicist **Georges Lakhovsky**, employed Tesla-coil electrotherapy in successful treatments of plants and patients with cancers. In 1925 he wrote a book called “The Secret of Life” from the case studies he had amassed using the “multi-wave oscillator” Tesla Coils he designed and manufactured. A paper entitled “Curing Cancer with Ultra Radio Frequencies” expressed his philosophy that the “amplitude of cell oscillations must reach a certain value in order that the organism be strong enough to repulse the destructive vibrations from certain microbes.” He went on to say, “The remedy in my opinion is not to kill the microbes in contact with the healthy cells, but to reinforce the oscillations of the cell either directly by reinforcing the radio activity of the blood or in producing on the cells a direct action by means of the proper rays.” With his multi wave oscillator he found that “the cells with very weak vibrations, when placed in the field of multiple vibrations, finds its own frequency and starts again to oscillate normally through the phenomenon of resonance.”

Also, in the early 1920s a Russian histologist Dr. **Alexander Gurwitsch** discovered the mitogenic wave communication of vital information exchanged between living cells with biophotons. About that same time, Danish physician and professor **Niels R. Finsen** at the Finsen Medical Light Institute, was performing research on the use of visible naturally occurring light and artificial light to cure disease conditions, including cancer.

In 1932, Tesla’s non-invasive electrotherapy was publicly acclaimed before the American Congress of Physical Therapy. “Tesla’s high-frequency electrical currents are bringing about highly beneficial results in dealing with cancer, surpassing anything that could be accomplished with ordinary surgery.”

**Albert Einstein**
Einstein’s contributions to the field of quantum physics, goes without saying. In particular, his theory of stimulated emission of radiation offers an understanding of how a tiny signal can instigate a growing three-dimensional cascade effect of light energy transduction to deeper tissues, and ultimately the entire system.

**Royal Raymond Rife**

Dr. Rife was a research physician at the University of California at Riverside in the 1930’s. He was inspired by medical cures claimed by Lakhovsky and others of the time who borrowed from Tesla’s non-invasive electrotherapy. Rife was out to prove that specific disease pathogens could be identified by their unique resonance response to a variable-wavelength light source. He developed what was called a “Universal Microscope” which offered insight into the role of the light spectrum of electromagnetic energy in living tissues and disease. The 1944 Annual Report of the Smithsonian Institution published a brief description of how Rife’s microscope worked. Essentially, using block crystal quartz prism optics between the subject and the light source for the purpose of polarizing the light passing through the specimen. This is because light waves vibrate in all planes perpendicular to the direction in which they were propagated. When the portion of the spectrum is reached in which both the organism and the color band vibrate in exact accord. There is a definite characteristic spectrum emitted by the organism. Cancer is purple/red, tuberculosis emerald green and Bacillus thypous is turquoise.

With this Universal Microscope, Rife was able to study in vivo living blood and tissue cells and dynamically monitor a patient’s diet, immune health, and disease responsive to non-invasive electrotherapy. Once he proved his thesis that disease pathogens could be identified by their unique resonant response to a specific wavelength of visible light, Rife was lead to another insight. He found a new way to study a diseased cells response to specific energy structures in vivo using a modification of Tesla’s Radio Frequency (RF) waves, to his own shorter blue light wavelengths.

The first clinical work of Dr. Rife described the frequency-specific protocol’s efficacy in the treatment of cancer. A special Medical Research Committee of the University of Southern California was the setting for a clinical trial of 16 terminal cancer cases, supervised by Milbank Johnson, MD. All 16 were treated for varying types of malignancy. After three months, 14 of these cases were signed off as clinically cured by the staff of five medical doctors and pathologist for the group, Dr. Alvin G. Foord, M.D. Unfortunately, the report issued by this esteemed committee was destroyed in a suspicious arson in his laboratory.

**Other Pioneers in the Field**

In the 1940s, a controversial biochemist and psychologist William Reich discovered faint blue light around living blood cells. Another pioneer, orthopedic surgeon Dr. Robert Becker compiled compelling evidence under government grants supporting an electronic explanation of the efficacy of acupuncture, and the importance of the earth’s magnetic resonance for human health and wellbeing. The fact that he was twice nominated for a Nobel Prize did not seem to impact the lack of funding for his continued research. His extensive work in peer-reviewed journals has been ignored among conventional physicians and medical researchers. In the 1950s and beyond, advances in quantum mechanics began to accept earlier electrotherapeutic discoveries.
In the 1970s, Dr. Fritz Popp was able to measure mitogenic waves emanating from seedlings of various plants. His study revealed that mitogenic plant communication appears in the red-to-green wavelengths and has illumination intensities as low as a few tens of photons per second per square centimeter. He went on to show that given the highly variable loss of its cells, the human body could only remain in balance through mitogenic communication among its cells on the time scale in which atomic electrons change orbit to emit an information carrying photon. He is credited with the discovery that, although our body appears to have a solid slow to change countenance, on the atomic level, we are changing every microsecond as cells are constantly dying and being replaced. For example, the pancreas reproduces most of its cells daily, stomach lining renewed every three days, etc. The body essentially renews itself every four weeks. Dr. Popp surmised that mitogenic luminescence or biophoton emission is an essential component of life.

Dr. Paul Nogier identified seven frequencies natural to our bodies, the three tissue types: ectoderm, endoderm and mesoderm, as well as four additional frequencies. His research shows that the application of these frequencies helps to bring organs and tissues back to their resonant frequencies.

The work of these pioneers supports the hypothesis of biophysics inventor and author Alexis Guy Oblensky which suggests that the healing of disease is attributable to the reversal of entropy in affected cells through biophotonics, and achieved specifically by autoparametric, phase-conjugate amplification of life saving emissions of mitogenic biophotons.5

The Frequencies and Low Power Laser
A non-heat producing Class 2 Low Level Laser (5mW and 7.5mW) with visible light wavelengths of 635nm (red) and 405nm (violet) with the ability to program frequencies within, is an option that exists, and is the laser device system used by this author. At one hundredth of the power of Class 4 lasers, these Class 2 lasers cause vasodilation and photobiomodulation without generating heat. Wavelengths that are in the visible light spectrum are not subject to concerns for retinal scarring, and thus eye protection is not generally needed. This feature makes it extremely user friendly in the field of animal therapy, especially when treating in metal cages, or from a distance becomes necessary. Originally considered a Class 3 laser, the classification was changed to reflect the decreased risk due to the line-generated beams that distribute the energy density to a larger surface area.6

Studies have been documented that demonstrate the affect that frequency has on seizure activity when focused on the vagus nerve.7 There are also numerous studies in the literature pertaining to the benefits of frequency applied to different energy sources such as micro-electric current, ultrasound, as well as LLLT on macrophages, immune mediated disease such as rheumatoid arthritis, Crohn’s disease and bone healing.

A Potpourri of Case Responses
The multiple species represented in the case responses accompanying this lecture demonstrate the versatility of the addition of frequency specificity to the individual protocols.\(^8\)

**Conclusions**

The combined abilities of varying the frequencies of the laser light, the known tissue regenerative benefits of the 635nm wavelength, and the bactericidal/sporicidal qualities of the 405nm wavelength, offers a veritable palate of options in painting a picture of health. This combination of features follows the pioneering works of Tesla, Einstein, Rife, and others who supported vibrational healing through returning diseased states to resonant harmony. This is truly where healing can be an art form. Healing is optimized when combining this and other forms of vibrational energy, with modalities that address re-establishing harmony in other systems. Rehabilitation of the spinal/neuronal integrity (acupuncture, osteopathy, VOM, chiropractic) connective tissue stability (myofascial release techniques), cellular enhancement (nutritional status, hydration, exercise for circulation, mental enrichment for decreasing stress cortisol), and adding to it, the power of our genuine intention, can only expedite healing. To quote Nikola Tesla: “If you want to know the secrets of the Universe, think in terms of energy, frequency, and vibration.”

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Objective

- To show that there are non-invasive possibilities for calming and increasing appetite and vitality through signaling the body's innate pharmacy through Photobiomodulation.
- To show the ability of non-thermal light energy to decrease sympathetic tone and increase parasympathetic responses for calming patients can result in inspiring colleagues to a new tool in the management of anxieties, as well as pain management, hypertension, anorexia, and gut motility.

Introduction

Low Level Laser Therapy (LLLT) also currently termed Photobiomodulation, has become an accepted healing modality in the areas of pain management, rehabilitation, wound healing and fracture repair. Photobiomodulation is described as a non-thermal enhancement of cellular processes that result in enhanced healing.

The unique Class 2 low power (5mW; 7.5mW) non-heat producing, frequency specific, visible light wavelength (635nm; 405nm) laser is 1/100 of the power of a common Class 4 laser. The visible light does not scar retinal tissue, allows for a blink response, and thus there is no need for protective eyewear. The line generated beams and the ability to vary the frequency of the pulsation of the light energy allows the ability to target varying surface areas, affecting different tissues and systems. Individualized frequency settings are based on the vibrational frequency variations of different tissues and the studies of Nikola Tesla, Royal Raymond Rife, Paul Nogier, among others.\(^1\)

A unique ability of this combination of specifications of visible light and low power, allows for an energy density that affects, without damaging, the autonomic nervous system. Along with calming, this effect allows for increasing appetite in anorexic animals.\(^2\)

Numerous species (including but not limited to, horses, dogs, cats, birds, small mammals, large exotic cats, and wildlife, have been documented by the author to show similar increase in parasympathetic responses with concurrent decrease in sympathetic tone. Lowered heart rates and blood pressures have been recorded immediately post treatment on dogs, as well as decrease in digital pulse rates on laminitic horses. Calming of fractious animals, increase in appetite and gut motility, as well as allowing restorative sleep are the observed benefits. The ability to achieve these healing responses, without sedation, from a short distance, without need for eye protection, allows for a truly non-invasive treatment protocol.\(^3\)

This Class 2 non-thermal laser system has been used globally in the human field in the areas of rehabilitation medicine, sports performance, neurodegenerative disease, Alzheimer’s and traumatic brain injuries, as well as burn units, owing in part to its FDA Clearance in acne and onychomycosis.\(^4\) Veterinarians are able to utilize the benefits of the frequency specific low level laser therapy for cellular enhancement beyond pain and inflammation. Stem cell stimulation and nerve regeneration have been described in the literature, when low power non-heat generating lasers and LEDs are used.\(^5,6\)
A recent peer reviewed double blinded study using low power non-heat producing lasers in autism spectral disorders, demonstrated that all study subjects had reduced irritability after laser treatment.\textsuperscript{7}

The ability to affect the Autonomic Nervous System is perhaps the most exciting response few have been able to be made aware of. The author has experienced and documented lowered blood pressure within seconds of the completion of the therapy implemented using specific frequencies that can be programmed into the device. There are documented studies on the benefits of vagus nerve stimulation with various energy sources which result in decreased inflammation, decrease in seizure activity.\textsuperscript{8} Also reported in the literature is management of immune mediated disease conditions such as rheumatoid arthritis and Crohn’s disease. This author hopes to inspire more to investigate these responses further.

True Photobiomodulation involves cellular enhancement using low power lasers and LEDs without resultant thermal change within the tissues.\textsuperscript{9} This term has erroneously been generalized to include high power heat producing therapy lasers, and thus confusion will occur until specific guidelines are enforced in future studies.

There is no question that higher power Class 3b (200mW) and 4 (500mW) lasers demonstrate beneficial results in areas of joint and muscular rehabilitation, as they inhibit pain with variable additional heat increase in the tissues.\textsuperscript{10} However, there exists the potential to cause thermal injury either due to improper device handling, or to fragile endocrine (adrenals, pancreas) or gonadal tissues intolerant of this temperature variation. Proper training can minimize this risk, however, colleague reports of the smell of burning feathers, thermal burns to an equine spine, as well as described animal discomfort has this be an unacceptable risk when other non-invasive options are available. Suitable required eye protection using high power lasers can be cumbersome, as well as impractical.

**Materials and Methods:**

A Class 2 low power (5mW; 7.5mW) non-heat producing, frequency specific visible light wavelength (635nm; 405nm) Laser System with line generated beams, was used to perform therapy. LLLT treatments were performed using three 60-120 sec modules. A 5mW laser unit with two diodes composed of two line-generated 635nm wavelength beams was used to allow for simultaneous stimulation of nerve root as well as area of involvement. Alternately, sequential treatment of the nerve root and the area of involvement were also used with single diode lasers of identical power and wavelengths. The frequencies selected were referenced from studies by Rife, where electric current was used, which is another form of electromagnetic energy.

1. **“Sympathetic Overstimulation:”** placing one diode that is preset with neurologic settings through the brain via the foramen magnum, and the other diode with settings for sympathetic nervous system, pain relief and circulation, over the thoracolumbar spine where the sympathetic ganglia reside. (Once light stimulation stops, the sympathetic tone drops, and allows the parasympathetic responses to increase gradually).
2. **“Parasympathetic Stimulation:”** placing the preset neurologic diode and the diode set with the parasympathetic and colon settings both over the cranium and dorsal spine.
including sacral area. (This can enhance the parasympathetic response that has been allowed to increase with the now decreasing sympathetic tone).

3. “Pain/Inflammation:” which includes settings for lymphatic drainage, muscle, nerve, and liver. Both diodes are placed over entire cranium, spine, and body.

NOTE: It is important to note that animals that are in a near death crisis such as a hit by car, anaphylactic shock, anesthetic emergency, it is imperative that the PARASYMPATHETIC ONLY be performed. Stimulating the sympathetic nervous system may push a critical patient over the edge.

Treatment with the sympathetic and Parasympathetic settings are mainly performed once in a 12-24-hour period as the effects are lasting. Anecdotal evidence of use of this laser system prior to fireworks on the New Year’s Day 2020 revealed all 15 dogs responding with less anxiety, and more focus. One owner found that her dog seemed to benefit with these attributes even 1 week beyond the treatment.¹¹

Applications
There will be numerous documented case responses in the lecture involving all applications mentioned below:

Exam Presentations:
The veterinary setting can be full of stressors that can overwhelm an animal’s ability to cope. Recognizing that animal’s emotional state is the first step in managing the fear, anxiety and stress being exhibited with a proper treatment plan. A prey animal has a heightened sympathetic fright or flight response, which if not managed, could result in aggression, immune suppression, hypertension, capture myopathy, and even death from cardiovascular or respiratory distress. If the emotional currency for each emotional state is properly managed (approach retreat, pattern interrupt, for the timid; treat and play rewards for the confident), this may be all that is required for advancing the veterinary diagnostic and treatment plan in a stress-free manner. For timid, or overanxious highly stimulated animals, LLLT has been a valuable tool for causing a refocus. Often, the effects are within 3-6 minutes. There will be responses varying from lying down, falling asleep, standing in a “Zen-like” state, to rocking back and forth cooing-in the case of parrots. Fractious cats can often be handled enough with appropriate Fear Free and Feline Friendly concepts in place (pheromone spray, quiet room, leaving in bottom of carrier with towel over the top), to obtain a blood sample. The effects of the light therapy are not a sedative effect, merely a shifting from fright/flight to more that of being more subdued. The degree of the response has a lot to do with the animal’s inherent spirit level. Low energy animals tend to be the ones that fall asleep, whereas higher energy animals may just come down a few notches in energy expression.

Painful animals
Another application for the calming effects of LLLT is shifting the high sympathetic tone in severely painful animals, to the rest and digest parasympathetic tone. Animals exhibiting severe pain from intervertebral disc disease, fractures, dislocations, trauma, surgery, feline lower urinary tract disease/obstructions, and post dental extractions are candidates. This author has seen previously obstructed cats be able to urinate once calmed post LLLT.
**Anorexia; Gut Motility Disorders**
The benefits of increased appetite in anorexic cats, dogs, rabbits and other exotics, as well as horses, have been documented. The Parasympathetic responses cause animals to urinate and defecate post LLLT, often necessitating the owner to allow this to occur after leaving the exam even if they performed these duties before entering the hospital.

**Hypertension**
Due to the vasodilation that occurs, the author has witnessed blood pressure normalize, or decrease significantly as a result of LLLT. One small poodle had a drop of 40mmHg down to normal after a 120 sec LLLT tx, while the BP cuff was still on. Another hypertensive Cushingoid husky demonstrated a drop from 210/138 down to 148/72 within 25 minutes of LLLT- with 2 IV catheter placement attempts within that time period.

**Presurgical, Intraoperative, and Post-Surgical Applications**
Pre-treatment with the LLLT protocols described above is beneficial in decreasing the stress and forwarding healing. The author treats surgical patients 1-2 hours prior to surgery with the sympathetic/parasympathetic balance. Also, worth noting is that the benefits of the laser to tissue prior to tissue trauma, has been documented in Tuner and Hode. Tissues become primed for healing with release of Nitric oxide and ROS. If no trauma occurs, these chemical responses dissipate.12

Intraoperative treatment can be performed to facilitate healing by using settings to increase circulation and lymphatic drainage, while decreasing pain and inflammation. Shining the beam into an open abdomen, bladder, or intestinal anastomosis is common. The author has witnessed improved color to a circulatory compromised intestinal bowel loop within seconds of LLLT application. Because of the bactericidal violet laser, and tissue regenerative red laser beams, dental surgery and orthopedic surgeries benefit as well. Post-surgical treatment can be performed immediately prior to awakening, and/or several hours later, especially if a second treatment is warranted. It is suggested to allow time for physiologic changes to occur before offering a second treatment in order to gain the best benefit.

**Discussion**
Photobiomodulation is a promising versatile healing modality with an amazing ability to signal the body’s own innate pharmacy to expedite healing in its many forms. Also, the distinction in the terminology of true photobiomodulation is evolving to include only those light therapies that do not produce a thermal response. Clearly there are a lot of unanswered questions in how quantum medicine truly works. A quote from astrophysicist Dr. Neil de Grasse Tyson reminds us in that “The universe is under no obligation to make sense to us.” Consequently, the ability of photobiomodulation in the form of non-thermal laser irradiation to affect the Autonomic Nervous System is perhaps the most exciting response few have been able to be made aware of. With documented variations in vital statistics in multiple species, including lowered blood pressure within seconds of the completion of the therapy implemented. Using specific frequencies programmed into the device, this author hopes to inspire more to investigate these responses further. The lack of need for eye protection, ability to enhance tissue regeneration systemically,13
the ability to treat broad areas from a short distance without sedation, while in motion, offers exciting possibilities for sensitive wildlife.

“Magic is science not yet explained” …Isaac Asimov.

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Successful Treatment of Laminitis, Colic in Horses
Janet Gordon Palm, DVM, CVCP

Objective
- To inspire colleagues to recognize the non-invasive potential of non-thermal LLLT in not only advancing safe and efficient healing in equine inflammatory conditions, but also the unique abilities in decreasing anxieties.

Introduction
Like any new frontier, exploration of appropriate treatment applications and protocols are fraught with results that can be difficult to reproduce. Along with the surge of interest and promising responses, there has been an equal amount of confusion, misinformation, and often less than stellar results. Laser devices vary in power, wavelength, frequencies, and whether they are in fact a true laser, or in some cases an LED. Often there is a lack of knowledge of vital information regarding the device specifications prior to purchase. An understanding and awareness of the specifications of the laser allows appropriate and safe use as well as optimum results. Improper or cavalier use can result in poor results and occasionally harm. Although there can be no question that High power Class 3b and 4 units can have beneficial results in areas of joint and muscular rehabilitation, they have potential to cause thermal injury to tissues intolerant of this temperature variation. Using a device that generates heat within the tissue on an acute injury or incision is counterproductive. If currently using a Class 3b or Class 4 Laser device, it is recommended to abide by the safety restrictions. Common sense would dictate use on tissues that are tolerant of thermal increase.

A non-heat producing Class 2 Frequency Specific Low-Level Laser (5mW and 7.5mW) with visible light wavelengths of 635nm (red) and 405nm(violet) is a safer option that exists. This is the laser system that this author has been successfully using for 10 years. This Class 2 laser causes vasodilation and photobiomodulation without generating heat.

This presentation offers an insight into what is possible with increased versatility using this Class 2 laser. Examples in the equine include expediting major wound healing, musculoskeletal issues such as multiple limb lameness, arthritis, laminitis, abscesses, infections, immune stimulation, and endocrine balance. Also demonstrated is the ability to affect the sympathetic and parasympathetic nervous system to calm animals and improve gut motility. This is especially important in colic management.

Versatility of Low Power Class 2 Lasers
The outdated concept that "more power is essential to penetrate deep tissues" is being replaced by studies showing that cellular enhancement occurs using less power and visible light wavelengths. It may be true that more power and longer infrared wavelengths deliver a calculated therapeutic "dose" to a measured distance in a mathematic calculation as well as a cadaver leg in a relatively short time. The concept loses relevance however, when considering a living biological system with the properties of bio-photons, biologic water, and the intercellular Integrin system of signal transduction. Therapeutic response can occur to deeper structures (6cm) within a treatment time of 6 minutes, as measured by MRI.1 This is a far cry from the four hours that has been suggested by high power laser marketing. Established laser experts Tuner
and Hode have since discussed that the idea of therapeutic dose needs to be re-evaluated.\(^2\) Albert Einstein proposed this Stimulated Emission of Radiation phenomenon. Absorption of the light energy results in the photons exciting the electrons orbiting the nucleus of the atom to a higher orbit. When these electrons decay back to the ground state, they emit a photon to the neighboring atom, whose electrons excite, also emitting a photon as they retreat to ground state, and the process continues in a 3-dimensional cascade effect eventually affecting the entire organism. Lending credence to this continuing cascade effect, Mester has shown that laser effects are systemic.\(^3\) Studies on burn victims have shown the laser treated area healed faster than the control group, however the opposite non-treated area also healed faster than the controls. Incisions on rats behaved similarly. This concept is important to note, as many of the treatment protocols involving lameness and laminitis involve treating the supporting legs simultaneously in order to strengthen tissues to aid in prevention of future breakdown. This has been successfully performed in managing canine ACL ruptures as well.

**Communication and Case Selection**

It must be reminded that therapy laser is not a magic wand. Rehabilitation at the cellular level works best when considered as an adjunct to healing along with rehabilitation at the spinal and connective tissue levels with some form of neuronal modulation such as Acupuncture, chiropractic, VOM and myofascial release techniques. Other building blocks for healing include adequate nutrition, hydration, exercise for lymphatic drainage and circulation, as well as mental enrichment to aid in managing the deleterious effects of stress.

Having performed thousands of laser therapies over 10 years on multiple species including birds, dogs, cats, pocket pets, horses, raptors, and other wildlife, the author is familiar with a myriad of responses. This can range from the "wow" response (horse able to bend his neck immediately) seen typically with managing some acute pain and inflammation; to gradual improvement noticed after several treatments as tendons and ligaments heal.

In the event of slight to no response within 6 laser treatments, the rationale includes several possibilities. 1) Either the cells have rehabilitated to the extent they can, (prompting a review of nutrition, hydration, nutraceutical status) as healthy cells do not respond to biostimulation as pathologic tissues do; 2) There may be an underlying condition yet to be diagnosed; 3) the wrong diagnosis has been made; 4) the treatment protocol needs to be tweaked and thus the need for close follow up and progress exams.

Communicating these factors to owners is paramount to compliance and expectations. It is not practical to imply a prediction of who will receive a Wow response, and who may offer a previously non-existent left lead canter in 1-2 weeks. That is why close follow up calling is imperative within 1-3 days and medical progress exams initiated when appropriate.

**Role of Frequency Specific LLLT in Healing**

There is controversy concerning the validity and importance of frequency (oscillations or pulsations) of the laser light in the overall effects of healing response. Frequency does make a difference. It is worth pursuing in an evidence base medicine research setting.\(^4\)
**Autonomic Nervous System Applications**
The Autonomic Nervous System controls all life functions and is always in a state of balance. When the sympathetic tone is high (fright or flight) the parasympathetic tone is low, (homeostasis, digestion, appetite).

The sympathetic ganglion reside along the paralumbar muscles between T1-L3-4. The line-generated beams of the laser device can access this entire area. As photonic energy is absorbed, causing the excitation of electrons to higher orbits, then subsequent photonic emissions to neighboring atoms in a cell-to-cell cascade, the sympathetic tone is continually stimulated. When the pre-programmed light stops in 120-180 sec, the sympathetic tone plummets, allowing the parasympathetic tone to increase. Within minutes, a fractious, painful, or emotional animal can be calmed to a more harmonious state. Appetite, peristalsis, and focus are restored. Blood pressure has been documented to decrease. Similarly, the parasympathetic tone can be further enhanced. The areas to receive the laser light input would be cervical and sacral, where the Parasympathetic ganglion reside.

It is important to note that the Sympathetic stimulation should NOT be used in shock, anesthetic emergencies, or near-death cases. In these cases, the Parasympathetic stimulation ALONE is indicated. Further stimulation of a sympathetic tone in these fragile patients could be detrimental and send them over the edge.

**Treatment Protocols**

This is a Class 2 non-thermal frequency specific low power laser. The protocols used with this laser system cannot translate to other lasers with higher power, and non-visible spectrum wavelengths. These unique specifications are found to be tissue friendly, non-heat generating, and thus have more tissue versatility than other laser devices.

The treatment protocols vary on a case-by-case basis, which is where the true "Art" of medicine comes in. Determining factors are as follows:

- Physical exam / Supporting Diagnostics
- Diagnosis- or list of differentials
- Chronicity of Condition or Symptoms
- Owner Compliance to Schedule and Costs
- Response to Treatment, and thus follow up is imperative!

**A) Accelerated Plan: Severe trauma, pain**, 2 treatments 90 + min apart; 3 days in week 1; 1 treatment / day for 3 days in week 2, then 1 treatment/day for 2 days per week; Total 8-13 treatments; 180 seconds for each module in horses.

Allowing 70-90 min between treatments allows physiologic changes from biostimulation to occur in order to receive optimal benefit as a second treatment. LLLT is cumulative, the benefits will be seen sooner with the “Accelerated Plan.” Noticeable benefits may be witnessed within hours with acute injuries, or several days if healing connective tissues and fractures.

**B) Chronic Plan: Long Term, Low Grade Pain,** 2 treatments on day one; 2 treatments once weekly for 2 weeks, then 1-2 treatments/week.
C) "Try and See" Plan: *Diagnosis Open*, or owner has financial limitations. 2 treatments day one, then; one treatment/week.

**Immune System**
Borrowing on the concept of varying the frequencies for specific tissues, allows for access to enhancing the immune system. Accessing the entire chest and abdomen with the line generated beams for the preprogrammed time (120-180sec), allows stimulation of lymphatics including the thymus, (Bursa of Fabricius in birds), and spleen. Combining this immune protocol with a treatment for arthritis can allow more effective management of immune mediated conditions such as rheumatoid arthritis, Lyme nephritis, as well as any infectious diseases. Low-level laser therapy has been found to stimulate mesenchymal stem cell proliferation.7

**Applications to Disease Conditions**

**Endocrine Disease**
Endocrine diseases can also be affected. Since there is conceivably cell pathology in many disease conditions, tissue regenerative abilities of photobiomodulation can be beneficial. There exists no contraindication due to the non-heat producing qualities of this laser’s ability to cause photobiomodulation. Although a cure is not suggested, there have been cases of reversal of early onset diabetes in a cat when pancreatic inflammation has been decreased, and islet cells stimulated to regenerate their insulin producing abilities. Similar anecdotal responses in treating hypothyroid and Cushing’s disease has been reported, resulting in minimizing treatment dosing. Hirsutism in the PPID horse has been affected and shedding initiated with LLLT.

**Laminitis**
The goal is to use a combination of conventional and alternative tools to get the horse out of pain ASAP! Successful management of these cases involves a well- choreographed "dance" between the veterinarian, farrier, owner compliance, as well as the horse’s attitude. I am a fan of neuronal adjustment (chiropractic, VOM, Acupuncture) and Myofascial release to rehabilitate the spine and connective tissue or living matrix. These areas often spasm as a result of compensatory mechanisms. Rehabilitating these areas will free up the body, add to total comfort, and aid in accessing the body's own innate pharmacy. I would caution as to the degree of myofascial release performed on a severe acute laminitic episode due to inevitable flood of circulating toxins released from the areas treated. Bute or Banamine will often be on board by the time the author’s service is implemented.

That being said, the contribution of the tissue friendly non-thermal laser, is to safely stimulate tissue regeneration, while further allowing increased circulation to the hoof via vasodilation. The increased lymphatic drainage and resulting toxin removal will further aid in decreased pain and inflammation. It is wise to inform the farrier and owner that due to the tissue regenerative capabilities of LLLT, sole and heel growth is expedited, and this will require more frequent farrier visits. The additional cost of the farrier is more than made up in the speed of recovery and improved overall prognosis.

**Laser Protocol:** To manage the horse's attitude and pain it is advantageous to reduce the fright/flight response and resulting stress hormone cortisol release. This is performed by programming the settings for Sympathetic Overstimulation into the laser, followed by the
Parasympathetic stimulation for further calming. This also increases appetite and gut motility. Neurological settings applied to either the poll, or nerve root segment such as cervical and thoracic spine for front legs, and thoracolumbar/sacral spine for hind legs. Pain inflammation settings along spine and affected hooves, is easily accessible with the line generated beam.

The violet/red combination with settings to combat infection and encourage tissue regeneration is selected. This has been helpful for treating hoof abscesses as it speeds the response time of abscess eruption and drainage.

Depending on the severity of the case, an Accelerated Protocol, or modification thereof would be appropriate, tapering down to a maintenance protocol if indicated.

**Colic**
Similar pain consideration and treatment protocol used in laminitis would be implemented. Neuronal adjustment and myofascial release is very helpful in restoring nerve communication to the end organ system including peristalsis to the gut.

**Laser Protocol:** Along with the sympathetic and parasympathetic balance, as well as pain and inflammation settings, I will often add the immune system enhancement. This involves lasering through the thoracic inlet, as well as over the entire chest and abdomen, especially the spleen. The light energy absorption and eventual response to the thymus, spleen and lymphatics is intended to speed the production of macrophages and killer T-cells.

**Arthritis, DJD, Distal Hock, Stifle, Kissing Spine, Fractures**
Depending on the degree of pain, anxiety, Horsenality, the Sympathetic/Parasympathetic calming can be used prior to laying a hand on the horse. This author is an advocate of developing a rapport with the horse and managing his/her primary need before proceeding. Approach and retreat, calm and slow approach for the insecure, versus treat rewards and finding "the itchy spot" for the more confident. A form of neuronal adjustment/myofascial release is again indicated ideally.

Physical exam including heat scanning with your hands, palpation, observation of gait and relationship with owner and rider, and ultimately tools you feel necessary to offer the best chance at diagnosis or list of differentials. From this, you can determine the modules you may want to include in the laser prescription.

**Laser Protocol:** Sympathetic / Parasympathetic balance if appropriate. Nervous system settings for the nerve root that innervates the area of involvement, as well as pain/inflammation settings for the area of involvement would be suggested. These can be accessed simultaneously with some Class 2 lasers that offer two probes, or sequentially as with single probes. The line-generated beam allows for entire spine, leg, or multiple legs lasered at the same time.

**Wounds, soft tissue, tendon, ligament injury, Post-op Applications**
The proposal that laser energy merely promotes cellular energy rather than changing cell function explains why injured tissue cells respond to laser therapy whereas there is little effect on
non-injured cells.\textsuperscript{9}

Laser energy is more effective in treating pathological states, therefore, when healthy subjects are used, the outcomes may be subdued. Although tissue healing is accelerated, no hyper plastic effects have been reported. During wound healing, laser wounds had more collagen and a higher tensile strength than the controls, until healing was complete, at which time both lasered and control groups were similar. Laser energy catalyzes normalization rather than creating a super normal effect. Thus, proud flesh would not be accelerated beyond that of non-lasered. Other modalities in addition to LLLT may be beneficial. Ultrasound when combined with LLLT showed better response when performed individually.\textsuperscript{10}

\textbf{Laser Protocol:} Varying degrees of wounds would determine mixing and matching protocols to the issues each individual demonstrates. A combination of the immune system enhancement, with treating over the nerve root or entire spine, along with pain/ inflammation settings over the wound or soft tissue injury itself would be in order.

The violet wavelength and its documented bactericidal and sporicidal properties allow for benefits against bacteria and fungi. The author has used LLLT successfully to manage cellulitis, "scratches," wire cuts, decubitus ulcers, and nodular necrobiosis masses.

LLLT is used for pre and post-op surgical applications in soft tissue as well as orthopedics. Studies have shown that when using the bactericidal Violet 405nm 5mW on osteoblasts in cell culture when studying infected arthroplasties, over 15mW altered osteoblast function. It was concluded that 5mW was the maximum power recommended to stimulate osteoblast function.\textsuperscript{11,12} As a reminder, popular Class 3b units are generally over 60mW and Class 4 are 500mW. Use of the violet/red low power laser in orthopedics for fracture repair and infection control is exciting.

\textbf{Vaccinations}

When the benefit of vaccinations are deemed to outweigh risks, LLLT can be used to decrease pain and inflammation at the vaccinated site, as well as stimulate circulation, lymphatic drainage, and stimulate the immune system using these modules.

\textbf{Conclusion}

LLLT and particularly Class 2 non-thermal visible light wavelength laser, offers a myriad of non-invasive treatment options available to the horse. The ability to affect the Autonomic Nervous System to calm, as well as stimulate appetite and gut motility, is groundbreaking. Ability to treat endocrine tissue, gonads, laminitis and sensitive tissues not amenable to heat, shows promise. Managing arthritis and joint disease, expediting wound and fracture healing effectively without the inherent risks of higher power units has been proven. The low risks and lack of need for eye protection with the non-thermal laser allows for confident staff use and client safety.

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Objective

- To discover new non-invasive science supported tools to combat antibiotic resistant infections.

Introduction

Low Level Laser Therapy (LLLT, 3LT) has shown benefits that are well documented in the human and animal species. The purpose of this presentation is to demonstrate the capabilities of the low power frequency specific visible light wavelength 405nm, 635nm, 5mW laser in expediting wound healing. A brief review of the science behind laser therapy is necessary in order to assess the appropriate use and application. Examples of treatment protocols using specific low power (5mW, 7.5mW), frequency specific, visible light wavelength (635nm, 405nm) therapy lasers are given and are based on a case-by-case basis. Setting up and implementing a diagnostic and treatment plan, as well as the importance of case selection and communication for optimum results, will be discussed. For the sake of showing a variety of wounds, case results involving multiple species including dogs, cats, horses, cattle, birds, exotics and wildlife will be highlighted, emphasizing the non-invasive healing capabilities. Another application exclusive and unique to this laser system is the ability to affect the autonomic nervous system as an aid in calming fractious animals, as well as increase in gut motility and appetite. Immune enhancement applications have also been experienced by the author and are demonstrated in the case responses.

A Laser Review

Therapy lasers produce a *Photochemical* reaction, where light energy is absorbed through chromophores on the cell membrane, resulting in a cascade of beneficial responses. This contrasts with surgical lasers that result in a *Photothermal* reaction. LEDs or Light Emitting Diodes have shown benefits on a superficial level, but wavelengths vary and are not coherent. To ensure proper depth of penetration and tissue stimulation, laser light that is coherent is vital. Care must be taken in interpreting conclusions from studies performed, as extrapolation of data from true laser results with variation of power and wavelengths have erroneously occurred. Therapy using *Light Amplification by Stimulated Emission of Radiation (LASER)* is a means of directing concentrated coherent (polarized) monochromatic (one wavelength or color) light to certain tissues of the body. This unidirectional concentrated in-phase light wavelength is responsible for the cascade of chemical reactions that result in *photobiomodulation*. In the familiar example of photosynthesis, radiant energy from the sun results in an electron transport chain of events stimulating chemical reactions ultimately causing plant cell regeneration. The concept is similar in tissue cells. Research supports wavelengths within the visible light spectrum influence absorption through chromophores on the cell membrane. A series of electron transport reactions occur which stimulates mitochondria to produce more ATP. Increase in cellular regeneration and cell communication result from these energy enhanced cells. Enhanced wound healing decreased pain and inflammation, and neural reintegration are some of the resultant effects.
The Science That Defines LLLT
The primary mechanism that defines LLLT is rooted in quantum physics and based on the Niels-Bohr model of subatomic particles. Considering the properties of an atom, there exist a nucleus, and a surrounding electron cloud at varying orbital levels. Electrons are capable of undergoing quantum leaps from a ground state to a higher energy excited state upon absorption or emission of a photon. The electron eventually falls back to its ground state, emitting an identical photon to the original photon responsible for the excitation. This is termed *Stimulated Emission.*

The Electromagnetic Spectrum, Einstein’s Electron Volt Theory, and Arndt – Schultz Law
In the electromagnetic spectrum, visible light occurs between 400nm and 660nm, correlating to blue red. Photobiomodulation occurs when electrons are enhanced by electromagnetic energy to a higher orbit and the resultant photons released would excite neighboring electrons. Einstein proposed that the electron volt energy (eV) within wavelengths shorter than 400nm (towards the ultraviolet) was so high that the electrons would be catapulted out of the atomic orbit. This ionization accounts for the damaging effects UV and x-ray wavelengths have to tissue cells. Wavelengths between 400nm-660nm (visible light) have enough eV to excite electrons to higher orbital levels required for photobiostimulation, without leaving the atom. Wavelengths higher than 660nm (near infrared and infrared) do not possess enough eV to excite electrons to higher levels without addition of more power output in the form of Watts. It is this extra Wattage that results in heating of tissues. This characteristic needs to be taken into consideration as certain tissues do not benefit from thermal heating, and too much heat can damage even the more tolerant tissues. The Arndt-Schultz Law simply states that for therapeutic substances, small doses stimulate, moderate doses begin to inhibit, and large doses can damage to the point of termination. This concept has been applied to LLLT as well as other modalities.

Biochemical Mechanisms and Physiologic Responses
Light therapy in the green-red visible spectrum has been shown to induce physiologic responses in cells. The primary reaction within the mitochondria of increasing ATP production is followed by an immediate secondary reaction of three-dimensional cell-to-cell energy transference resulting in a cascade of systemic responses. LLLT has been shown to suppress apoptosis and promote viable cell growth. Laser therapy has been shown to preserve membrane and genetic material of cells that are nutritionally starved, revitalize erythrocytes enhancing their oxyphoric function, enhance fertilization potential of spermatozoa, stimulation of satellite stem cells, and reduce the extent of myocardial infarctions and ischemic strokes. The ability to modulate cellular metabolism and promote a biological response is dependent on the intensity, wavelength and frequency emitted by the specific device. Within the electron transport chain of the mitochondria is the terminal enzyme cytochrome c oxidase. This enzyme is responsible for mediating electrons from cytochrome c to molecular oxygen within the mitochondria. This respiratory chain enzyme was later found to be capable of absorbing photonic energy. Cytochrome c oxidase has been identified as the photo acceptor molecule responsible for the various responses following LLLT.

A “fourth phase” of water (H302), a gel like “liquid crystalline” state that occurs when electromagnetic energy stimulates the cells, has been determined to play a role in speeding the conduction of photonic energy through the cells. For a given wavelength of light, Energy Density is an important factor in determining the tissue reaction. Research indicates that ED in
the range of 0.5-4J/cm² is most effective in triggering a photo biological response in tissue.⁹

There is ongoing research working to support and fine tune this claim.

**Studies in Support of 405nm Blue Light for Managing Infections**

Irradiation with red and near infrared light promotes tissue repair, while treatment with blue light is known to be antimicrobial. Infected wounds benefit from combined blue and red/infrared light therapy as evidenced by D.D. Masson, who concluded that irradiation with blue light at low fluence (3-10J/cm²) does not impair in vitro wound healing, increases protein synthesis, and that it is anti-inflammatory.¹⁰ Blue Laser light was capable of inhibiting bacterial growth (Staphylococcus aureus, Pseudomonas aeruginosa, E-Coli) at low fluences (3-18J/cm²) over time, thus presenting no time dependent effects.¹¹ The 405 nm light produced a dose dependent bactericidal effect on Pseudomonas aeruginosa, and Staphylococcus aureus, achieving as much as 95.1% and 90% kill rate for each respectively.¹²,¹³ Low doses of HINS light were found to have no significant inhibitory effects on fibroblast populated collagen lattice contraction (in vitro model for wound healing), cell proliferation, or alpha smooth muscle actin expression. Doses of up to 18J/cm² had no significant inhibitory effects on FPCL cell numbers, and this dose was shown to cause almost complete inactivation of bacteria. These results show that HINS light has potential for disinfection applications without adversely influencing wound healing.¹⁴ Another study established that Campylobacter jejuni is particularly susceptible to violet/blue light at a wavelength of 405nm. This finding, coupled with the safety in use advantages of this visible (non-ultraviolet wavelength) light, suggests that high intensity 405nm light may have applications for control of Campylobacter jejuni contamination levels in situations where this type of illumination can be successfully applied.¹⁵ Another study validates the sporocidal claims and findings in case responses. Lethal effects of high intensity violet 405nm light on Saccharomyces cerevisiae, Candida albicans, and on dormant and germinating spores of Aspergillus niger. The results of this study indicate that fungal organisms can be inactivated by exposure to high intensity light from within the visible light spectrum and specifically violet light of wavelength 405nm. Of the two yeast species tested, and dormant and germinating spores of A. niger.¹⁶

**Communication and Case Selection:** Therapy laser is NOT a magic wand. Rehabilitation at the cellular level works best when considered as an **adjunct** to healing. Ideally, cellular enhancement would support rehabilitation at the spinal and connective tissue levels. This can be accomplished by performing neuronal modulation and myofascial release techniques including, but not limited to acupuncture, chiropractic, osteopathy, or VOM. Other building blocks for healing include adequate nutrition with appropriate supplementation, hydration, exercise for lymphatic drainage and circulation, as well as mental enrichment. In the event of slight to no response within 6 laser treatments, or when there is a plateau, the rationale includes several possibilities. 1) The cells may have rehabilitated to their full extent, or there are no viable germinal cells. This would prompt a review of nutrition, hydration and nutraceutical status; 2) There may be an underlying condition yet to be diagnosed; 3) The wrong diagnosis has been made; 4) The treatment protocol needs to be tweaked and thus the need for close follow up and medical progress exams. Communicating these factors to owners is paramount to compliance and expectations. Close follow up is imperative in the form of staff callbacks within 1-3 days and medical progress exams. In four plus years of performing LLLT, the author has yet to have an owner regret their investment as realistic expectations were explained.
**Treatment Protocols**

Not all lasers are created equal, thus there is no universal treatment protocol. The specifications including power, wavelength and frequency define, and the individual condition determines the protocols. This author is familiar with a low power truly non-invasive laser system utilizing the specifications described above. Under no circumstances should this treatment protocol be applied to other laser systems. The treatment protocols vary on a case-by-case basis, and this is where the true “Art” of medicine comes in. Determining factors are as follows: a) Physical exam and supporting diagnostics, b) Diagnosis or list of differential diagnoses, c) Chronicity of condition or symptoms, d) Owner compliance to schedule and costs, e) Response to treatment—follow up imperative! Case reports involving birds, exotics, dogs, horses, and wildlife will be discussed including diagnostic results, selection of treatment protocols and response to treatments.¹⁷

**Accelerated Plan:** For severe trauma or pain, or chronic condition: Two treatments 90 minutes or more apart to allow for physiologic changes to occur. The 2 treatments /day would occur 3 days in week one, then 1 separate treatment 3 days in week 2, then 2 treatments per week for a total of 12-13 treatments. Since the effects of the LLLT are cumulative, benefits would be seen sooner in the course of treatment. Noticeable benefits may be witnessed within hours with acute exacerbations, or several days if healing ligaments and fractures. **Chronic Plan:** Long Term, Low Grade Pain: Two treatments on day one, then two separate treatments each week for 2 weeks, then one treatment weekly. **Try and See Plan:** Diagnosis Open, or Owner has Financial Concerns: Two treatments on day 1, then 1 treatment weekly. Follow up is imperative!

**Wounds, Soft Tissue, Tendon, Ligament Injury, Post-Op Applications**

The proposal that laser energy merely promotes cellular energy rather than changing cell function explains why injured tissue cells respond to laser therapy whereas there is little effect on non-injured cells. Laser energy is more effective in treating pathological states, therefore, when healthy subjects are used, the outcomes may be subdued. Although tissue healing is accelerated, no hyperplastic effects have been reported. During wound healing, laser wounds had more collagen and a higher tensile strength than the controls, until healing was complete, at which time both lasered and control groups were similar. Laser energy catalyzes normalization rather than creating a super normal effect. Thus, proud flesh (in the case of a horse) would not be accelerated beyond that of non-lasered individuals. **Laser Protocol** Varying degrees of wounds would determine mixing and matching protocols to the issues each individual demonstrates. A combination of the immune system enhancement, with treating over the nerve root or entire spine, along with settings to increase circulation and lymphatic drainage over the wound or soft tissue injury would be in order. The violet wavelength and its documented bactericidal and sporicidal properties allow for benefits against bacteria and fungi. The author has used LLLT successfully to manage cellulitis, "scratches," wire cuts, decubitus ulcers, and nodular necrobiosis masses. LLLT is used for pre and post-op surgical applications in soft tissue as well as orthopedics. Studies have shown that when using the bactericidal Violet 405nm 5mW on osteoblasts in cell culture when studying infected arthroplasties, over 15mW altered osteoblast function. It was concluded that 5mW was the maximum power recommended to stimulate osteoblast function.¹⁴
Conclusions
The delivery of light in the form of laser (monochromatic, coherent, and directional) allows for biostimulation. LLLT affects tissue cells in a manner that stimulates cellular biochemical reactions that enhance cell regeneration and cell communication. This photobiomodulation results in decreased pain and inflammation, as well as increased vasodilation resulting in enhanced wound healing. Studies are showing that wavelengths in the range of 400nm-660nm along with low power, appears to have beneficial responses, with the least amount of risk to patient and operator. Irradiation with red and near infrared light promotes tissue repair, while treatment with blue light is known to be antimicrobial. Infected wounds benefit from combined blue and red/infrared light therapy. Studies also show that Low Power Lasers do result in effective management of deep tissue pain and inflammation, contrary to current competitive marketing claims. Low power lasers at wavelengths of 405nm and 635nm, with 5mW and 7.5mW power output are showing systemic responses. More investigation into this non-invasive technology is encouraged. In addition, the Blue/Violet Laser has been found to be bactericidal and sporicidal, which can benefit infected wound management as well as disinfection of surgical suites.

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Objectives

- To demonstrate a safe and effective non-invasive means of calming and expediting healing of wounds and organ systems.
- To demonstrate that treatment can occur from a short distance, with minimal to no restraint, as well as no eye protection needed, makes this system invaluable for critical species.

Introduction

Low Power Laser Therapy was performed on multiple species using lasers that are 5mW and 7.5mW and wavelengths of 635nm (red) and 405nm (violet).

The discussion will focus on numerous case results involving birds, exotics, raptors and wildlife. The tissue regenerative, low power visible light wavelength non-heat producing qualities of this laser, along with the line generated beams allows treating from a short distance un-sedated. There is also no need for eye protection. This allows for a safer stress-free treatment option. Examples including pre and post op applications, expediting wound healing, as well as managing arthritis and lumbar disease are documented. The ability to manage abscesses and infections, immune stimulation, and endocrine balance will be highlighted. Also discussed is the ability to affect the sympathetic and parasympathetic nervous system to calm fractious animals or revive fragile shock patients. Besides exotic companion pets from the clinic experiences, the author has spent 10 years gathering case responses from volunteer contributions to The Raptor Center in St. Paul Minnesota, The Wildlife Clinic, St. Paul Mn; The WildCat Sanctuary, Sandstone, Mn, The Children’s Nature Center, Grand Junction, CO, among other rescue organizations.

Autonomic Nervous System Applications for Calming

The Autonomic Nervous System controls all life functions and is always in a state of balance. When the sympathetic tone is high (fright or flight) the parasympathetic tone is low, (homeostasis, digestion, appetite).

The sympathetic ganglion reside along the paralumbar muscles between T1-L3-4. The line-generated beams of the laser device can access this entire area. As photonic energy is absorbed, causing the excitation of electrons to higher orbits, then subsequent photonic emissions to neighboring atoms in a cell-to-cell cascade, the sympathetic tone is continually stimulated. When the pre-programmed light stops in 120-180 sec, the sympathetic tone plummets, allowing the parasympathetic tone to increase. Within minutes, a fractious, painful, or emotional animal can be calmed to a more harmonious state. Appetite, peristalsis, and focus are restored. Blood pressure has been documented to decrease.

Similarly, the parasympathetic tone can be further enhanced. By following the sympathetic protocol with Vagus nerve frequencies, the calming can be even more enhanced. The areas to receive the laser light input would be cervical and sacral, where the Parasympathetic ganglion reside.
It is important to note that the Sympathetic stimulation should NOT be used in shock, anesthetic emergencies, or near-death cases. In these cases, the Parasympathetic stimulation ALONE is indicated. Further stimulation of a sympathetic tone in these fragile patients could be detrimental and send them over the edge.

It is advised to prepare the staff to have the laser available, set for parasympathetic settings to have at hand for any shock, severe trauma, anesthetic emergency, collapse, or fragile state. This will save time in the event of an emergency. If there can be a fraction of a second plateau in an otherwise downward spiral that can make the difference between life and death, it is well worth it.

Role of Frequency in Healing
There is controversy concerning the validity and importance of frequency (oscillations or pulsations) of the laser light in the overall effects of healing response. In this author’s experience, as well as other operators of laser devices with similar specifications and capabilities, the answer is clear. Frequency does make a difference. It is worth pursuing in an evidence base medicine research setting.

Considering that the String Theory of Quantum Physics suggests that the physical universe consists of a series of vibrations, James Oschman’s book, Energy Medicine: The Scientific Basis, denotes that all tissues have a vibrational state unique to it.

Royal Raymond Rife discovered in the 1930s that varying the frequencies of micro electric current, different microorganisms are affected. Laser light, another form of electromagnetic energy can be pulsed in varying frequencies. This altering of the vibration or oscillation of the beam is measured in Hertz. Numerous studies have documented the benefits of frequencies in managing seizure activity, bone healing, as well as immune mediated diseases such as rheumatoid arthritis and Crohn’s disease.

When varying the laser frequencies, combined with the tissue compatible (non-heat producing) low power, visible light wavelength, different tissues can be affected more specifically. This allows the practitioner to practice the “Art” of veterinary medicine as individualized treatment protocols can be prescribed.

Treatment Protocols
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**Immune System**

Borrowing on the concept of varying the frequencies for specific tissues, allows for access to enhancing the immune system. Accessing the entire chest and abdomen with the line generated beams for the preprogrammed time (120-180sec), allows stimulation of lymphatics including the thymus, Bursa of Fabricius in birds, and spleen.

Combining this protocol with treatment for pain and inflammation can allow more effective management of immune mediated conditions such as Rheumatoid arthritis.

**Endocrine Disease**

Endocrine diseases can also be treated, as there exists no contraindication due to the non-heat producing qualities of this lasers ability to cause photobiomodulation. Although a cure is not suggested, there have been cases of reversal of early onset diabetes when pancreatic
inflammation has been decreased, and islet cells stimulated to regenerate their insulin producing abilities.

**Cancer**
Palliative care for cancer patients is indicated, as the benefits of improved circulation, lymphatic drainage and decreased pain and inflammation in a non-heat producing effect has been demonstrated. The non-thermal laser with the ability to program various frequencies has been used in human cancer clinics for treatment of mucositis and stomatitis secondary to chemo and radiation treatments. Although not considered a cure, the size of some cancers have diminished as a result of implementing a combination of immune system enhancement, autonomic nervous system capabilities to improve appetite and digestion, and managing pain and inflammation. The photobiomodulation essentially accesses the body’s immune system and innate pharmacy to fight more effectively. It is again stressed that adjunctive modalities also come in to play such as nutrition, hydration, exercise, as well as mental enrichment to decrease stress.

**Conclusion**
Treatment and rehabilitation of exotic wildlife and zoo animals poses a challenge of attempting to ensure that the risk/benefit equation is managed at all times. The abilities of the non-thermal laser with its line generated beam, low power and visible light wavelengths, and ability to implement various frequencies, allows safe treatment of a myriad of infectious, inflammatory and degenerative diseases in these stress sensitive animals. The ability to treat from a safe distance without sedating the animal, with no risk of retinal damage, is invaluable.

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Objective
To understand the structure and function of the endocannabinoid system as well as the potential
detriment of endocannabinoid deficiency.

Introduction
Cannabis has been integrated within human civilization for over 4000 thousand years. It has been
used for food, fiber, fuel, and as medicine. The naturally occurring phytocannabinoids and
terpenes produced by cannabis exert a profound physiologic effect on both humans and animals.
By accessing the endocannabinoid system, cannabis has multiple actions as example; anti-
inflammatory, analgesic, anti-neoplastic, and anticonvulsant, all while promoting homeostasis
within the body. The keys to successfully using cannabis as medicine in veterinary patients lies
in understanding the physiology of the endocannabinoid system and how that system interacts
with cannabis.

Basic Terminology

Cannabis
The genus of a flowering plant has three different species that have been recognized including
*Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis*. All cannabis used for medicine is
derived from *Cannabis sativa L*. Both hemp and marijuana are classification systems for the
umbrella term, cannabis.

Industrial Hemp and Medical Hemp
Previously, hemp-derived cannabis products came from industrial hemp and they were often low
quality and contained chemical residues due to farming methods. Currently, medical grade hemp
is phenotypically similar to marijuana plants and is grown to be used as medicine, specifically
for its cannabinoid (CBD mostly) content. Properly grown hemp products are considered safe
and may contain a variety of other plant compounds such as minor cannabinoids, terpenes, and
flavonoids.

Materials manufactured from hemp has been dated to over 10,000 years ago. The stalk produces
fibers that can be used to manufacture textiles, rope, food, clothes, paper, etc. Hemp contains
<0.3% of THC by dry weight at the time of harvest, which is the intoxicating compound of the
plant.

Marijuana (High THC Cannabis)
Compared to the industrial hemp plant, the marijuana variety of the cannabis plant contains
>0.3% of THC by dry weight at the time of harvest. Most marijuana chemovars tend to have
>20-30% THC, with a few exceptions.

Endocannabinoid System (ECS)
One of the body’s most ubiquitous neurotransmitter networks found within all animal systems
from nematodes to humans.
**Cannabinoids**
A class of diverse chemical compounds that act on cannabinoid receptors in cells that alter neurotransmitter release. Ligands for these receptor proteins include the endocannabinoids (naturally made in the body), the phytocannabinoids (natural compounds that come from the plant), and synthetic cannabinoids.

**Terpenes**
Aromatic hydrocarbons found in the oils and resin of all plants. They produce the unique smell and flavor of the plant varieties. Terpenes produce their own pharmacological effects on the body.

**The Endocannabinoid System**
The endocannabinoid system (ECS) was originally discovered by Israeli researcher Raphael Mechoulam in the 1970s. A complex regulatory system that is present in almost every system in the body that helps maintain balance and homeostasis. The endocannabinoids are generated on demand by the body, especially in times of stress, disease or injury.

The Endocannabinoid System is composed of three essential parts:

1. The endocannabinoid receptors (part of the G-protein coupled receptors)
   a) CB1 - found predominantly in the central nervous system but is also found in other tissues such as hepatic, gastrointestinal, skin, lungs, urinary bladder and reproductive organs. Due to its distribution these receptors are responsible for pain modulation, movement, appetite, nausea, memory processing and temperature regulation. CB1 plays an inhibitory role on multiple neurotransmitters such as Dopamine, Glutamine, Serotonin, GABA, Noradrenalin and Acetylcholine.
   b) CB2 - found predominantly in the spleen, tonsil and immune system (especially B-cells, natural killer cells, monocytes and mast cells) but also found in other tissues like bone and lung. These receptors play a role in immune modulation, inflammation, and bone density.
   c) Other non-classic receptors such as: ligand-gated ion channels, serotonin, glycine and nuclear receptors.

CB1 receptors have the ability to dimerize with a variety of other receptors such as opioid, serotonin, dopamine, adenosine and chemokine, and receptors. Heterodimerization changes can increase or decrease the signal generated from the receptor or even change signaling pathways. It can also change the affinity of the ligand to its receptors as well as change the location of receptor.

2. Endocannabinoids (ligands)
   a) Anandamide (AEA) - primary endogenous ligand for CB1 receptor
   b) 2-AG - primary endogenous ligand for CB2 receptor
   c) Others: n-arachidonoyl dopamine (NADA) and Virodhamine (OAE) and Noladin Ether
The endocannabinoids are formed from lipid-based compounds that are generated on demand by the body, especially in times of stress, disease or injury. Endocannabinoid deficiency has been linked to a variety of chronic disease such as fibromyalgia, migraines and irritable bowel disease.

3. Regulatory Enzymes
   a) Fatty Acid Amide Hydrolase (FAAH)-degrades anandamide
   b) Monoacylglycerol Lipase (MAGL)-degrades 2-AG
   c) Cyclooxygenase-2 (COX-2)-degrades both anandamide and 2-AG
   d) Fatty Acid Binding Proteins (FABP)-mediates the transport of anandamide to FAAH

Endocannabinoid signaling occurs either as tonic or phasic. Tonic signaling is what establishes endocannabinoid tone/basal level of signaling. Multiple factors can affect tone including reduced synthesis or increased degradation of endocannabinoids. Deficiency of endocannabinoids can be caused by genetic factors or be acquired secondary to chronic disease or illness. Examples of abnormal endocannabinoid tone include inflammatory bowel disease, anxiety, chronic stress, and epilepsy. Furthermore, clinical endocannabinoid deficiency (CED) has been studied and documented in three treatment resistant conditions: migraine, fibromyalgia and irritable bowel syndrome.

Conclusion
The endocannabinoid system is a complex neuromodulatory system that has profound effects on multiple body systems. The role of the endocannabinoid system is to maintain homeostasis of multiple physiologic processes within the body. This intricate system is integrated throughout all body systems with important implications in energy balance, immune modulation and nervous system communication. Decreased or altered endocannabinoid levels can lead to imbalance and potentially the development of chronic diseases.

References
Cannabis is the most common taxonomic designation of the plant that is under so much discussion within the medical communities. Technically, the term “cannabis” can indicate any plant within the Cannabis genus.

The genus of a flowering cannabis plant has three different species that have been recognized including Cannabis sativa, Cannabis indica and Cannabis ruderalis. All cannabis used for medicine is derived from Cannabis sativa. Both hemp and marijuana are classification systems for the umbrella term, cannabis. These two classifications are the basis of the regulatory definitions of Cannabis and have important legal implications for veterinary practitioners working with these products.

Industrial Hemp and Medical Hemp
Previously, hemp-derived cannabis products came from industrial hemp and they were often low quality and contained chemical residues due to the farming methods. More recently, medical grade hemp is phenotypically similar to marijuana plants and is grown to be used as medicine, specifically for its cannabinoid (CBD) content. Properly grown hemp products are considered safe and may contain a variety of other plant compounds such as minor cannabinoids, terpenes, and flavonoids.

Materials manufactured from hemp has been dated to over 10,000 years ago. The stalk produces fibers that can be used to manufacture textiles, rope, food, clothes, paper, etc. Hemp contains ≤0.3% of THC by dry weight at the time of harvest, which is the highly intoxicating compound of the plant.

Marijuana (High THC Cannabis)
Compared to the industrial hemp plant, the marijuana variety of the cannabis plant contains >0.3% of THC by dry weight at the time of harvest. Many marijuana chemovars tend to have >20% THC, with a few exceptions.

Endocannabinoid System
One of the body’s most ubiquitous neurotransmitter networks found within all animal systems from nematodes to humans. 3

Cannabinoids
A class of diverse chemical compounds that act on cannabinoid receptors in cells that alter neurotransmitter release. Ligands for these receptor proteins include the endocannabinoids.
(naturally made in the body), the phytocannabinoids (natural compounds that come from the plant), and synthetic cannabinoids.

**Terpenes**
Aromatic hydrocarbons found in the oils and resin of all plants. They produce the unique smell and flavor of the plant varieties. Terpenes produce their own pharmacological effects on the body.

**Molecules Produced by The Cannabis Plant**[^2][^27]
Plants from the *Cannabis* genus are capable of producing three types of compounds currently of interest to medical professionals; phytocannabinoids, terpenes, and flavonoids.

**Phytocannabinoids**
Phytocannabinoids consist of over 100 naturally occurring compounds with chemical structures related to the endocannabinoids. They are exogenous, plant-based compounds that bind to the endocannabinoid receptors as well as other receptors in the body. There are multiple phytocannabinoids that have been studied but the two most common ones are detailed below. THC is a partial agonist for both CB1 and CB2 and is largely responsible for the neurological effects noted with cannabis use. Some of the most notable physiologic effects of THC include:
- Analgesia
- Anticonvulsant
- Anti-inflammatory
- Antineoplastic
- Appetite stimulant and antiemetic
- Bronchodilatory
- Gastrointestinal support
- Promotes sleep

CBD, unlike THC, is not intoxicating and in fact can reduce the negative effects associated with THC via negative allosteric modulation of CB1 and CB2 receptors and inhibition of cytochrome P450 (which slows the metabolism of THC to the potentially more psychoactive metabolite 11-hydroxy Δ9 THC). CBD is an antagonist, with low binding affinity at CB1 and CB2 receptors. CBD is unique in that it can inhibit FAAH in rodent models, which can allow anandamide (or THC) to act on the receptors longer. We do not know if the same occurs in companion animals. Also, CBD binds to FABP which reduces the degradation of AEA by FAAH, allowing the body to be exposed to AEA longer. Some of the most notable physiologic effects of CBD include:
- Analgesia
- Antiemetic
- Antidiabetic
- Anti-inflammatory
- Antineoplastic
- Anxiolytic/Antidepressant
- Cardioprotective
- Improved fracture healing
- Neuroprotective and anticonvulsant
There are several other phytocannabinoids that have been shown to have medicinal benefits, both in vitro as well as in vivo. For example, cannabidiolic acid (CBD-A) is a precursor to CBD and has been shown to have potent anti-emetic, anti-neoplastic and anti-inflammatory properties. A 2008 study showed CBD-A had essentially equal COX-2 inhibition compared to two NSAIDs. A subsequent study showed that cannabigerol (CBG), (cannabigerol acid) CBG-A, and tetrahydrocannabinolic acid (THC-A) had COX-2 inhibition as well.

**Terpenes**

Terpenes are aromatic oils that are responsible for giving cannabis varieties different smells and tastes. The development of terpenes within cannabis began for adaptive reasons, specifically to repel predators, protection (antibacterial and antifungal effects) and to attract pollinators. There are over 200 different terpenes that have been identified in the cannabis plant and every cultivar (strain) has a unique terpene profile. Practitioners already have some familiarity with these molecules from their presence in essential oils and the practice of aromatherapy. These molecules are usually found in quite small quantities in the cannabis plant but can have significant therapeutic effects within the body. The most significant characteristic of terpenes is their ability to interact synergistically with the other compounds within the plant to enhance the effect it has on the body. The distinctive terpene profile is truly what results in the specific physiological effect that differentiates between the chemovar varieties. Some terpenes are responsible for more of relaxing or anti-anxiety effect while others may produce an uplifting or energetic effect.

**Flavonoids**

Flavonoids are a diverse group of naturally occurring polyphenolic compounds that play a role in providing the color pigmentation of the plant as well as attract pollinators. They are plant-based antioxidants found frequently in nature. There are over 29 flavonoids that are considered highly pharmacologically active compounds that work synergistically with other compounds within the cannabis plant to produce medicinal benefits.

**Entourage Effect**

The importance of understanding whole plant medicine is to appreciate the phenomenon of the entourage effect. This is defined as the intricate synergy between the different parts of the plant (cannabinoids, terpenes, and flavonoids) that result in powerful medicinal benefits. It is believed that utilizing a complex profile of molecules achieves better clinical outcomes than pharmaceutically isolating a fraction of the plant (for example, THC or CBD alone). Keep in mind, the entourage effect is essential until we truly figure out the exact compounds required to treat a specific disease. The author postulates that the future of cannabinoid medicine will to transform to personalized medicine. Everyone has a unique ECS which can vary depending on several factors including genetics, chronicity of condition, age, co-morbidities, and environmental influences such as stress. This concept is essential to understanding why each patient (human or veterinary) should have individual formulations created for their unique ECS and disease.

The clinical effects of many of the molecules produced by the cannabis plant are not fully understood. However, the improved clinical outcome from products with complex molecular
spectrums is well supported. Cannabis products that incorporate as much of the plant’s diverse molecular profile is ideal.

**Veterinary Cannabis Studies**

To date, we have an ever-growing list of relevant studies for practical use of cannabis in companion animals. Most notably, we now have the results from three studies, two conducted at Colorado State University (CSU) and one from Cornell University, to help shed light on effective and safe dosing of CBD dominant cannabis products in dogs. In the Colorado State University study, conducted by Dr. Stephanie McGrath, dogs were given three different dosing strategies. A group of 30 healthy beagle dogs were randomly assigned to receive a cannabidiol dominant product in the form of a capsule, oil, and CBD transdermal cream at a dose of 10 mg/kg/day or 20 mg/kg/day for 6 weeks. In the study, the dogs had complete blood counts, chemistry panels, urinalysis, and bile acids performed at 0, 2, 4, and 6 weeks.

The most notable effect was elevations in serum alkaline phosphatase (ALP) that occurred in some dogs. All the dogs in the study also experienced diarrhea, while the dogs that received the transdermal formula had reddened skin after application that was not of clinical concern. Because the products used in the study were plant-based, the variability between batches were measured. Variability was <10% for the CBD-infused transdermal cream and CBD-infused oil. There was considerable variation, 28–31%, between the CBD concentration in the capsules and the amount stated on the label. Higher systemic exposures were observed with the oral CBD-infused oil formulation, and the half-life after a 75 mg and 150 mg dose was $199.7 \pm 55.9$ min and $127.5 \pm 32.2$ min, respectively. Exposure was dose-proportional, and the oral CBD-infused oil provided the most favorable pharmacokinetic profile. The study mentions that the diarrhea was not related to the formula but instead environmental factors.

In a canine study conducted at Cornell University under the direction of Dr. Joseph Wakshlag, evaluated both pharmacokinetic and clinical efficacy study on dogs with osteoarthritis (OA). A single dose pharmacokinetic study was performed using two different doses of CBD enriched oil. The industrial hemp used in this study has ~10 mg/mL CBD and an equal mix of ~10 mg/mL cannabidiolic acid (CBDA), 0.24 mg/mL THC, 0.27 mg/mL cannabichromene (CBC), and 0.11 mg/mL cannabigerol (CBG). All other cannabinoids were less than 0.01 mg/mL with a robust terpene profile.

The initial investigation into single-dose oral pharmacokinetics was performed with four beagles. Each dog received a 2 mg/kg and an 8 mg/kg oral dosage of CBD oil. The dogs were fed 2 h after dosing. Blood was collected at 0, 0.5, 1, 2, 4, 8, 12, and 24 h after oil administration. Pharmacokinetics demonstrated that CBD half-life of elimination median was $4.2 \text{ h (3.8–6.8 h)}$ for the 2 mg/kg dose, and $4.2 \text{ h (3.8–4.8 h)}$ for the 8 mg/kg dose. These results led to dosing during the clinical trial at 2 mg/kg every 12 h. For the clinical efficacy study, which assessed the use for dogs with radiographically confirmed OA, a randomized placebo-controlled, veterinarian and owner blinded, cross-over study was used. Dogs received CBD oil (2 mg/kg) or placebo oil every 12 hours. Hematology, serum chemistry, and physical examinations were performed on every visit. A canine brief pain inventory and Hudson activity scores showed a significant decrease in pain and an increase in activity with CBD oil. Veterinary assessment showed decreased pain during CBD treatment. Owners reported no adverse side effects; however, serum
chemistry showed an increase in alkaline phosphatase (ALP) similarly to the CSU study during CBD treatment, which normalized over time. Conclusions of the clinical study suggest that 2 mg/kg of a CBD-dominant product twice daily can help increase comfort and activity in dogs with OA. It should also be noted that some dogs in the study were also on traditional nonsteroidal anti-inflammatory drugs with no adverse effects.

A recent study evaluating single dose PK in dogs and cats as well as determined safety over 12 weeks of administration of CBD-dominant hemp. A total of 16 patients were treated (8 dogs and 8 cats) with 2mg/kg BID of CBD hemp product. The pharmacokinetics revealed a mean maximum concentration (Cmax) as well as systemic exposure of drug (area under the curve (AUC) significantly less in cats vs dogs. But the time to maximal concentration (Tmax) was similar in both species. Serum chemistry and CBC results showed no clinically significant alterations; however, one cat showed a persistent rise in alanine aminotransferase (ALT) above the reference range for the duration of the trial. It was concluded that in healthy dogs and cats, an oral CBD-rich hemp supplement administered every 12 hours was not detrimental based on CBC or biochemistry values. Cats do appear to absorb or eliminate CBD differently than dogs, showing lower serum concentrations and adverse effects such as excessive licking and headshaking during oil administration.

A 2020 publication out of Canada evaluated the safety and tolerability of escalating doses of three cannabis oil formulations vs placebo in dogs. It was a randomized, placebo-controlled, blinded, parallel study with 20 healthy beagle dogs. Dogs were randomly assigned to one of five treatment groups: CBD-dominant, THC-dominant, CBD/THC (1.5:1), sunflower oil placebo or MCT placebo. Up to 10 escalating doses of the oils were planed via oral gavage with three days separating doses. Results showed that dose escalation of the CBD-dominant oil was as safe as the placebo and safer than dose escalation containing THC. Generally side effects profile was low except for the dogs receiving THC or THC/CBD combination, they had moderate to severe side effects including (ataxia, hypothermia and lethargy). All of these adverse effects are not surprising with THC, especially when considering that the experimental design did not account for tolerance that occurs when appropriately dose escalating THC in a clinical setting. That would require slow titration with dose increase, and that significantly lowers or eliminates toxicity seen with THC. In addition, they found the residual CBD and THC in the plasma seven days post last dose which means without an appropriate wash out period, they were getting cumulative dose toxicity.

Conclusion
The use of cannabis in animals is an area of growing interest, largely due to the therapeutic benefits. Though THC and CBD are the most well- known cannabinoids, it is important to understand that the minor cannabinoids, terpenes, and flavonoids have significant clinical benefit. Continued research is imperative to confirm safety and efficacy of the variety of compounds within the plant.

References


Clinical Application of Cannabis: Therapeutic Implementation, Dosing Rational, and Toxicity Information
Trina Hazzah, DVM, DACVIM (Oncology), CVCH

Objectives
- To understand the main considerations when implementing cannabis into a treatment plan including knowing which conditions are most appropriate to introduce cannabis therapy.
- To learn the importance of product selection, safety, and dosing rational.
- To review the clinically relevant veterinary literature

Introduction
Cannabis is being utilized for a variety of different disease processes in human medicine and there are multiple publications (both in vivo or in vitro) supporting its medicinal use. Due to the legal environment surrounding cannabis, there are only a few in vivo studies performed in veterinary medicine thus far. Here are a few examples of medical conditions, which represent the most common and scientifically justified clinical applications of cannabis:1-28

- Anti-inflammatory
  - Eosinophilic dermatitis and hypersensitivity in cats
  - Atopic dermatitis in dogs
- Analgesia
  - Osteoarthritis
  - Neuropathic pain
- Anticonvulsant
- Neuroprotection
- Anxiolytic
- Antineoplastic
- Gastrointestinal support

Product Selection
Although CBD and THC are only two of the many molecules produced by the cannabis plant, these two molecules frequently make up the largest portion of any cannabis product. Products that contain higher concentrations of CBD are most effective for immune system imbalances, anxiety disorders, mild pain control, and a subset of seizure conditions. Products that contain a more balanced ratio of CBD to THC provide stronger pain control, stronger anti-inflammatory effects, improved nervous system regulation, and greater success in a subset of behavior disorders.

Products appropriate for human medical patients are not automatically safe for animal administration. The contamination testing limits that are appropriate for human patients may be dramatically different from those that are safe for animals. Additionally, products from the human cannabis market that are utilized for animals should be carefully evaluated to avoid extra additives, coloring or sweeteners. Pet owners should be carefully counseled to avoid products with known toxins such as xylitol, chocolate, raisins, etc.
Selecting the correct product is critical for all patients, but especially veterinary patients. The following are a few important points that need to be considered when obtaining a medical cannabis preparation:

- “Full spectrum” means the product contains the various components of cannabinoids, terpenes and flavonoids, in the original plant strain, which contributes to the entourage effect. Utilizing the entourage effect tends to provide the patient with the best chance of success. When the product has many compounds but not all of what was found in the original strain, it is referred to as “broad spectrum.”
- CBD isolates are pharmaceutically purified CBD. CBD isolates have no entourage effect and typically require much higher dosages to see a similar benefit compared to full or broad-spectrum products.
- Be sure the product is free of pesticides, fungicides, herbicides, heavy metals, harmful pathogens/mycotoxins and residual processing solvents. This can be accomplished by reviewing a certificate of analysis.
- The product should have labeled amounts (in mg) of each cannabinoid (THC, CBD, etc.) so that appropriate dosing is feasible.

**Toxicity**

THC is the limiting factor when it comes to dosing veterinary patients and careful selection of products and proper dosing is essential. Dogs, in particular, have higher amounts of CB1 receptors in their cerebellum compared to any other species. When dogs receive excessive amounts of THC (either via accidental ingestion or overdose) they develop a unique toxicity known as Static Ataxia. Dogs with this condition frequently present with severe ataxia and a sawhorse stance where they sway back and forth and abruptly catch themselves from falling.

Excessive THC exposure in dogs can also lead to urinary incontinence, severe lethargy, agitation, tachycardia or bradycardia (dose dependent), hypersalivation, and hypothermia. The majority of dogs experiencing intoxication after marijuana ingestion recover completely with supportive care and monitoring. However, dogs with severe clinical signs that are unable to eat or drink without support, intravenous fluids and even hospitalization may be warranted. The use of intralipid therapy to bind the highly lipophilic THC is another treatment option to reduce clinical signs in severe cases of toxicity. Theoretically, depending on the timing of when the pet presents after overdose, treating with CBD can also reduce the THC induced intoxication. Unlike opioid receptors, there are no cannabinoid receptors in the respiratory centers of the brain. Thus, even with extreme overdoses of cannabis, there is no chance of respiratory depression.

CBD, by contrast, has very few side effects in both humans and veterinary patients. A recent study found that CBD was well tolerated in dogs at a dose of 10-20 mg/kg/day. This is much higher than what is typically given in a clinical setting. The only hematological effect noted was an elevation in serum ALP, which was likely due to CYP450 interactions. Physiologic side effects were limited to mild gastrointestinal signs (diarrhea), pinnal erythema, and oculonasal discharge noted.

**Dosing**

The majority of medications in veterinary medicine follow a linear dosing curve. In other words, as the dose increases, drug efficacy increases (or reaches a plateau). Similarly, side effects
develop with increasing dosage. With cannabis however, dosing follows a biphasic dosing curve, meaning after the “optimal” dose is achieved, a further increase in dosing leads to diminished clinical efficacy. Dosing cannabis beyond the optimal dose also increases the risk of developing side effects, particularly with THC.

When considering the above information regarding biphasic dosing and realizing that THC is the dose-limiting compound, it is imperative that pets are dosed with a full spectrum product initially at very low doses. Based on human data, it has become clear the importance of starting low and titrating slowly (every 5-7 days) until efficacy or dysphoria is noted. Overtime, as the receptors are “primed” and the therapeutic window widens, higher doses of THC can absolutely be used in patients as tolerance to the intoxicating effects occur. Depending on the disease state (i.e., specific cancers or severe pain), higher amounts of THC may be warranted. Most cannabis products are dosed orally at an interval of every 12 hours, however depending on the condition treated (i.e., seizures, anxiety, pain) every 6-8-hour dosing may be implemented.

Cannabis dosing guidelines must incorporate an understanding of the product’s molecular profile, the influence of the individual molecules on multiple body systems, the synergistic effects of and between these molecules, and the individualized response of each patient.

**Pertinent Clinically Applicable Veterinary Studies**

**Osteoarthritis**

**Cornell Study**
A prospective, randomized, placebo-controlled, double-blind crossover study was conducted using 16 client-owned dogs with radiographically confirmed evidence of osteoarthritis who were enrolled and who completed this study. Dogs were randomized to receive either 2 mg/kg q12h orally of CBD oil, or a placebo consisting of olive oil with a benign herbal extract at a similar volume q 12 h for 4 weeks. Subjects were given a 2-week washout period and then the treatments were crossed-over, and each subject received the other treatment twice daily for 4 weeks. Veterinary assessment of lameness, movement, and response to manipulation, owner questionnaires (Canine Brief Pain Inventory (CBPI), Hudson activity scale), objective kinetic analysis on a pressure-sensitive walkway, hematology and chemistry analysis were obtained at weeks, 0, 2, and 4 for both oils.

Assessment of pain and mobility showed a significant decrease in pain and increase in activity (p<0.001) at week 2 and 4 during CBD treatment as compared to baseline at each bi-weekly evaluation. It was found that the CBD oil resulted in reduced pain scores when compared to baseline on both bi-weekly examinations (p = 0.03). No side effects were reported by owners, but serum chemistry demonstrated an increase in serum alkaline phosphatase (9/16 dogs: 56%) while receiving the CBD oil, which reached significance at week 4 (p<0.005).

**Colorado State Study**
The purpose of the study was to assess the impact of a full-spectrum hemp extract on dogs with chronic osteoarthritis. A total of the 32 dogs were enrolled and completed a 90-day pilot study. Dogs received CBD oil at 0.25mg/kg delivered on food once daily for 3 days and then every 12 hours. Pain assessments (physical exam and gait analysis) were conducted every 2 weeks for the 90-day period. The CBD dose was escalated by 0.5-0.75mg/kg every 12 hours at each 2-week recheck until the pain score was 0 or 1 (out of 10).
Results showed that 30 total dogs demonstrated improved pain support with their pain scale scores decreased from 3.2 to 0.97 (on the 1-10 scale). Six dogs experienced an improvement in their overall pain scores of 5 or better. Of the 23 dogs that were taking gabapentin at the time of enrollment, 10 dogs were able to discontinue taking gabapentin after the addition of the CBD oil to their pain management protocols. Of the remaining 13 dogs, 11 dogs were able to reduce their gabapentin dose. Among these 30 dogs that had a positive response: the dose of CBD ranged from 0.3 up to 4.12 mg/kg BID. The only clinically meaningful change in blood parameters obtained was an increase in ALKP. Feedback from 94% of the owners (n = 30) indicated they felt their dogs’ quality of life had improved after starting the CBD product.

**Epilepsy**

A prospective, double-blinded, placebo-controlled study assessing the short-term effect of CBD (2.5 mg/kg/day x 12 weeks) on seizure frequency in poorly controlled epileptic dog. The study consisted of 16 client-owned dogs who were diagnosed with idiopathic refractory epilepsy. All dogs were required to stay on their standard anticonvulsant drugs (AED). Routine blood work and CBD levels were determined every four weeks. AED levels were measured at the conclusion of the trial. Dogs in the CBD group had a significant (median change, 33%) reduction in seizure frequency, compared with the placebo group. However, the proportion of dogs considered responders to treatment (≥ 50% decrease in seizure activity) was similar between groups. Plasma CBD concentrations were correlated with reduction in seizure frequency. Elevations in alkaline phosphatase (ALP) were recorded for the treatment group, and one dog in the control group. There was no significant elevation in either potassium bromide or phenobarbital groups. This is an interesting finding because there has been a concern that CBD, which is metabolized through the CYP450 may interfere with the metabolism of CYP450 substrates (like phenobarbital).

**Conclusion**

As with any medication, veterinary practitioners should seek to understand the underlying mechanisms of action in order to appropriately match the product’s molecular profile to the patient’s condition. In addition, other factors like patients age, comorbidities, any contraindications, and pet and owner temperaments need to also be considered when deciding if cannabis therapy should be considered. Product selection should be taken very seriously as there are hundreds of products currently available. Finding products that have clear and accurate molecular profiles (including full cannabinoid and terpene concentrations) and an up-to-date certificate of analysis (COA). A COA provides the practitioner with the profile of the cannabis product as well as evidence of the lack of contaminants (pesticides, heavy metals, mold, bacteria and residual solvents).

**References**

Integrating Cannabis into Veterinary Cancer Therapy: Part 1
Trina Hazzah, DVM, DACVIM(Oncology), CVCH

Objective
- Become familiar with the relationship between the ECS and cancer as well as understand the antineoplastic mechanisms of the various compounds of the cannabis plant.

Introduction
Cannabinoids have been used as medicine for almost 5,000 years. There is evidence that the ancient Chinese, Egyptians and Indians used cannabis for a variety of conditions including inflammation, GI disorders, reproductive disorders, cancer, glaucoma and others. During the last decade numerous studies have been published suggesting that endocannabinoids, phytocannabinoids as well synthetic cannabinoids have antineoplastic properties.

Cancer is recognized as a disease characterized by uncontrolled proliferation of cells and the ability of these cells to invade into other tissues and metastasize. Understanding the true definition of cancer and the common traits (or hallmarks) that control the transformation of normal cells to malignant cells is essential.

This is a summary based on peer-reviewed articles published by cancer researchers Douglas Hanahan and Robert Weinberg, identifying the six hallmarks of cancer. The hallmarks constitute an organizing principle for rationalizing the complexities of neoplastic disease.¹

The original six hallmarks of cancer are described with the below characteristics:
1. Stimulate their own growth (self-sufficiency in growth signals)
2. Resist inhibitory signals that might otherwise stop their growth (insensitivity to anti-growth signals)
3. Resist programmed cell death (evading apoptosis)
4. Multiply indefinitely (limitless replicative potential)
5. Simulate the growth of blood vessels to supply nutrients to tumors (sustained angiogenesis)
6. Invade local tissue and spread to distant sites (tissue invasion and metastasis)

And then about a decade later, the same researches proposed two additional hallmarks:²
1. Cancer cells have the capability to modify or reprogram cellular metabolism in order effectively support neoplastic proliferation (abnormal metabolic pathways); and
2. Cancer cells can evade the immune system, in particular, by T and B lymphocytes, macrophages, and natural killer cells (evading immunological destruction)

The Endocannabinoid System and Cancer
There are several lines of evidence which support the hypothesis that tumor development and progression may indeed be associated with the disturbance of the endocannabinoid balance. This is especially noted in metastatic cancers.

Specifically, endocannabinoids, including anandamide and 2-arachidonoylglycerol, are involved in cancer pathophysiology in several ways, including tumor growth and progression, peritumoral...
inflammation, nausea and cancer pain. In cancer patients, it has been noted that alterations of
plasma endocannabinoids occur, and similar changes were seen in rodent models with local and
metastatic cancers.3

The endocannabinoid pattern in the tumor microenvironment depends on the tumor’s origin and
site of primary growth and metastasis. For example, tumor growth is associated with an increase
of 2-arachidonoylglycerol (2-AG) both at the site of the primary tumor and in the plasma while
endocannabinoids (eCBs) anandamide (AEA), oleoylethanolamide (OEA) and
palmitoylethanolamide (PEA) decrease in the tumor microenvironment and in plasma likely
because the growing tumor displaces normal cells that produce these eCBs. These three eCBs
decrease as the tumor grows and metastasizes and they are all primarily metabolized by fatty
acid amide hydrolase (FAAH), which is upregulated in various types of cancer.3

Some scientists have concluded that overactivation of the endocannabinoid system may be
protumorigenic and such overactivation of the ECS has been correlated with tumor
aggressiveness. Both anandamide and 2-AG have been shown to be overexpressed in several
types of tumors, including glioblastoma multiforme, meningioma, prostate, colonic carcinoma
and others. In addition, several studies revealed that upregulation of CB1 was correlated with
disease severity and a poor prognostic indicator in a variety of carcinomas such as ovarian,
colorectal, pancreatic and prostate. However, the opposite was noted in patients with
hepatocellular carcinomas, where overexpression of both CB1 and CB2 receptor were correlated
with an improved prognosis. Similar discrepancies regarding prognosis was noted with levels of
CB2 receptor, endocannabinoids and degradative enzymes (both FAAH and MAGL).4

Due to the inconsistent findings, the ability to reliably dictate prognosis based on alterations in
the components of the ECS is not possible at this time. Further studies, including ones that
involve manipulation of the endocannabinoid system, are needed to help clarify which
components of this complex system acts pro-oncogenic or as a tumor suppressor.

The Antineoplastic Effects of Cannabinoids
Despite the above conflicting data relative to the role of the endocannabinoid system in tumor
generation and progression, over the past 20 years there have been an emerging body of research,
mainly using in vitro models of different cancers, to further elucidate the antineoplastic activity
of cannabinoid receptor agonists (like THC, anandamide, 2-AG or synthetic compounds) and
other cannabinoids and terpenes.5

Proposed Mechanisms of Anti-Tumor Effects of Cannabinoids
Inhibition of Tumor Proliferation5-8
Cannabinoids have been shown to inhibit proliferative and oncogenic pathways. CB1 specifically
reduces one such pathway called adenylate cyclase-cAMP-protein kinase A. This signaling
pathway leads to downregulation of the anti-apoptotic factor, survivin. Survivin overexpression
is associated with poor clinical outcomes and reduced tumor apoptosis in patients with colorectal
cancer.

Research has demonstrated that cannabinoid compounds can modulate different portions of the
cell cycle checkpoints. as well as downregulate cyclin dependent kinase (CDK)1 and induce
CDK inhibitors (i.e. p21). Furthermore, cannabinoids have been shown to decrease expression of multiple growth factors such as epidermal growth factor receptor (EGF-R), nerve growth factor, prolactin and vascular endothelial growth factor receptor (VEGF-R).

Cannabinoids (specifically CBD) suppresses ID1 gene (Inhibitor of DNA Binding 1) which has been shown to be overexpressed in more than 20 different tumors and is critical to growth and metastasis of tumors. In addition, activation of PPARγ by cannabinoids can inhibit tumor proliferation and induce apoptosis. Lastly, an in vivo study in mice with gliomas proved that CBD exerted its antitumoral effects through modulation of the LOX pathway. CBD significantly reduces LOX activity by 40%.

**Induction of Cancer Cell Death**

A significant amount of the research conducted so far on the mechanism of cannabinoid antitumor activity has focused on glioma cells. Cannabinoid-induced apoptosis relies on the stimulation of endoplasmic reticular (ER) stress and autophagy. Treatment with THC results in enhanced expression of the stress-regulated protein p8, a transcriptional regulator that has been responsible for tumorigensis as well as tumor progression. Along with several downstream targets (ATF-4, CHOP and trib3), inhibition of AKT and subsequent mTORC1 inhibition is achieved. This process stimulates autophagy-mediated cell death. This specific mechanism of cannabinoid-induced autophagy (leading to apoptosis) is noted in glioma, pancreatic, and hepatocellular carcinoma cells. The role for pro-apoptotic Bcl-2 family members, such as Bad, has also been hypothesized in cannabinoid-dependent apoptosis.

**Inhibition of Invasion and Metastasis**

As discussed above, tumor neovascularization is a hallmark of cancer progression and it has been observed to be suppressed by cannabinoid therapy. In vivo experiments provided proof that cannabinoid-induced inhibition of tumor vascularization was associated with downregulation of the proangiogenic factors such as vascular endothelial growth factor (VEGF), placental growth factor (PlGF) angiopoietin (Ang)-2 and hypoxia-inducible factor 1α (HIF-1α).

Also, cannabinoids cause a lower distribution of CD31-positive cells, a common angiogenesis marker, in experimental tumor xenografts of glioma, melanoma, lung cancer and nonmelanoma skin cancer.

The main receptors of VEGF (VEGF1 and VEGF2) are downregulated when treated with cannabis in skin carcinomas, gliomas, and thyroid carcinomas. Contrary to the above results, few in vitro studies have proved cannabinoids may induce, rather than inhibit, angiogenesis at lower concentration through direct interaction with endothelial cells. Keep in mind, this contrast the numerous studies that uniformly report inhibition of tumor vascularization by cannabinoids.

Cannabinoids as well as degradative inhibitor (FAAH) can work together to modulate regulation of ID1, MMPs, TIMPs and adhesion markers. This may be a therapeutic option to help reduce or inhibit tumor migration, invasion and metastasis.
Modulation of the Immune System

Cannabinoids may elicit an antitumor immune response via multiple mechanisms, enabling a more effective action of immune cells to combat cancer or by favoring conditions that result in local reduction of inflammation in the tumor microenvironment. It has been previously documented that chronic inflammation is associated with the development of neoplasia; therefore, reducing inflammation may, to some extent, contribute to the prevention of carcinogenesis. Phyto cannabinoids with high affinity for CB2 receptors, such as THC, exhibit modulatory effects on both cellular and humoral immunity. THC action was linked to the inhibition of IFN-γ production and suppression of T-cell proliferation.

Despite studies supporting the hypothesis that cannabinoids may enhance immune responses against the progressive growth and spread of tumors, there are some reports that found drastically different results and, in fact, showed cannabinoids have immunosuppressive action via activation of CB2 receptors, as well as causing upregulation of the regulatory T cells (Tregs) which leads to the inhibition of normal (antitumor) immune response.

A 2005 study evaluating both human breast cancer cells lines and mouse mammary carcinomas that had low to undetectable levels of cannabinoid receptors had enhanced tumor growth when exposed to THC. It was theorized, THC caused direct suppression of the antitumor immune response. The reduction of the antitumor immune response is mediated primarily through CB2 as opposed to CB1 receptor. A recent study showed that cannabinoids can promote the progression of Human Papilloma Virus (HPV) related positive head and neck squamous cell carcinomas through the promotion of cell growth, migration, and inhibition of apoptosis through p38 MAPK pathway activation.

The Antineoplastic Mechanisms of Cannabinoids and Terpenes

Below is a list of some of the known antineoplastic mechanisms of the major cannabinoids. There have been proposed mechanisms of antitumor effect with CBDA, THCA, CBG, CBGA, and CBC but they haven’t been studied as thoroughly as THC and CBD.

CBD
- Causes apoptosis via binding to TRPV1, TRPV2, GPR18 and GPR55 as well as inducing reactive oxygen species
- Inhibits cell proliferation via inhibition of ID-1 (inhibitor of DNA binding 1) and helix loop transcription factors (works with ID-1) and activation of PPARγ
- Inhibits inflammatory cytokines including COX-2 and LOX
- Inhibits P-glycoprotein

THC
- Results in apoptosis and autophagy via binding to CB1, CB2 and GPR18 as well as inducing reactive oxygen species
- Inhibits angiogenesis, growth, invasion and metastasis
- Inhibits P-glycoprotein
- Inhibits epithelial mesenchymal transition
- Inhibits inflammatory cytokines including TNFα
Terpenes that have been shown to have anti-neoplastic activity include: D-Limonene, α-Pinenes (also moderate cytotoxicity seen with β-pinene), Myrcene, α-Caryophyllene, β-Caryophyllene and P-Cymene. In addition, a 2019 study performed by Dana Farber and Harvard showed an isomer of Cannafavin B had anti-neoplastic effects on pancreatic carcinoma cell lines and this was further supported when this compound delayed metastatic disease in animal models with pancreatic carcinoma.

Conclusion
Cannabinoids, terpenes and flavonoids have all shown to have antitumor activity in cancer cell lines as well as in animal xenograft models. Cannabinoids can induce autophagy, apoptosis, cell cycle arrest, reduce angiogenesis, tissue invasion and metastasis, without affecting normal cells. However, due to the potential of THC suppressing the host immune response against specific cancers, it is crucial that the legal environment changes to allow for additional research and well-prepared clinical trials. The author feels strongly about the need for cannabinoid-based genetic testing (of both the patient and the tumor) to allow for a more specific targeted treatment. At this time, it is unclear if that will overcome the rare, but known, immunosuppressive effects which can be potentially protumorigenic, but at least it will be a start.

References


Integrating Cannabis into Veterinary Cancer Therapy: Part 2
Trina Hazzah, DVM, DACVIM(Oncology), CVCH

Objectives
- Become familiar with some of the potential clinical applications of cannabis in the cancer patient including product selection and dosing strategies.
- Be aware of some of the oncology in vitro and in vivo studies involving cannabis.

Until recently, most of the cannabinoid application in the cancer patient has been focused on palliative uses such as antiemetic, reduction in pain and increase in appetite. The discovery of the potential value of these compounds as direct antineoplastic effects has led to more research and advancements in cannabinoid implementation in the cancer patient treatment protocol. It was in 1975 where Munson et al demonstrated that the administration of Δ⁹ THC, Δ⁸ THC and CBD (at high doses) inhibited the growth of Lewis lung adenocarcinoma in vitro as well as in vivo after oral administration in mice.¹

Cannabis Therapy Along with Conventional Therapies
The use of combination anticancer therapies has several advantages over single-agent strategies, because they allow for the simultaneous targeting of tumor growth as well as metastatic lesions. Recent evidence suggests that the combined administration of cannabinoids with other anticancer drugs acts synergistically to reduce tumor proliferation. For example, the administration of THC (+/- CBD) and temozolomide exerts strong antitumoral action in glioma xenografts, an effect that is also evident in temozolomide-resistant tumors. The results support that administration of TMZ, and these cannabinoids could enhance the efficacy of standard TMZ-based antitumoral therapies for glioma cases.² A subsequent study revealed that CBD and THC prime glioma cells to respond better to ionizing radiation therapy. Pretreated cells with a combination of THC and CBD for four hours prior to irradiation increase the radiosensitivity compared to pre-treated cells exposed to either cannabinoid individually. The additive effect of cannabinoids to radiation therapy was associated with increased markers of autophagy and apoptosis. A similar effect was observed when THC and CBD were combined with radiation therapy in animal models of glioma. No toxicity was observed in mice treated with combinations of THC and temozolomide.³

Another study recently showed the first evidence that the gemcitabine and cannabinoid combinations exerted a strong synergistic antiproliferative effect on pancreatic adenocarcinoma gemcitabine-resistant cell lines by inducing death via reactive oxygen species (ROS) whereas it had no toxicity toward normal cells. In vivo studies strongly encourage the addition of cannabinoids to gemcitabine protocols for pancreatic cancer treatment.⁴ The findings support a key role of the ROS-dependent activation of an autophagic program in the synergistic growth inhibition induced by GEM/cannabinoid combination in human pancreatic cancer cells. Other interesting synergistic effects were noted with endocannabinoid, anandamide that was shown to enhance paclitaxel-induced apoptosis, through the activation of caspase-3, 8, and 9 (pro-apoptotic family of enzymes). The conclusion of the study suggested that cannabinoids could be a good palliative agent for cancer patients receiving paclitaxel.⁵ Lastly, a 2009 study proved that an anandamide analog and 5-FU produced synergistic effects in certain human colorectal carcinoma cell lines.⁶
Considering that future clinical studies investigating antitumor effects of cannabinoids will most likely not be conducted as monotherapy, but in combination with conventional chemotherapeutics, recent research suggests cannabinoids can work additively and synergistically with a number of chemotherapy agents. CBD and THC enhance the cytotoxic impact of several chemotherapeutics, including vinca alkaloids, cytarabine, doxorubicin, mitoxantrone, carmustine, temozolomide, bortezomib, carfilzomib and cisplatin.\(^7\) Also, a 2008 study showed enhanced cell death with the combination of multiple chemotherapy agents (cytarabine, doxorubicin and vincristine) when given along with THC in leukemia cells.\(^8\) Transient receptor potential vanilloid type-2 (TRPV2) activation by CBD significantly increased doxorubicin (DOX) uptake and apoptosis in triple negative breast cancer (an extremely aggressive form of breast cancer with few effective treatment options available).\(^9\)

The use of cannabinoids in an oncology setting raises the question of whether they act to modulate the effectiveness of concurrently administered anticancer drugs by altering P-glycoprotein expression (P-gp). P-gp confers multiple drug resistance (MDR) by effluxing a diverse array of anticancer agents. A few separate studies examined the effects of cannabinoids on P-gp. One study found that THC and CBD after prolonged exposure (72 hours) resulted in a decrease in P-gp expression, similar to curcumin. This correlated with an increase in intracellular accumulation of Rhodamine 123 (P-gp substrate) and enhanced sensitivity of the cells to the cytotoxic actions of vinblastine.\(^10\) Another article showed that CBD enhanced the intracellular accumulation of known P-gp substrates, Rhodamine 123 and doxorubicin, in a concentration-dependent manner.\(^11\) These results provide preliminary evidence that cannabinoids do not exacerbate P-gp mediated MDR but instead are moderately effective in reversing MDR by reducing P-gp expression. This is helpful information for oncologists to know as many of our chemotherapeutics fail to work due to upregulation in P-gp causing a subsequent multidrug resistance mechanism.

There are a handful of publications evaluating cannabinoid use in the radiation therapy setting. The first one showed radiation-induced emesis was blocked in a dose-dependent manner by the CB1/CB2 receptor agonists, Δ\(^9\) THC and Δ\(^8\) THC.\(^12\) As mentioned above regarding using cannabis along with RT for gliomas, results from that paper demonstrated a duration and dose-dependent reduction in cell viability with each cannabinoid and suggested that THC-BDS (full spectrum/botanical) was more efficacious than THC-P (pure), whereas, conversely, CBD-P (pure) was more efficacious than CBD-BDS (full spectrum/botanical). Similarly, pretreating cells with THC-P and CBD-P together for four hours before irradiation increased their radiosensitivity when compared with pretreating with either of the cannabinoids individually. The increase in radiosensitivity was associated with an increase in markers of autophagy and apoptosis. This data along with the in vivo murine glioma model information highlights the possibility that these cannabinoids can prime gliomas to respond better to ionizing radiation.\(^3\)

Another group explored the potential for enhancing the effectiveness of pancreatic and lung tumor cell kill via the combination of cannabinoids with RT and the use of smart biomaterials loaded with cannabinoids for sustained in situ delivery. Results revealed significant synergy was observed when combining RT and cannabinoids, hypothesized to be secondary to the increased level of apoptosis and resultant DNA damage caused by the combination therapy. When evaluating the in vivo portion for the study, the results support the hypothesis that sustained
delivery with prolonged exposure of tumor cells to cannabinoids may be more effective in inhibiting tumor growth than direct intra-tumoral administration of the same dose of cannabinoids.\textsuperscript{13}

**Cannabis Use in The Palliative Care Setting**

In the oncologic setting, the discussion about palliative care and palliative options for reduction in pain, nausea and improvement in quality of life is a very common topic. Unfortunately, pet owners are receiving little information or support from veterinarians due to the lack of available education on the topic for veterinarians as well as the legal limitations that currently exist. Current research shows that there is a potential role for medical cannabis in cancer palliation. However, the scale and quality of studies conducted to date are somewhat limited. Below I have reviewed some of the seminal articles on the subject.

Increasing preclinical evidence suggests that the endocannabinoid system plays a role in the regulation of both nausea and vomiting. For example, THC reduced the emetic effects of cisplatin chemotherapy induced in the least shrew. In addition, CBD-induced suppression of vomiting was reversed by systemic pretreatment with a 5-HT\textsubscript{1A} antagonist, suggesting that the antiemetic effect of CBD is likely mediated by activation of 5-HT receptors. Another interesting mechanism includes substance P being a key neurotransmitter in chemotherapy-induced nausea and vomiting and cannabinoids can modulate the release of substance P.\textsuperscript{14}

There are several publications from the 1970-80’s on the topic of cannabis for chemotherapy induced nausea and vomiting in humans, therefore, I am focusing on the more recent studies. A 2001 systematic review performed to quantify the antiemetic efficacy and adverse effects of cannabis used for sickness induced by chemotherapy. It was a randomized study evaluating patients that received cannabis, placebo or antiemetics. Results revealed cannabinoids were more effective antiemetics than conventional antiemetics such as prochlorperazine, metoclopramide, chlorpromazine, and domperidone. Many patients in the study had a strong preference for cannabinoids.\textsuperscript{15} In addition, in 2007, Meiri and colleagues randomized patients receiving moderately to highly emetogenic chemotherapy to dronabinol (synthetic THC), ondansetron, both, or a placebo in addition to standard antiemetic treatments. Dronabinol performed relatively equal to slightly superior to ondansetron in specific categories to prevent chemotherapy-induced nausea and vomiting, with no additive antiemetic effects on the combination of both, and all treatment groups were more effective than the placebo.\textsuperscript{16} In a more recent study, Duran et al evaluated 16 patients on chemotherapy who experienced chemotherapy-induced nausea or vomiting despite standard antiemetic treatment. Patients were randomized to either an oromucosal cannabis-based spray containing THC and CBD (1:1 ratio) or a placebo. Those in the treatment group experienced less nausea and vomiting than those on the placebo. Despite the low number of cases in the study, the conclusion revealed when cannabis therapy was added to standard antiemetic therapy it was well tolerated and provided better protection against delayed chemotherapy-induced nausea and vomiting.\textsuperscript{17} Lastly, cannabinoid therapy has been shown to have antiemetic effects for only specific chemotherapies, not for all of them.

The etiology of cancer-related pain is complex and not well understood. There is evidence that cannabis can affect both sensation (signal transduction in the nervous system) and perception (the experience of symptoms).\textsuperscript{14} A recent, 2018 study by Bar-Lev Schleider and colleagues
showed that 52.9% of patients with cancer reported a pain level of 8–10 on a 10-point scale at baseline, and only 4.6% reported that intensity of pain after 6 months of cannabis treatment. It was concluded that cannabis appears to be a safe and effective palliative treatment for patients with cancer pain. A previous multicenter, double-blind, randomized, placebo-controlled, parallel-group study evaluating the efficacy, safety, and tolerability of THC:CBD extract and THC extract in patients with intractable cancer-related pain revealed that CBD extract is efficacious for relief of pain in patients with advanced cancer pain not fully relieved by strong opioids. Interestingly, there was no significant change in the THC group. Also, there was a decreased use of strong opioids observed within both treatment groups. A subsequent study by the same author showed that the long-term use of 1:1 THC/CBD spray was generally well tolerated, with no evidence of loss of effect for the relief of cancer-related pain with long-term use. Furthermore, patients who kept using the study medication did not seek to increase their dose of this or other pain-relieving medication over time, suggesting that the adjuvant use of cannabinoids in cancer-related pain could provide useful benefit.

Chemotherapy-induced peripheral neuropathy is a serious dose-limiting adverse effect associated with several commonly used chemotherapeutic agents, including taxanes, platinum agents and vinca alkaloids. In veterinary medicine, this particular side effect is rarely seen secondary to chemotherapy, and in the authors experience it has been seldom noted in large breed dogs with vinca alkaloid therapy. The preclinical data on this subject has shown that CBD prevents the development of paclitaxel-induced mechanical sensitivity in mice and that its clinical use may be enhanced by co-administration of low doses of THC.

Cannabis offers many opportunities for supportive and palliative care in cancer, and recent changes in the social climate and legalization of cannabis will hopefully facilitate and increase in the number of high-quality studies to more accurately weigh the risks and benefits of cannabis use and expand on dosing and administration methods. Currently, clinical evidence in populations with cancer is beginning to emerge to support the use of cannabis for treating chemotherapy-induced nausea and vomiting, loss of appetite, pain, and peripheral neuropathy. Also, data from other disease conditions suggest that cannabis could be used to potentially alleviate anxiety, depression, fatigue and sleep disorders. The more clinical information and data we collect (human and veterinary), the more guidance we will have when discussing cannabis with pet owners.

**Preclinical and Clinical Data**

Numerous studies have been published suggesting that endocannabinoids, phytocannabinoids as well synthetic cannabinoids have antineoplastic activity. There are at least 15 different tumors that have been evaluated pre-clinically exposing cannabinoids to multiple cell line xenografts. I have focused on the top three tumors including gliomas, breast cancer and colorectal cancer. Below is a detailed summary of the current knowledge of cannabinoids and cancer based on preclinical and clinical research for those three tumor types.

**Gliomas**

When normal cells transition to malignancy, they tend to develop more cannabinoid receptors which potentially makes them more sensitive to cannabis therapy. In many brain tumors, the endocannabinoid system is unregulated and appears to be under epigenetic control. In glial
tumors, initial *in vitro* studies show the synergy of both CBD and THC via multiple antineoplastic mechanisms including; inhibition of cell proliferation, modulation of the cell cycle, induction of reactive oxygen species, promotion of apoptosis, as well as modulation of extracellular signal-regulated kinase (ERK) and caspase activities. Interestingly, these effects were not observed with either compound individually. A systematic review of the literature on clinical and experimental trials on the antitumor effects of cannabinoid in gliomas revealed that in all 16 *in vivo* studies performed to date, there were statistically significant reductions of tumor volumes when compared to controls.

A clinical phase 1 pilot study evaluated nine patients with recurrent glioblastoma multiforme who received THC intra-tumorally. All the patients in the study failed previous treatments including surgery and radiation therapy. The delivery method was safe without psychoactive effects. Steroid administration was used to help with cerebral edema, and there was no apparent drug interaction between THC and steroids. Median survival from the beginning of cannabinoid administration was 24 weeks. Two of the patients survived for approximately 1 year. Due to the small sample size, it is truly unclear the effect of THC on survival time. Although intra-tumoral delivery of THC may allow for higher concentration of localized therapy in the brain, it is extremely invasive and therefore is not recommended in veterinary patients. GW pharmaceuticals set out to evaluate the combination of cannabinoids along with temozolomide therapy in a proof of concept study. It was a phase II, randomized, placebo-controlled clinical trial evaluating 21 patients with recurrent glioblastoma multiforme. Twelve patients received dose-intense temozolomide along with Sativex (1:1 THC:CBD oral spray) while nine patients were randomized to receive placebo plus standard of care. The results from this exploratory study showed that patients treated with combination therapy had an 83% one-year survival rate compared with 53% for patients in the placebo group (received standard of care). The median survival time for the combination group was 550 days (vs 369 days for the placebo group). Sativex was generally well tolerated.

**Breast Cancer**

Preclinical research demonstrated that cannabinoids produce an antitumor response in breast cancer. Dr. Cristina Sanchez and team in Madrid compared THC isolates to THC rich plant extract *in vitro*. Both formulations had antitumor properties, but THC rich plant extract was more potent than the THC isolate for the three different breast cancer subtypes (ER+/PR+, HER2+, and triple negative breast cancer lines). The combination of cannabinoids with estrogen receptor therapy, HER2 targeted therapy or with chemotherapy (cisplatin) produced additive antiproliferative response in cell culture, up to 25% more antitumor effect. However, the same did not hold true, *in vivo*. Specifically, for hormone sensitive breast cancer, THC’s antitumor effect in HER2-positive breast cancer was mediated by the CB2 receptor. CB2 receptor results in dimerization with HER2, and that bond has been associated with poor treatment outcome in breast cancer. When THC binds to the CB2 receptor, it breaks the CB2-HER2 dimer, which results in downstream signaling, causing tumor regression. A previous study, unexpectedly found that CBD (followed by CBG and CBC) acted as more potent inhibitor of cancer growth then THC. The efficacy of pure CBD and CBD-rich extract were confirmed to have antitumor effects *in vivo* in mice bearing highly invasive breast cancer xenografts. Furthermore, both compounds inhibited the formation of lung metastasis after inoculation of breast cancer cells.
The mechanism behind CBD’s inhibition of growth, invasion and metastasis of breast cancer cells is partially due to induction of ROS as well as downregulation of Id-1.  

Colorectal cancer

Previous data demonstrates endocannabinoids inhibit the proliferation of colorectal cancer cell lines via CB1 activation. Anandamide and other endocannabinoids are present throughout the gastrointestinal tract and have the ability to control cell proliferation. These endocannabinoids are transported into the cell and can be metabolized by cyclooxygenase 2 (COX-2). COX-2 is overexpressed in the majority of colorectal cancers which is associated with the promotion of tumorigenesis, angiogenesis and immune modulation. Anandamide significantly inhibited tumor cell growth and induce cell death (in a non-apoptotic fashion) in COX-2 expressing colorectal cell lines and had no effect on the low COX-2 expressing cell lines. Anandamide (or a similar acting phytocannabinoids; i.e., THC) may prove to be beneficial in treating tumors that have developed a resistance to apoptotic death. In fact, a subsequent study proved that THC induced apoptosis of colorectal cancer cells. THC treatment resulted in CB1-mediated inhibition of both RAS-MAPK/ERK and PI3K-AKT survival signaling cascades; two key cell survival pathways frequently deregulated in colorectal tumors.

Dosing and Product Selection in The Veterinary Cancer Patient

Until more research is performed and we can identify specific compounds within the plant that provide antitumor effects for specific tumors, it is recommended to consider products that are as diverse as possible. The key to dosing pets with THC is having patience and careful monitoring. The combination of both THC and CBD in formulations can enhance the antineoplastic effect due to the synergistic or additive effect, but also CBD neutralizes the adverse effects seen with the THC.

The author feels strongly about the importance of creating custom formulas for the individual patient based on the specific disease (including type of cancer) and the formula should be adjusted for the presence of comorbidities, breed, age, drug interaction, pet and client tolerability for side effects and ultimate goals (palliative vs definitive intent). The formula should contain as many cannabinoids as possible along with an antineoplastic profile of terpenes. If custom products are not available in your area, then consider combining multiple products, and it is recommended to mix and match from different manufacturers to allow for a wider spectrum of terpenes, flavonoids as well as minor cannabinoids. The concept is reinforced by studies demonstrating that cannabis full-spectrum plant extracts which contain multiple compounds had superior antineoplastic effect compared to pure isolate compounds. It should also be noted, due to the immunosuppressive effects of cannabis, it is recommended to avoid giving any cannabis product to a patient while undergoing antitumor immunotherapy as there is evidence to support that it can negatively affect response rates when used simultaneously.

Conclusion

Cannabinoids may play an integral role in treating veterinary cancer patients in both a definitive and palliative setting. Incorporating cannabis products (either marijuana or hemp-derived) may help palliatively by reducing adverse effects seen with chemotherapy-induced nausea, vomiting, inappetence, pain and other ailments. It may also work synergistically with conventional therapies (chemotherapy and radiation therapy) as part of an effort to increase the antitumor
therapeutic potential. Unfortunately, due to the legal constraints that exist for veterinarians surrounding cannabis, there are no published in vivo clinical trials evaluating the use of cannabinoid therapy in the veterinary patient. As cannabis is becoming legal in many states, pet owners are looking to veterinarians for advice and guidance on how to effectively and safely treat their pet. Once the legal landscape is less restrictive, it is imperative that we collaborate to collect data and perform well-prepared clinical trials to further establish the details involved in the antitumor activity of cannabinoids in veterinary medicine.

References


Objectives
- To understand the clinically relevant pathophysiology of CCD.
- To understand the action of the common pharmaceuticals to treat this condition.
- To understand integrative therapeutic approaches to treating CCD.
- To understand how integrative treatment can help maintain a good quality of life for the patient and their family.

Introduction
Canine Cognitive Dysfunction (CCD) is a common medical condition that occurs in dog over 8 years of age. It has been called the analog of human Alzheimer’s disease (AD). The disorder is characterized by slow deterioration of cognitive abilities associated with altered mentation and dementia. In older dogs this manifests as behavioural changes such as disorientation, house soiling, changes in sleeping patterns and decrease in interaction with other family members.1-4

The pathophysiology of both CCD and AD involves brain vascular disease and the accumulation and aggregation of amyloid-β peptide (Aβ). Aβ accumulates in the brains of dogs with CCD and people with AD. It forms plaques in the forebrain and causes neurodegeneration because it is a neurotoxic protein. Other pathological processes contribute to cognitive dysfunction as well. There are several misconceptions in the veterinary community regarding CCD in regard to prevalence, treatment and general pathophysiology and relevance of the disease.

Prevalence and Pathophysiology of CCD and AD
CCD is an age-related disorder similar to AD in humans and occurs in older dogs. Dr Elizabeth Head from the Center on Aging at the University of Kentucky stated “The extent of Aβ deposition in the canine brain is linked to the severity of the cognitive deficit”5 so it seems that the deposition of Aβ is a hallmark for AD as well as CCD. This makes the canine the best naturally occurring animal model to study human AD. It has been estimated that the prevalence of CCD is between 14% and 35% of the companion dog population. It is likely, however, that this is underestimated as often signs of CCD are simply dismissed as a normal function of canine aging.1-3 As with people with AD, the prevalence of CCD dramatically increases with age with a recent study showing 28% of dogs 11-12 years of age and 68% of dogs 15-16 years of age suffering from CCD.1-3

The pathophysiology of CCD and AD is complex and multifactorial. Pathologic similarities exist between the brains of people with AD and dogs with CCD. Ventricular dilatation, meningeal thickening, gliosis and cerebral vascular changes occur in both species. (See Table 1)
Table 1. Structural Brain Abnormalities

<table>
<thead>
<tr>
<th>Structural brain abnormalities identified grossly and on MRI in both people with AD and dogs with CCD</th>
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</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
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<tr>
<td>Infarcts</td>
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<tr>
<td>Microhemorrhage and occasionally macro hemorrhages</td>
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<tr>
<td>Cerebral atrophy</td>
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<tr>
<td>Meningeal thickening</td>
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<tr>
<td>Ventricular dilatation</td>
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<td>Gliosis</td>
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</table>

There are many forms of CCD and often they involve depletion of neurotransmitters or disruption of neuronal pathways. All cases of neurodegeneration and cognitive decline involve oxidative stress and mitochondrial dysfunction. Table 2 below summarizes the common pathologic brain abnormalities between CDD and AD.

Table 2. Pathologic Brain Abnormalities

<table>
<thead>
<tr>
<th>Pathologic brain abnormalities identified in both people with Alzheimer disease and dogs with canine cognitive dysfunction</th>
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</thead>
<tbody>
<tr>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Aβ accumulation</td>
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<tr>
<td>Oxidative brain damage</td>
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<tr>
<td>Neuronal mitochondrial dysfunction</td>
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<tr>
<td>Glutamate-mediated excitotoxic neuronal damage</td>
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<td>Impaired neuronal glucose metabolism</td>
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<td>Microglial dysfunction</td>
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<td>Astrocyte dysfunction</td>
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Mitochondrial dysfunction is central to the development and progression of AD / CCD. The mitochondria undergo functional and morphological changes (including gene expression) some of which is attributed to Aβ deposition. A mitochondrial-mediated impairment of autophagy potentiates Aβ deposition. When the cell is unable to catabolize proteins, this leads to proteins being deposited as plaques and an intraneuronal accumulation of neurofibrillary tangles or tau proteins. Tau proteins belong to a family of microtubular proteins that are located within the neurons. During neurodegenerative diseases, tau proteins undergo hyperphosphorylation and accumulate within the neurons interfering with neurotransmission. Normally the mitochondria have the ability to decrease the toxic effect of Aβ on cellular function, however this function diminishes as the mitochondria decline. The declining mitochondria have a decreased ability to generate cellular energy in the brain and the neurons affected by AD/CDD have an impaired ability to uptake and use glucose.

An imbalance of neurotransmitters in the brain has been documented in both AD and CCD. This imbalance may consist of damage and depletion of dopamine and altered cholinergic transmission; a disruption of the serotonergic pathway; noradrenergic transmitter disruption; and glutamate mediated excitotoxic neuronal damage. Excessive stimulation of the glutamate receptors (AMPA and NMDA receptors) contributes to neuronal ecotoxicity and death.

Astrocytes and microglia are the main immune cells in the CNS. Both of these cells function to reduce the production of Aβ and remove it before formation of senile plaques can occur. In early AD large numbers of microglia accumulate to slow down the deposition of Aβ. However, this deposition continues suggesting that the ability of the microglia to clear Aβ declines with age. The failure of the microglia to perform their function appears to be a direct result of the Aβ-induced inflammatory response. TNF α is a pro-inflammatory cytokine produced by the microglia which upregulates Aβ production so the microglia which were recruited to clean the Aβ protein from the brain end up promoting the deposition of plaques. Astrocytes and microglia are responsible for uncontrolled neuroinflammation that is associated with the progression of both AD and CDD.

**History, Clinical Signs, and Diagnosis**

The typical history for CCD is a dog over 8 years of age with a slowly progressive history of cognitive decline over the last several months. No association has been found with body size, breed or sex.

Four main clinical features are apparent:
1. disorientation in home and yard
2. changes in social interactions with human family members,
3. decline in house training,
4. alterations in sleep-wake cycles
A dog must have signs of dysfunction in one of the categories greater than once a week for 1 month of more to be considered for a diagnosis of CCD. Dogs with CCD often show anxiety, abnormal mentation, compulsive circling, absent or inappropriate response to visual stimuli, resistance to even minimal restraint, transient vestibular episodes and recent onset of seizure activity. Dr Gary Landsberg developed DISHAA test to screen for CD but need to remember it is a diagnosis of exclusion. Medical must be ruled out in order to make a definitive diagnosis of cognitive dysfunction syndrome. Medical problems may include, but are not limited to Cushing’s disease, parathyroid disorders, thyroid disorders, diabetes mellitus, chronic kidney disease, cancer, cardiovascular disease, incontinence, liver disease, musculoskeletal disease, dental disease, prostatic disease, and sensory loss.

Behavioral problems that look like CDS may include generalized anxiety, separation anxiety, fear-related aggression, pain-related aggression, noise or storm phobias, lack of housetraining, attention-seeking behaviors, and compulsive disorders. Often there will be concurrent behavioral and medical illness as medical and cognitive disorders may exacerbate existing, previously undiagnosed, behavior problems.

Treatment Overview

Remember that certain diseases increase progression of CD. There are many but some examples would be: diabetes, osteoarthritis, hypo/hyperthyroidism, obesity, Cushing’s disease, CRF, CHF, pancreatitis, cardiomyopathy, liver disease, seizures, stress and chronic infection. Major disease is a significant risk factor for cognitive decline and progression of CD. When treating diseases treat the entire patient and consider the impact any drug or herb you use will have on the disease progression. For example, a dog with neuropathic pain that is on gabapentin—consider switching to amantadine as it has the same effect (dopamine agonist) but has positive benefits for CD. Minocycline is also effective for neuropathic pain and it reduces microglial inflammation. Switch from phenobarbital to zonasimide and potassium bromide as it does not increase CD. Use propofol for anesthesia instead of gas, glycopyrrolate instead of atropine. Remove from patient all drugs that increase cognitive decline and find alternative therapies whenever possible. A partial list would include barbiturates, benzodiazepines, anticholinergics, chemotherapeutic agents, some flea and tick medications, some heartworm preventives, corticosteroids and gas anesthesia.

Other thoughts for other conditions:
- Excess pacing—use melatonin not benzodiazepines
- Atopy—avoid steroids
- Urinary incontinence—avoid PPA—use DES if not using herbsals
- URI—Avoid Benadryl use Cerenia or no sedating anti histamines as they don’t cross BBB

Remember that CD can have many different causes—inflammatory, vascular, toxic, nutritional, viral or drug induced and often involves depletion of neurotransmitters and disruptions of neural pathways. We are not sure which our patient is suffering from so a multimodal approach is best. All CD involves oxidative stress and mitochondrial dysfunction.
Other factors that increase CD progression→lack of exercise, lack of sensory input, excessive pacing, abnormal sleep patterns, blindness/deafness.

Nutritional factors that increase CD progression→High CHO diets, excessive calorie intake, hyperglycemia, obesity, omega 3 deficiencies, B vitamin deficiencies.

**Drugs**
Selegiline (Anipryl) is a selective and irreversible inhibitor of monoamine oxidase B. It may enhance dopamine and other catecholamines in the cortex and hippocampus and has been shown both in the laboratory and clinic to improve signs consistent with CDS in dogs. It may also be neuroprotective possibly by reducing free radical production and/or increasing enzymes that scavenge free radicals such as superoxide dismutase and catalase. It may take a few weeks to work and is not labeled in cats. Do not give with other SSRI or TCAs. Dose is 0.5-1 mg/kg q 24 hours in morning.

Amantadine at 3-5 mg/kg once daily may be helpful
NSAIDs may have some anti-inflammatory effects that are beneficial

Mitochondrial dysfunction is often associated with pore opening in the mitochondrial outer membrane called mitochondrial permeability transition port (MPTP). Supplements or drugs that close that pore are very effective in reducing mitochondrial damage and cell death and can reduce neurodegeneration. Apoaequorin is a supplement from Jellyfish that acts as an MPTP blocker and has been used in dogs and humans (Neutricks)

**Diet and Nutraceuticals**
In both human AD and CCD of dogs, diet and dietary supplements have a substantial impact on both the development and progression of cognitive decline. As stated above, high CHO diets, excessive calorie intake, hyperglycemia, obesity, omega 3 deficiencies, and B vitamin deficiencies will contribute to progression of CD. Nutrients that are often deficient in such individuals include B vitamins (e.g., B12), vitamin C, vitamin E, mitochondrial cofactors (e.g., L-carnitine, DL-a-lipoic acid), and carotenoids from green leafy vegetables. The addition of carotenoids and flavonoids as natural antioxidants from fruits, and particularly vegetables, has been associated with improvements in CCD. These antioxidants are much more than just antioxidant in their actions. They can also act as mitochondrial cofactors and increase cellular endogenous antioxidant upregulation.

Commercial diets for CCD include Hill’s B/D diet and Purina Neurocare. Both are high in MCT and have added carnitine, lipoic acid, long-chain omega-3 polyunsaturated fatty acids, vegetable-based carotenoids, vitamin E, and vitamin C. Homemade diets that are low in high glycemic carbohydrates and balanced with antioxidant and MCT oil seem to be effective.

MCTs are recommended in dogs with CCD, either as part of a formulated diet or a supplement, for several reasons. The AD/CCD brain has an impaired ability to use glucose, the brain’s main energy source; MCTs provide an alternative energy source for the brain in cognitively impaired patients. These ketone bodies are rapidly converted to glucose precursors through interactions of astrocytes and glial cells with the surrounding neurons. MCTs may also improve brain
mitochondrial activity and decrease the level of brain amyloid precursor protein. MCTs are commonly included in ketogenic diets for both people and dogs. In one study, a proprietary mix of MCTs was shown to improve cognitive function in aged beagle dogs when incorporated into commercial food at 5% of the dry matter.¹ Foods rich in MCTs are limited to only coconut and palm kernel oils having the right profile. Proponents of using these oils suggest using them at approximately 5% of the dry matter in the diet initially by either providing as top dressing on a commercial food or providing primarily coconut oil as a fat source in a properly formulated home-prepared diet. This amount of coconut or MCT oil addition provides between 10% and 5% of the caloric content of the diet respectively. This additional oil can begin to create imbalance in the diet regimen, particularly if extra treats are being given as well.

Omega 3 fatty acids particularly DHA can be helpful to reduce lipid peroxidation as well. Dose your combination fish oil at EPA + DHA at 100 mg/kg daily.

SAM-e, alpha lipoic acid, melatonin, and gingko are also possibilities. Senilife is a combination product that contains many of these nutraceuticals.

**Cognitive Enrichment and Physical Therapy**

Regular exercise, social interaction, new toys and increased stimulation has been shown to improve cognitive dysfunction in old dogs. Old dog socialization classes that include basic obedience, scent discrimination tasks and obstacle course target balance, proprioception and cognitive skills. Owners can be taught to challenge their dogs at home with hide and seek games and other physical interactions to serve both as preventive and after onset of CCD.

There is an inverse relationship between physical activity and β-amyloid deposits in mice brains.¹² Therefore, physical activity might be a useful strategy in therapeutic management by delaying loss of neuromusculoskeletal functioning and the usual complications of the dementia. Regular exercise should be promoted by veterinarians in the treatment of all dogs, especially those that are aged. Specialized exercise programs can be designed to safely exercise dogs after individual physiotherapy assessments are completed and take into account other orthopedic, neurological or medical problems. Swimming or underwater treadmill walking for example could be great modes of exercise that do not impart the same concussive forces on potentially arthritic joints of older animals.

**Chinese Herbs and Acupuncture**

The table below summarizes single herbs that have been used for the treatment of AD in humans. Some combination formulae such as Liu Wei Di Huang have been used for this as well. Sai Luo Tong formula, which consists of the bioactive components of the 3 herbal extracts from Panax ginseng, Ginkgo biloba, and Crocus sativa, showed significant improvement in AD patients in neurocognitive function, learning, and memory.¹ Other Chinese herbal formulas such as Fu Fang Dan Shen, Ba Wei Di Huang Wan, and Yi Gan San, have also shown encouraging data on treating cognitive and psychological symptoms in patients with dementia.¹ Acupuncture particularly electroacupuncture may be beneficial in treating patients with CCD. Acupuncture is thought to cause “enhanced neuronal glucose use (as verified by PET scans), decreased accumulation of Ab in the brain (via inhibition of the mTOR [mammalian target of rapamycin] pathway), increased production of neurotrophic factors
(such as brain-derived neurotrophic factor [BDNF]) with subsequent proliferation of neuronal stem cells, and protection from or reversal of synaptic loss and dendritic atrophy in the hippocampus. Overall, the various mechanisms that have been uncovered experimentally are thought to enhance brain neuroplasticity and improve cognitive function.”

Effective acupuncture points have included: Yin-Tang, LI-20, GV-20, GV-14, ST-36, HT-7, PC-6, CV-6, CV12, CV-17, SP-10, LI-4 and LIV-3

**Summary**

Remember the key is multi-modal!

<table>
<thead>
<tr>
<th>Mild cognitive Dysfunction</th>
<th>Diet</th>
<th>Drugs</th>
<th>Nutraceuticals</th>
<th>Exercise</th>
<th>Herbs</th>
<th>Acupuncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homemade with MCT or Bright Minds, Calorie Restriction, Veggies and fruits</td>
<td>Homemadem with MCT or Bright Minds, Calorie Restriction, Veggies and fruits</td>
<td>Selegiline or Neutricks</td>
<td>Fish oil Melatonin B vitamins Senilife,</td>
<td>½ hour of walking, swimming then ½ of interactive play and brushing and combing</td>
<td>Gingko, Green tea, Turmeric Rehmannia 6</td>
<td>As above monthly</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate to Severe Dysfunction</th>
<th>Diet</th>
<th>Drugs</th>
<th>Nutraceuticals</th>
<th>Exercise</th>
<th>Herbs</th>
<th>Acupuncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homemade with MCT or Neurocare, Calorie Restriction Veggies and fruits</td>
<td>Homemade with MCT or Neurocare, Calorie Restriction Veggies and fruits</td>
<td>Selegiline or Neutricks Aricept (Donepezil) perhaps</td>
<td>Fish oil Melatonin B vitamins Senilife, SAM-e</td>
<td>Aricept (Donepezil) perhaps</td>
<td>Depending on pattern</td>
<td>Weekly to every other week</td>
</tr>
</tbody>
</table>
### References


Rehabilitation for Hospice/Palliative Care Patients
Janice L Huntingford, DVM, DACVSMR, CVA, CVPP, MS-TCVM

Objectives
- To understand how a blend of physical and pharmaceutical medicine can be used for palliative patients.
- To understand how to improve and sustain function and comfort for palliative and hospice patients.

Introduction
Rehabilitation is most commonly prescribed for post-surgical or post injury patients or those with neurological disease. Patients in palliative or hospice care are those who are approaching the end of their lives and for whom aggressive therapy is not desired. Palliative care focuses on the comfort and wellbeing of the patient and the caregiver to maintain a good quality of life. Palliative rehabilitation focuses on long-term impairments, working within the patient’s illness dependent limitations to enable participation in as many activities of daily living (ADLs) as possible. Every hospice patient must be treated as an individual, with great care for underlying issues and have frequent re-evaluation as the disease changes and progresses.

Some of the aims of rehabilitation for palliative care patients are:
1. Pain control—both pharmaceutical and non-pharmaceutical
2. Restoration and or maintenance of function
3. Increase or improve mobility and activity
4. Prevent muscle atrophy and joint contracture
5. Improve circulation
6. Improve mental well being
7. Stabilize cognitive decline
8. Involve owners in care for their pets
9. Improve quality of life

Managing mobility can be challenging for the owners of hospice patients particularly if these patients are large and relatively immobile. The decline in mobility is also connected to many disease processes, such as the neuropathies seen in poorly regulated diabetes and the weakness associated with degenerative myelopathy. As death nears, a decline in mobility toward becoming recumbent or moribund is expected.

Four types of mobility issues are dealt with in hospice care.
1. Acute mobility associated with a serious disease (IVDD)
2. Chronic condition which has stabilized but is slowly progressive (DM, DJD, neuropathies)
3. Weakness associated with a specific disease (low potassium)
4. Decreased mobility due to approaching death

A thorough physical, orthopedic and neurological examination should be done on all hospice to patients to determine the extent of mobility issues as well as whether these impairments are likely to be permanent or temporary. Questions regarding activities of daily living and mobility
goals that the clients may have for these patients are of paramount importance. A mobility questionnaire and an activity questionnaire such as appears at the end of these notes could be used to determine mild, moderate or severe disability. The practitioner can then determine the appropriate course of action.

According to Shearer, regardless of the cause of the challenge there are 2 main areas of focus for all mobility-impaired pets. 3

1. Preservation of physical and emotional quality of life. Not addressing mobility problems can lead to pain, urinary tract infections, decubital ulcers, hygromas, pneumonia and decreased ROM.
2. Behavioral risks of boredom and anxiety including decline of cognitive dysfunction

Through applying basic care tips, such as treating pain in the pet, modifying and enhancing the environment, maintaining hygiene of the pet, offering mobility assistance, and performing simple therapy, many problems associated with mobility impairment can be prevented3.

Pain management is best treated with multi-modal therapy. Pharmaceuticals such as NSAIDs and gabapentin can be used with many of these patients but the primary DVM or a CVPP should be available to manage on going pain in these patients. Many of the rehabilitation modalities we will discuss below are aimed at pain management.

Environmental Modifications and Hygiene Assistance
Simple environmental modifications can have a positive effect on mobility impaired patients. Raising food and water dishes, providing multiple water dishes, putting down yoga mats, area rugs or carpet to reduce slipping, installing ramps and using baby gates to limit dangerous areas are all good ideas for household modifications. A foam bed or other soft area to lie on can cushion old joints and prevent hygromas and decubital ulcers.

A disabled pet’s hygiene should be checked every 2 hours or more frequently. Diapers, incontinence pads, pull ups and sanitary clipping can decrease amounts of urine and feces that is in contact with the pet’s skin. Cleaning with wash clothes and wipes around the genital areas, feet, face and perineum is key to comfort. A barrier cream or corn starch can be used to help prevent urine scald. Clients can also be taught how to express a pet’s bladder or do catheterization if necessary.

Assistive Devices
Harnesses, slings, booties, power socks, toe grips, braces and orthotics are all examples of assistive devices that can be used. In my experience Help Em up Harnesses are great for patients with hind end weakness and mobility challenges. Protective clothing such as is made by Dog Leggs can help prevent decubital ulcers and hygromas.

Sometimes carts and wheelchairs are also necessary allow pet who have hind end difficulty to still get around. Sometimes, these help emotionally with pets who are depressed when they are immobile. Simulated mobility can also be helpful for these pets. Owners can use wagons, strollers, bike trailers and baskets to allow the pet to enjoy the outdoors with his/her owner.
Rehabilitation for hospice care patients requires the practitioner to have a good knowledge of basic veterinary sciences and an in-depth knowledge of neurology, pain medicine and exercise physiology as well as additional training in rehabilitation. Often these patients are treated by a team involving a veterinarian, a technician, a physical therapist, a chiropractor, a massage therapist and an acupuncturist as well as an educated owner. Sometimes these modalities may be employed by one person or many.

The rehabilitation techniques generally employed for palliative care patients are: 2-6

1. Thermal modalities (cold/heat/therapeutic ultrasound)
2. Massage
3. ROM
4. Stretching
5. Chiropractic
6. Joint mobilization
7. Acupuncture
8. Myofascial trigger point release
9. Therapeutic laser
10. Electrical stimulation
11. Targeted pulsed electromagnetic field therapy (tPEMF)
12. Therapeutic exercise.

A few of these techniques will be discussed below. For more information consult one of the textbooks on rehabilitation therapy.

**Manual Therapies 2-6**

Massage is soft tissue massage and soft tissue mobilization. Massage can decrease excessive tissue tension by aiding in removal of chemical substances in soft tissue that activate chemical nociceptors. Soft tissue massage can also, by the Gate Theory, reduce pain by stimulating large rapidly conduction fibers, selectively closing the gate against smaller pain fiber input.

Joint mobilizations - a manual technique used to assess a joint and improve its movement (arthrokinematics). Joint mobilizations improve joint lubrication, modulate mechanoreceptors, and decrease sensory input thus relieving pain. Therapeutic glides are ranked Grade I to V using the Maitland Mobilization Scale.

Passive range of motion (PROM) is defined as therapist assisted placement of the joint through its normal range of motion. These exercises are very important for neurological patients and post-surgical patients to reduce pain and edema, maintain functional range of motion and improve joint lubrication. Neurologic patients are at risk of contractures of tendons and ligaments. PROM mitigates this condition. In neurological patients PROM works best after heating the tissue with hot packs to warm up the muscles. Do each joint of the affected limb in flexion and extension approximately 10 times before entire limb is flexed. This avoids pain and spasm.
Many manual therapies can be taught to owners, so that therapy can be done in the pet’s home environment. This is also beneficial for strengthening the human-animal bond and allows the owner to be part of the treatment team.

**Laser**

LASER is Light Amplification by Stimulated Emission of Radiation. By definition, a laser must be collimated and monochromatic. Penetration of laser energy is determined by the wavelength, and many wavelengths are patented. The physiological effects of laser stimulation include accelerated cell division via mitochondrial stimulation, increased leukocyte phagocytosis, stimulation of fibroblast production, enhanced synthesis of ATP, and angiogenesis. Treatment with laser is indicated for pain management, control of inflammation, and tissue healing.

**Pulsed Electromagnetic Field Therapy (PEMF)**

PEMF has been used in humans in Europe for a number of years and by equine practitioners in North America. Its use in small animals has increased with the development of affordable and portable field devices. Mats containing coils that generate the field or portable loop devices are most commonly used. PEMF has been used to reduce pain, inflammation, the effects of stress on the body, platelet adhesion, improve circulation, and help with cell regeneration. It is used in non-healing fractures to accelerate bone repair and improve wound healing. With the proper field intensity and frequency, treatment with PEMF appears to be disease-modifying. The stimulation of TGFβ may be a mechanism by which PEMF favorably affects cartilage homeostasis. Through calcium-calmodulin-dependent pathways, PEMF may also increase nitric oxide activity. A study with rats showed the animals receiving PEMF exposure, had an increase in tensile strength of up to 69% at the repair site of the rat Achilles’ tendon at 3 weeks after transection and repair compared with non-stimulated control animals. Further studies exist for this modality.

**Exercises**

*Rhythmic stabilization—Weight shifting* is used to increase weight bearing and balance. Weight shifting should be done while the dog is standing. Place your thumbs over the dog’s pelvis bones and your hands down their sides. Slowly sway side-to-side making sure both legs are weight bearing. Do not use enough force to cause the dog to lose his balance.

*Assisted standing*

This exercise is important to build and maintain muscles needed for balance, proprioception, and locomotion. These muscles quickly become atrophied if not used as frequently occurs with paresis. A therapy ball, rolled towel, cushion, foam roller or other device (depending on the size of the dog) is placed under the dog’s abdomen.

*Proprioceptive Neurological Facilitation (PNF) patterns*

PNF patterns mimic the dog’s running motions and other normal functions of daily living (scratching, digging). PNF patterns help with ROM, stimulate the neural pathways and help redevelop new axonal pathways for movement. To perform a PNF pattern for running, lay the dog on his side and mimic the running pattern. The therapist should use one hand to mimic the ground contact at the appropriate part of the gait cycle.

*Tapping*
Tapping over a muscle belly can elicit muscle contractions and stimulate the neural receptors (Muscle Spindle Fibers and Golgi Tendon Organs) in muscle and tendon. This should be done for 3 to 5 minutes a few times a day as part of the nursing care for animals recovering from paralysis.

**Tensor Bandaging, Thundershirts, or Snuglis**

The principle of using tensor bandages or thunder shirts for neurological dogs is to connect the front and back end of the dog and create body awareness. The slight pressure that the wrap puts on the body helps with neurological co-ordination. Many of these dogs can wear such shirts or wraps throughout recovery.

**Tactile Stimulation**

This is beneficial to provide stimulation to the superficial receptors in the patient’s skin. Brushing the dog, tapping, pinching, or using a vibrator provides additional sensory stimulation to increase input into the nervous system.

**Mental Stimulation of Neurological Patients**

The therapist should be aware that the patient’s mental state plays a big role in recovery. Dogs can become depressed if they cannot move, get outside or interact with their family. Dogs can be mentally stimulated by taking them outside or “walks” in a wagon or stroller, moving them around the house frequently if they are unable to move, giving them new treats or squeaky toys. Anything that can engage the patient will be mentally stimulating and speed recovery.

**References**

Box 1
Mobility questionnaire

Owners should assign a grade to each question based on the rating scale.
Rating System: 0 = none; 1 = mild; 2 = moderate; 3 = severe

- Difficulty with walking: 0, 1, 2, 3
- Difficulty to move from lying down to stand: 0, 1, 2, 3
- Difficulty to move from stand to lying down: 0, 1, 2, 3
- Difficulty to move from sit to stand: 0, 1, 2, 3
- Difficulty to move from stand to sit: 0, 1, 2, 3
- Difficulty to hold posture to defecate: 0, 1, 2, 3
- Difficulty to hold posture to urinate: 0, 1, 2, 3
- Difficulty ascending stairs: 0, 1, 2, 3
- Difficulty descending stairs: 0, 1, 2, 3
- Difficulty with jumping: 0, 1, 2, 3
- Difficulty with running: 0, 1, 2, 3
- Difficulty with climbing inclines: 0, 1, 2, 3
- Difficulty with losing weight: 0, 1, 2, 3
- Difficulty with gaining weight: 0, 1, 2, 3
- Difficulty with endurance: 0, 1, 2, 3
<table>
<thead>
<tr>
<th>Box 2</th>
<th>Questionnaire on activities of daily living</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Is the pet an indoor or outdoor pet?</td>
</tr>
<tr>
<td></td>
<td>What type of terrain is outside? Rugged, inclines, flat?</td>
</tr>
<tr>
<td></td>
<td>What type of flooring is in the house?</td>
</tr>
<tr>
<td></td>
<td>Does the pet have steps to climb? How many and where?</td>
</tr>
<tr>
<td></td>
<td>Does the pet sleep in the pet owner's bed?</td>
</tr>
<tr>
<td></td>
<td>Does the pet travel in the car?</td>
</tr>
<tr>
<td></td>
<td>What activities does the pet participate in?</td>
</tr>
</tbody>
</table>
Geriatric Rehabilitation
Janice L. Huntingford, DVM, DACVSMR, CVA, CVPP, MS-TCVM

Objectives
- To identify the common geriatric problems that face an integrative practitioner.
- To learn common and easy rehabilitation techniques that can be quickly implemented in any small animal practice.
- To understand how to integrate modalities, exercises and nutrition to improve QOL of our geriatric patients.

Introduction
Gerontology is the study of aging. The aging process is not a disease process but a decline in all body systems that increases the likelihood of developing a disease. Common medical conditions we see in our patients include degenerative joint disease, neurological disease, neoplasia, obesity, sarcopenia, and endocrine disease. A comprehensive physical examination, pain exam, nutritional assessment, and a thorough orthopedic and neurological examination including blood and urine testing is important to identify concurrent disease and assess how the patient will respond to rehabilitation therapy. Rehabilitation aims to improve function and mobility and address required medical and nursing care. Quality of life issues are paramount when dealing with geriatric patients.

Veterinary professionals consider dogs to be senior at an earlier age than owners do. Since the size of our patients is variable, a dog is considered senior when reaching 75% of his or her life expectancy. A giant breed dog would be geriatric at around 7 years, whereas a chihuahua may be considered a senior at 11 or 12. Cats should be considered geriatric at the age of 12 or greater.¹

Our geriatric patients can be divided into 3 categories:
1. Old but healthy—few age-related changes
2. Old with subclinical organ dysfunction
3. Old with overt disease—often multiple problems

Geriatric Changes that affect our patients and may affect our PT programs¹
- Cardiopulmonary changes
  - Decreased cardiac output
  - Decreased elasticity of pulmonary tissue
  - Decreased cough reflex
  - GOLPP
  - CHF and exercise intolerance
- Metabolic changes
  - Decreased metabolic rate
  - Protein requirements are increased
  - Obesity is common
- Immune changes
  - Maybe immunocompromised
- Slow wound healing

- Neurological changes
  - Decline of proprioception and co-ordination
  - Ataxia if decreased MS strength
  - Slower nerve conduction
  - Vision loss
  - Hearing loss
  - Cognitive dysfunction
  - Vestibular issues

- Musculoskeletal changes
  - Sarcopenia
  - Cartilage thinning
  - Bones more brittle due to fat infiltration
  - Lactic acid builds faster, and glycogen depletes faster
  - Type II muscle fibers decrease by 25%
  - Arthritis is common

Pharmaceutical, Nutraceutical, and Dietary Therapy
These subjects are well covered elsewhere but it is important to note that geriatrics require lower doses of many pharmaceuticals due to organ dysfunction and metabolic changes. Nutraceuticals such as Omega 3 fatty acids, Undenatured Collagen Type 2, Pentosan, Glucosamine, and Avocado Soy Unsaponifiables are all important to help control pain in geriatrics.

Environmental Modifications and Assistive Devices\textsuperscript{2,3}
Simple environmental modifications can have a positive effect on old painful patients. Raising food and water dishes, putting down yoga mats, area rugs or carpet to reduce slipping, installing ramps and using baby gates to limit dangerous areas are all good ideas for household modifications. A foam bed or other soft area to lie on can cushion old joints. Harnesses, slings, booties, power socks, braces and orthotics are all examples of assistive devices that can be used. Sometimes carts and wheelchairs are also necessary.

Physical Rehabilitation\textsuperscript{2-4}
The goals of rehabilitation include the restoration, maintenance and promotion of optimal function and quality of life as they relate to movement disorders. Health benefits of rehabilitation therapy for geriatrics include:
1. Improved daily function
2. Reduced pain
3. Improved strength
4. Better oxygen transport and capacity
5. Improved joint mobility
6. Bond building
7. Relaxation
Most rehabilitation therapeutics involves manual therapies including joint mobilizations, and therapeutic exercises. Equipment used on a regular basis in veterinary rehabilitation includes physio balls, therapy bands, rocker/wobble boards, cavaletti poles and land treadmills.

**Hydrotherapy** equipment can include pools, resistance pools and underwater treadmills. Modalities such as hot and cold therapy, laser, electrical stimulation, shock wave therapy and therapeutic ultrasound can also be used. Regenerative medicine with platelet rich plasma and stem cells is now also a part of rehabilitation and pain management.

**Thermal Therapy** - The effects of thermotherapy are vasodilation with secondary increased local circulation, decreased pain, relaxed muscle tone, reduced muscle spasm, increased tissue extensibility, increased cellular metabolism, and increased local tissue oxygenation. Heat is generally used to reduce pain from arthritis, trigger points and muscle spasms, and to prepare tissues for exercise or stretching.

**Cryotherapy** can be applied via ice bath, ice massage, ice pack, vapocoolant gel, or circulating ice compression units. The beneficial effects of cryotherapy include vasoconstriction; reduced cellular metabolism; decreased nerve conduction velocity, and decreased production of pain mediators, leading to analgesia; reduction of edema and decreased muscle spasm.

**Manual Therapies**

**Massage** is soft tissue massage and soft tissue mobilization. Massage can decrease excessive tissue tension by aiding in removal of chemical substances in soft tissue that activate chemical nociceptors. Soft tissue massage can also, by the Gate Theory, reduce pain by stimulating large rapidly conduction fibers, selectively closing the gate against smaller pain fiber input.

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Many manual therapies can be taught to owners, so that therapy can be done in the pet’s home environment. This is also beneficial for strengthening the human-animal bond and allows the owner to be part of the treatment team.

**Laser**
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**Therapeutic Exercises**

Therapeutic exercise contributes to pain management through Exercise Induced Hypoalgesia (EIH) which results from activation of the opioid system with beta-endorphin release from the pituitary. It is also believed that exercise can activate large afferents and that mechanical hypoalgesia is induced by repeated low load exercises regardless of exercise mode. Exercises are used for stretching, strengthening, balance, proprioception, flexibility, endurance and muscle re-education.

**Exercises for Geriatrics**

*Rhythmic stabilization—Weight shifting* is used to increase weight bearing and balance. Weight shifting should be done while the dog is standing. Place your thumbs over the dog’s pelvis bones and your hands down their sides. Slowly sway side-to-side making sure both legs are weight bearing. Do not use enough force to cause the dog to lose his balance.

*Trampoline, cushions, Air mattress*—These uneven surfaces help improve weight bearing as well as proprioception. The exercise can be done in many ways. Start with 2 paws on the uneven surface and move the patient around it then have the patient walk across the surface. Progress to standing on the surface while the therapist applies gentle pressure to each hip or shoulder in a back and forth motion to challenge balance. Be sure to use a harness to control the patient so he or she does not lose balance and fall.

*Cavaletti Course*—This helps with proprioception, strengthening and gait retraining. Pole heights can vary while the distance is case dependent, but the poles are evenly placed apart and the animal walks over the poles very slowly. The slow pace allows the animal to step over the poles.
one paw at a time and recognize their paw location. The goal is to walk over the poles without touching them. Generally, start with 5 minutes twice daily.

**Balance Boards or Balance Discs**- These are used for balance, proprioception, and strengthening legs. Place the weakest legs on the board or all 4 paws. Control the patient with a harness and rock the board back and forth. Balance discs or BOSU balls can also be used for this. To improve balance have the dog take treats from different location on the board so they will have to walk, stretch and not lose their balance. The goal is for the dog to maintain balance despite movement of the board or disc. Start with 3 to 5 minutes twice daily and progress as the patient strengthens. For home exercises, cushions can be used

**Weave Cones**— These are generally used to improve proprioception and increase core strength. Objects, normally 6-8, are lined up about 1-1/2 to 3 feet apart (depending on patient size) and the dog is weaved in and out of the objects. According to McCauley et al., odd number of cones work on proprioception and flexibility on one side only, even numbers work both sided. The dog needs to learn to pivot sharply at the end of the pattern. Normally, this exercise lasts about 5 minutes twice a day.

**Figure eights**
This exercise is also done with cones and is used to increase balance, coordination, spinal range of motion and for weight shifting. It is completed by walking the outline of the number “8” around 2 cones. The figure eight normally is twice the height of the dog and the activity should be performed a slow speed. The slow speed allows for an increase in spinal range of motion. This should be done a few minutes at a time to avoid dizziness.

**Backwards walking**
This exercise helps strengthen the pelvic legs (particularly the hamstring muscle group), increase balance, coordination and proprioception. This exercise is easier to start with the dog parallel to a wall, a sofa or anything straight. The therapist should hold a treat at his or her chest level and walk toward the dog saying “Back.” Most dogs will try to turn while they are learning the walk backwards; thus, it is important to reward the dog when he takes a step backwards. Another way of training this is to have a couch parallel to the wall just far enough from the wall that the dog cannot turn around. Lure the dog in forward with a treat, then say “Back” and encourage him to walk backwards for another treat. This is an important exercise to teach all dogs and puppies as at some time in their lives, all dogs will need more hindlimb strength. A backwards walking session should be 5 to 10 minutes twice daily.

**References**

**Further Reading**
Objectives

- To define glyphosate, introduce the history of this herbicide compound, and understand the sources and common uses and types of crops most commonly affected, etc.
- To understand the actions of glyphosate on plants and its effects on the nutritive value of plants.
- To understand the vast health impacts of glyphosate toxicity within the body; the carcinogenic affects and damage to gut integrity, kidney function, microbiome depletion, etc.

What is Glyphosate?

Glyphosate is an organophosphorous compound which acts to inhibit specific plant enzymes. This compound was discovered to be an herbicide in 1970 by Monsanto chemist, John E Franz, and it was brought to market for agricultural use in 1974 under the trade name RoundUp. Monsanto’s final US patents ended in 2000, and now there are over 750 products containing glyphosate for sale in the United States. Glyphosate is used as a broad-spectrum systemic herbicide and crop desiccant. It is most often recognized as an herbicide, but is also used to regulate plant growth, and to ripen specific crops as a crop desiccant. In addition to agricultural use, it is now used in forestry, on lawns, gardens, and industrial areas. Some glyphosate products are even used to control aquatic plants.

Farmers quickly adopted glyphosate for agricultural use, especially after Monsanto introduced glyphosate-resistant RoundUp ready crops, enabling farmers to kill weeds without killing their crops. By 2007, glyphosate was the most commonly used herbicide in the US agricultural sector and the second-most in home and garden, government, industry, and commercial applications. In fact, over the past 40 years we have seen a worldwide 100-fold increase in the frequency and volume of application of glyphosate-based herbicides (GBH), and this trend is expected to continue. Part of the reason for the massive volume increases being used is due to the global emergence and spread of glyphosate-resistant weeds, requiring greater application to maintain effectiveness. Glyphosate is the single most widespread herbicide used worldwide, with reports of detectable levels in 70% of the global rainfall.

How Does Glyphosate Work?

Glyphosate is a non-selective herbicide, meaning it will kill most plants. It prevents the plants from making certain proteins that are needed for plant growth. Specifically, it inhibits the synthesis of 3 aromatic amino acids: tyrosine, tryptophan and phenylalanine. It is therefore only effective on actively growing plants and is not effective as a pre-emergence herbicide. An increasing number of crops have been genetically engineered to be tolerant of glyphosate, with corn and soy being most recognized as common GMO crops. Indeed, the first genetically modified/genetically engineered crop to be resistant to glyphosate was the Roundup ready soybean.

The action of glyphosate to inhibit protein synthesis prevents a specific enzyme pathway that is necessary for plants and notably also for some microorganisms. In other words, glyphosate has
herbicide action on plants and an antibiotic action on soil microorganisms. This also means that 
glyphosate is currently the most common and widespread antibiotic used globally.

Glyphosate is now used on numerous agricultural crops, many that are genetically modified and 
many that are not. Common GMO/GME crops include alfalfa, apples, canola, corn, cotton, 
papaya, potatoes, soybeans, squash, and sugar beets. These crops were genetically engineered to 
be tolerant to glyphosate. Genetic engineering involves biotechnology that is used to alter the 
plant biology. In this way, the genes in plants are turned on or off, or in some cases they are 
completely removed and replaced with different genes. The intended purpose for using genetic 
engineering was to create crops that were not only tolerant to herbicides, but also more resistant 
to insects and more tolerant to droughts.

However, glyphosate is also applied to many more types of crops that are not genetically 
gineered. In this scenario, glyphosate is being used as a crop desiccant to allow for timing of 
harvesting and to hasten the ripening of some crops when harvested. Because these non-GMO 
crops are sprayed with glyphosate at the end of harvest, these foods have higher levels of 
glyphosate than do the GMO crops which are sprayed prior to growth. Common non-GMO 
crops being sprayed with glyphosate include oats, wheat, barley, rye, legumes, chickpeas, beans, 
potatoes, and peas.

Glyphosate Affects Plant Nutrients
Glyphosate decreases the nutritional quality of plants, therefore reducing the ability of plants to 
offer "food medicine." We now understand that this chemical is blocking the ability of the 
environment, i.e. the microbes and the soil, to create alkaloids in plants. Alkaloids are organic 
nitrogen compounds of plant origin that have diverse and important physiological effects on 
humans and animals. These components contribute to the “medicinal properties” in food. In fact, 
alkaloids possess a variety of pharmacological potential including effects that are analgesic, 
anticancer, anti-hyper glycemic, antiarrhythmic, antibacterial, and neuromodulatory.

Toxic Effects and Levels of Exposure
Although the most recent classification listed by WHO places glyphosate as a probable 
carcinogen, there are several known litigation cases (against Monsanto) which have awarded 
settlements to human cancer victims with high exposure levels to glyphosate. Routes of exposure 
to glyphosate toxicity include ingestion, absorption into the skin or eyes, and inhalation. 
Monsanto’s own studies have shown that farmers who get glyphosate on their skin have 10 times 
the levels in their bodies as those who use gloves.

The University of California San Diego school of medicine performed a study demonstrating the 
association between the glyphosate herbicide and negative effects upon the human liver. Other 
studies in humans have linked herbicide exposure to cancers of the colon, sinus, lung, prostate 
and ovary, lymphomas, and multiple myelomas.

The majority of glyphosate is excreted in urine and feces, and some can be measured in hair or 
skin samples. In the American population, 86% of people tested have detectable levels of 
glyphosate in their urine and their levels are an average of 38 times higher than 20 years ago. As 
alarming as these levels of growing exposure are for humans, we now have information showing
the dramatically higher exposure rates for dogs and other animals. Researches and independent laboratories, such as HRI (Health Research Institute) have found glyphosate levels in the urine of dogs in the United States to be an average of 30 times higher than their human counterparts, and cats at an average of 16 times higher than people. Horses have been found to have glyphosate levels that measure close to that of dogs.

Although foods are a large source of glyphosate exposure for dogs and other animals, it appears that dogs are getting a significant exposure from the environment as well. Many dogs spend quite a bit of time outside - walking, playing and rolling in the grass, lawns and other areas that are sprayed with Roundup and similar weed killers. This can add up to a lot of skin and contact exposure. Furthermore, dogs often spend a lot of time sniffing in areas of grass, other plants and along the ground, and therefore are likely to get a high level of sinus and inhalation exposure.

The National Cancer Institute (NCI) has reported that dogs are twice as likely to develop lymphoma if Roundup is applied on their properties 4 or more times a year. The Tufts University school of veterinary medicine reported that exposure to lawn chemicals raises the risk of canine malignant lymphoma by more than 70%, and veterinary studies at Purdue University have found links to bladder cancer in dogs.

The toxic actions of glyphosate on mucous membranes leads to numerous health issues. Glyphosate destroys the cellular matrix of linings that it interfaces with inside the body. The gut is dramatically affected with destruction of the intelligent barrier, leading to hyperpermeability and leaky gut syndrome. Leaky gut syndrome is known to be a root cause of most or diseases and chronic inflammatory conditions. Additionally, glyphosate in the body also interfere with the function of the kidney tubules (diminishing the ability to excrete wastes effectively) and affect the nasal membranes and sinus tissues.

Numerous studies have shown that the combination or interaction inside the gut between glyphosate and gliadin (the breakdown product of gluten) causes an exponential toxic synergy which markedly increases hyperpermeability in the gut lining, resulting in gastrointestinal inflammation and compromise, as well as chronic systemic inflammation and reactive immune response. Understanding the effects caused by the combination of gluten and glyphosate establishes an explanation for the significant increase in gluten sensitivity issues affecting the health of both animals and people over the last few decades. Although glyphosate was brought to market (as Round Up) in 1974, its widespread use became more common in the 1990s, when gluten reactivity was also beginning to be commonly recognized. The marked hyperpermeability caused in the gut allows for additional toxins (beyond glyphosate) to gain systemic access into the body too. Furthermore, the destruction of the gut barrier leads to a significant disruption in the microbiome, which impacts the immune system, gut health, brain health, and overall body systems.

References
2. Trends in glyphosate herbicide use in the United States and globally, Charles M. Benbrook Email author, Environmental Sciences Europe Bridging Science and Regulation at the Regional and European Level 2016 28:3


Objectives

- To develop awareness regarding current levels of glyphosate exposure for humans, pets, and other animals.
- To learn about research that has determined specific measurement levels of glyphosate in foods, pet foods, human urine, and animal urine and to have knowledge of resources available for testing animals and people.
- To discover options for minimizing the exposure to glyphosate and to minimize the effects of damage in the body.

Glyphosate Levels in Foods

Most pet foods have significantly high levels of glyphosate and one bowl of dry kibble dog food has an average of 400 ppb compared to a raw meat meal measuring at an average of only 1 ppb. In other words, a dog eating an average quality kibble will get 400x the level of glyphosates in one meal compared to a dog eating a high-quality raw food. This is a remarkable difference in the level of exposure to this particular toxin for pets eating a heavily processed diet compared with a fresh food diet. Furthermore, as non-GMO crops are known to contain higher levels of glyphosate than the GMO crops, this creates a significant concern regarding the levels of glyphosate in (non-organic) foods such as oats, lentils, chickpeas, beans, peas, and potatoes.

Interestingly, these foods are typically included in rather high portions in the grain-free varieties of pet food. Understanding that glyphosate is a notable offender to gut health, causing gut permeability and microbiome disruption, suggests there may be a link between the high levels of glyphosate in grain-free dog foods and the improper absorption and utilization of the amino acid taurine, in addition to many other issues. A recent white paper, titled Dilated Cardiomyopathy and Diet in Dogs, reports the taurine issue is “a multifactorial problem related to the change in the bacterial flora of the gut, perhaps from high percentages of legumes in the diet which can change the taurine absorption and alter its digestibility and bioavailability.”

Additionally, the writers state that problems may be related to the manufacturing processes of the protein sources. Thermal (high heat) processing of proteins causes altered digestion, creates pro-inflammatory mediators, and leads to a shift in microbiome bacteria. This type of shift can promote an intestinal environment that favors increased numbers of taurine-degrading bacteria. There are many issues interacting here, but glyphosate levels may be one of the important factors.

Glyphosate Testing

The Health Research Institute (www.hrilabs.org) is an independent, non-profit laboratory and research program which performs quality testing techniques and offers direct-to-consumer testing of people and animals. The HRI lab performs high complexity testing with limits of detection (LOD) much more sensitive than most government and commercial labs. HRI has documented levels tested in numerous foods and commercial pet foods, in addition to testing urine, feces, and hair samples of humans, dogs, cats, horses, and farm animals.
HRI has tested organic foods and the urine of humans consuming organic foods vs. nonorganic foods and has shown that 95% of foods labeled organic do not contain any detectable levels of glyphosate. About 5% of foods labeled organic do contain traces of glyphosate, which happens as the result of several factors including: drift from nearby farms, co-mingling in transport, packaging or processing, and mislabeling or fraud.

**Minimizing the Damaging Effects of Glyphosate or Bind/Detox Glyphosate Accumulation**

One measure of protection from glyphosate and other toxins is to eat organic and clean foods as much possible. It can be difficult to find organic foods created for pets and/or difficult for most pet owners to afford these types of diets. Fortunately, simply feeding a raw food or meat-based diet is one sure way to significantly decrease pet’s exposure to glyphosate as well as other toxins.

However, even with dramatic reductions of glyphosate levels in the food, it is been shown that dogs can have a high rate of environmental exposure, due to their typical levels of physical interaction with grass, plants and other substrates outdoors. There are a few notable nutraceutical products to help combat the damage caused in the body by consistent exposure to glyphosate and other toxins in food and the environment.

ION BIOME Gut Health is unique and natural product which offers the ability to restore damage from glyphosate disruption in the gut and other mucous membrane linings (i.e. kidney tubules and nasal/sinus tissues). This product was created by Zach Bush, M.D., and was initially labeled RESTORE on the human product and LUMA-PET on the dog & cat product. Both products have been recently relabeled as ION BIOME Gut Health. This product is a liquid supplement (similar flavor and appearance to water) that uses soil-based, carbon-based redox molecules to help restore the communication between mitochondria, cells and bacteria. Specifically, Restore (ION BIOME Gut Health) was developed to help support glyphosate detoxification and repair gut permeability, additionally fostering a microbiome shift back into better balance.

Another natural product which can address the damages and support detoxification from glyphosate and other toxins is called Clinoptilolite. This natural zeolite, found in volcanic rocks, works much like a charcoal to bind toxins and remove their accumulations. Look for more information on this unique substance in the next presentation.

**References**

2. Environmental Pollution, Volume 243, Part B, 2018, Pages 1113-1118, ISSN 0269-7491,
Detoxification (And More) With Zeolite Clinoptilolite
Katie B. Kangas, DVM, CVA, CVCP

Objectives

- To define zeolites and gain an understanding of how the unique crystalline structure provides detoxifying effects.
- To discover the wide use of zeolite clinoptilolite applications in humans, animals, and the food animal industry.
- To learn about the antioxidant, inflammatory, anti-cancer, and immunomodulatory properties of micronized zeolite clinoptilolite.
- To understand the effects of zeolite clinoptilolite on the gastrointestinal tract.

What Are Zeolites?
Zeolite is a collective name for minerals and chemical compounds within the group of silicates. Natural zeolites are crystalline compounds of volcanic origin with microporous structures. The arrangement of the atoms affects the water-binding capacities in the zeolite minerals, like a “rock-sponge.” The term zeolite was coined by a Swedish mineralogist and chemist in 1756. The name is derived from the Greek language zeo (to boil) and lithos (stone) meaning “boiling stone.” Zeolites consist mainly of alumino-silicates with SiO₄ and AlO₄ structures connected by shared oxygen atoms. This grid structure of zeolites can act as inorganic cation-exchanger, adsorbent, and reservoir for metal-catalyzed reactions.

These properties have earned them extensive industrial applications. Zeolite’s use in medicine, especially micronized natural zeolite-clinoptilolite (ZC), is a relatively new subject of interest. However, numerous studies have demonstrated that natural zeolite-clinoptilolite (ZC) exerts immunostimulatory effects, modulates anti- and pro-inflammatory mechanisms, and potential use as an adjuvant in anticancer therapy. Other researchers describe zeolite’s capability to adsorb glucose, antidiarrheic effects, and its strong antioxidant activity.

Clinoptilolite is one of the most abundant natural zeolites, widely distributed throughout the world and used for its ion exchange and adsorbent properties. Because it has remarkable and unique ion-exchange properties in water, it has been employed for various medical, industrial and environmental uses, especially for sequestration of toxic pollutants from industrial wastes. At present, natural zeolite clinoptilolite (ZC) is recognized to have many positive effects due to the capacity to adsorb and therefore remove harmful substances like heavy metals, ammonia, or other small molecules in the gastrointestinal tract of humans and animals.

It is important to mention that this positive impact can improve through modifications of ZC due to micronization of ZC (M-ZC) or tribomechanical activation of ZC (TMAZ), or double tribomechanical activation of ZC (PMA-ZC) - known as Panaceo Micro Activation. This recently developed PMA (Panaceo Micro Activation) technology is a special micronization process that contributes to an increase of the surface charge and the cation exchange of the individual particles, improving the overall therapeutic performance of ZC.

The oral application of specific PMA-zeolite in human clinical trials suggest positive impacts on the intestinal tract as it supports intestinal wall integrity. Preclinical data also suggest a positive
impact on the intestinal microbiome. This connection is especially impactful understanding the role of microbiome in relation to chronic neurological disorders; i.e. the Gut-Brain Axis. The modified forms of ZC (M-ZC, TMAZ, PMA) are being highlighted for therapeutic aspects for overall well-being and as a potential preventive agent in Alzheimer disease and other neurological disorders. Mounting clinical research on ZC and its modified forms show promise as a potential agent for promoting human brain health and overall well-being.

**Detoxifying Effects**

Most of the clinical positive effects of ZC and modified ZC have been attributed to its reversible ion exchange and adsorption capacity. The first detoxifying effects of ZC in a modified form were observed in mouse models. In lead poisoned mice, the modified ZC reduced the accumulation of lead in the intestine by more than 70% with a protective effect on the brain tissue. In rats intoxicated with organophosphates, ZC was effective in restoring cholinesterase activity at the system level.

Some reports show that ZC in the intestine may bind to the organophosphate through a dipole–dipole interaction and therefore can be excreted in the feces. As a result, the role of ZC has been recognized in veterinary medicine where it has been seen to improve the physical fitness and efficiency of farm animals by removing numerous harmful substances from the body including ammonia, nitrates, mycotoxins, and other toxins. The presence of high levels of ammonia in the environment is the result of intensive agricultural industries which pour these pollutants into the environment, contaminating groundwater resources. ZC has shown a high ability to eliminate ammonia from the environment, especially from drinking water.

In addition, dairy cattle may undergo nitrate and mycotoxins intoxication from the water, which can generate alterations in protein and glucose metabolism. In these cows, the integration of ZC in the feed has reduced the assimilation of nitrates and concentration of aflatoxins in their milk, improving the systemic toxic effects. The detoxifying action on these ions has no effect on the physiological ionic equilibrium. In fact, the blood mineral levels of cattle, pigs and poultry were unaffected by integration with ZC. In this regard, ZC has shown a positive effect in farmed poultry in balancing the total intestinal microbial flora, reducing toxic effects of aflatoxins and increasing the antioxidant activity of peroxidase, catalase, and SOD (superoxide dismutase) as well as increasing levels of omega-3 fatty acids in eggs.

Clinoptilolite is becoming increasingly known as a biomedical feed ingredient, widely reported in the scientific literature, for use in farm animal nutrition as a candidate to replace antibiotic growth promoters (AGP), due to its unique antibacterial properties and safety and efficacy as a dietary supplement in food animals. This is of importance and notable benefit due to rising concerns over the rapid emergence of antibiotic resistant strains of pathogenic microbes in the biomedical industry and particularly within the agricultural animal industry. This issue has resulted from the non-clinical use and misuse of dietary antibiotics for many decades to prevent bacterial infections and to enhance performance in livestock production, (especially with chickens and pigs). Namely, the increased sanitary problems in intensive farming of food animals have been mitigated by adding antibiotic growth promoters (AGP) to animal feed in order to enhance production efficiency by increasing growth rate, improving feed utilization and reducing mortality from clinical disease. These practices have led to growing concerns about
drug residues in meat and other animal products. Furthermore, the continuous use of antibiotics contributes to drug-resistant bacteria which may be capable of transferring their resistance to pathogenic bacteria in both animals and humans.

So far, clinoptilolite has been successfully used in animal biotechnology as an agent to address mycotoxicosis, maintain gut health by acting favorably on intestinal microbiota, reduce, prevent, and treat diarrheal disease in farm animals, decrease the level of toxic heavy metals and ammonia, improve immunity, general health, and growth performance in animals of veterinary and biomedical importance.

**Antioxidant, Immune Enhancing, and Anti-Cancer Properties**
Currently, there are many reasons for ZC utilization in veterinary medicine beyond its detoxification capabilities. It also offers antioxidant, hemostatic, anti-diarrheic, and immune-stimulating properties. In human medicine, the experiments in vitro and in vivo have suggested that ZC could be used as an adjuvant in immunodeficiency conditions and anticancer therapy, antioxidative agent, or reducer of the levels of radioactive elements. Furthermore, toxicology studies on mice and rats demonstrated that micronized zeolite treatment did not have negative effects.

Recent research has evaluated clinoptilolite as a potential adjuvant in anticancer therapy, due to its antimetastatic and immunostimulatory effects. Clinoptilolite treatment of mice and dogs suffering from a variety of tumor types led to improvement in the overall health status, longevity, and decrease in tumor size. It also reduced lipid peroxidation in the liver of mice. Specific evaluations in research show that combined treatment with Doxorubicin and micronized zeolite resulted in strong reduction of the pulmonary metastasis count increasing anticancer effects of Doxorubicin. Another study showed that local application of clinoptilolite to skin cancers of dogs effectively reduced tumor formation and growth.

In vitro tissue culture studies showed that finely ground clinoptilolite induces expression of specific tumor suppressor proteins and blocks cell growth in several cancer cell lines. This new data indicates that clinoptilolite treatment might affect cancer growth by attenuating survival signals and inducing tumor suppressor genes.

**Impact on Gut Health**
Zeolites are crystalline compounds of silicates with microporous structures. In the gut, these silicates can act as adsorbents, ion-exchangers, catalysts, detergents, or anti-diarrheic agents. Studies have evaluated zeolite supplementation effects on biomarkers of intestinal wall permeability and parameters of oxidation and inflammation. ZC was shown to modulate intestinal wall integrity via impact on zonulin secretion from enterocytes, and to reduce pro-oxidative and pro-inflammatory processes in the gut via binding of oxidants. Other reports demonstrate that ZC reduces ammonia concentration and improves the integrity of the intestinal barrier. Furthermore, ZC acts on intestinal lymphoid tissues with a positive impact on the intestinal ecosystem, boosting the immune system. ZC contains metal ions within its structure which act as available cofactors for the activation of antioxidant enzymes.
The effects of zeolites on intestinal barrier integrity, inflammation, redox biology, as well as on physical performance have been established to have positive impacts. This information suggests nutritional solutions like zeolite supplementation could be of reasonable relevance for health and performance.

**Conclusion**
In conclusion, zeolites are porous minerals with high absorbency and ion-exchange capacity. Even though there are several synthetic or natural occurring species of zeolites, the most widespread and studied is the naturally occurring zeolite clinoptilolite (ZC). ZC is an excellent detoxifying, antioxidant, and anti-inflammatory agent. As a result, it is been used in many industrial applications ranging from environmental remediation to specific medical uses as a dietary/food supplement for animals and humans.

Cumulative research on zeolites is finding that using this as a food supplement can improve lifestyle and can provide advantages when combined with traditional pharmacological treatment. In fact, evidence shows a promising detoxifying role of ZC in the removal of toxic metabolites produced by drugs chronically administered during chemotherapy, diabetes, or cardiovascular diseases. However, more research is needed to explore all the potential benefits that ZC and other specific modified ZC can produce on human and animal health.

**References**
Objectives

- To understand the demands and tasks involved in different performance dog abilities.
- To understand how different herbal and pharmaceutical medications can affect the ability of performance dogs to accomplish their duties.

Depending upon the skill set of a performance dog, all or one of the senses may be involved in the duty of the dog. Sight, olfaction, hearing, taste may all be a specific sense a performance dog requires to advance in a career. It is often difficult to assess damage or loss of a sense specifically olfaction and taste. Therefore the aim should be to avoid medications that may have adverse reactions and negatively impact these senses.

Performance dog activities and job responsibilities can be divided into categories that reflect the type of activity performed by the athlete. Companion events include such activities as agility, obedience, rally, conformation, tracking, freestyle, flyball, disc dog, dock diving, weight pulling, and canine nose work. Performance events include lure coursing, greyhound racing, herding, field trials, hunt test, earth dog tests, fox hunting, schutzhund, French ring sport, mushing, and carting. Working dog activities include search and rescue, detection, police, patrol, and protection, farm dogs, service dogs, and canine actors. Scent detection activities are widespread and include brown tree snake detection, cadaver detection, conservation work, drug detection, explosive detection, fire accelerant detection, game hunting, identification of individuals, pipeline leak detection, termite and bed bug detection. Understanding the demands on each of these jobs is important to effectively implement treatment protocols. In addition, tailoring exercise programs and feeding strategies to optimize olfactory performance should be considered when working with these teams.

The following medications have been known to cause changes in the sense of smell in people and dogs: Amiodarone, amlodipine, bromocriptine, cimetidine, dexamethasone, doxycycline, nifedipine, and phenylephrine. In addition, various disorders are known to cause olfaction changes in people such as asthma, chronic kidney failure, cobalamin deficiency, Cushing’s disease, diabetes mellitus, head trauma, hepatic cirrhosis, hypothyroidism, nasal polyps, upper respiratory infections, and acute viral hepatitis.

The following medications have been known to affect vision: atropine, doxepin, SSRIs, tricyclic antidepressants, belladonna, buspirone, gabapentin, alprazolam, cetirizine, cimetidine, clonazepam, and trazadone. In addition, latanoprost has been known to change the iris pigment when applied to the eye. It also increases eyelash growth.

In regard to hearing, both aminoglycosides (i.e. Otomax) and erythromycin have been known to decrease or diminish hearing.
The sense of taste is difficult to assess in the canine patients, but several drugs have been known to negatively affect this sense in humans. Metronidazole, thyroid medications, and terbinafine have been implicated in taste deficiencies.

Many of our canine patients have job descriptions that are more than just companion. Treating performance dogs can be both challenging and rewarding. Becoming familiar with the job description or events that performance dogs are involved in can greatly increase our ability to positively impact their lives.

References
An In-Depth Look at The Anatomy, Neurology, and Treatment Approaches to The Temporomandibular Joint and Hyoid Apparatus
Dr. Lyndsay Klemens DVM, CVST, CVMRT

Objectives

- To understand the anatomy and neurology involved in both the temporomandibular joint (TMJ) and hyoid apparatus of carnivores and herbivores.
- To address underlying deficiencies of the TMJ and hyoid apparatus and effectively implement treatment protocols.

The temporomandibular joint (TMJ) and hyoid apparatus are two important components of the stomatognathic system. Along with the teeth, dental-alveolar ligaments, skull, mandible, sternum, and all the ligamentous and muscular attachments; the TMJ and hyoid apparatus are essential elements of the system. Across the species, there are both subtle and obvious differences in the anatomy depending on the predominant food substance in the animal’s diet. The differences can be grouped based upon herbivore, carnivore, or omnivore and are more dramatic in the TMJ than the hyoid apparatus. The importance of examining and diagnosing dysfunction in these two structures is important as small alterations can have widespread neurologic and functional impacts on the body as a whole. Utilizing basic palpation and manipulation in conjunction with imaging techniques when needed can add in diagnosis.

**TMJ**

The TMJ is a synovial joint with articulation between the mandibular fossa of the temporal bone and the condylar process of the mandible. It is surrounded by a joint capsule and supported by extracapsular ligaments. The joint capsule itself is divided into two distinct compartments by a cartilaginous meniscus, the articular disc. This articular disc lacks nerve endings and blood vessels and is not sensitive to pain. The upper or dorsal compartment allows movements of gliding, protrusion/retraction, and lateral excursion. The lower or ventral compartment allows for rotational and flexion/extension movement of the TMJ. Extension of the TMJ can occur when the condylar process has moved anteriorly in the dorsal compartment. Anterior movement is limited by the retroarticular process. Movement beyond the retroarticular process results in dislocation of the mandible.

Significant anatomical differences exist between the species and movement is predominately determined by the conformation of the mandibular condyle. The herbivore has a more flattened condyle allowing for greater lateral excursion of the dorsal compartment. The carnivore has a more hinge like or dowel rod appearance to the condyle allowing for more rotational flexion/extension in the ventral compartment. There is a two-phase motion of the joint where the ventral compartment supported by a tight joint capsule allows for rotational flexion/extension. The larger dorsal compartment allows for the major movement of lateral excursion. The carnivore has a more hinge like or dowel rod appearance to the condyle allowing for more rotational flexion/extension in the ventral compartment. There is
minimal translation (forward gliding) and minor lateral excursion. The articular disc is not as well developed and the retroarticular process is more predominant assisting in prevention of dislocation. The omnivore has a similar two compartment configuration and the conformation of the condyle is intermediate where there is both a flattening of the condyle and slight hinge like property. The movements of the TMJ are therefore diverse in allowing for rotation, translation, and lateral movement. The muscles of mastication can be divided into jaw openers and jaw closers. The main drivers of jaw opening or TMJ extension include digasticus and lateral pterygoid along with gravity. The major jaw closers or TMJ flexion include masseter, temporalis, and medial pterygoid. It should be noted that the muscle bellies of the TMJ flexors are much larger than the bellies of the muscles of TMJ extension.

**TMJ Extension**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Origin</th>
<th>Insertion</th>
<th>Innervation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digasticus</td>
<td>paracondylar process of occipital bone</td>
<td>angular process and body of mandible</td>
<td>trigeminal mandibular branch rostrally, facial nerve caudally</td>
</tr>
<tr>
<td>Lateral Pterygoid</td>
<td>sphenoid bone</td>
<td>Joint capsule/articular disc and neck of condylar process</td>
<td>trigeminal mandibular branch</td>
</tr>
<tr>
<td>Gravity</td>
<td></td>
<td></td>
<td>Gravity</td>
</tr>
</tbody>
</table>

**TMJ Flexion**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Origin</th>
<th>Insertion</th>
<th>Innervation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masseter</td>
<td>zygomatic arch</td>
<td>massenter fossa of mandible</td>
<td>trigeminal mandibular branch</td>
</tr>
<tr>
<td>Temporalis</td>
<td>temporal fossa</td>
<td>coronoid process of the mandible</td>
<td>trigeminal mandibular branch</td>
</tr>
<tr>
<td>Medial pterygoid</td>
<td>sphenoid bone</td>
<td>medial surface of mandible</td>
<td>trigeminal mandibular branch</td>
</tr>
</tbody>
</table>

**Hyoid Apparatus**

The function of the hyoid apparatus is to suspend the larynx and anchor the tongue. It allows for swallowing, lolling, lapping, and retching. The articulation with the skull is just caudal to the external acoustic meatus. In the carnivore, the apparatus consists of paired stylohyoid, epihyoid, ceratohyoid, and thyrohyoid bones. A single basihyoid bone unites the paired sides at the base of the tongue. The horse has an additional lingual process which is rostrally projected from the basihyoid bone.

Functionally, flexion/extension of the TMJ causes dorsal/ventral movement of the hyoid. Swallowing moves the hyoid apparatus rostral-dorsal.

The suprahyoid muscles originate on the skull and mandible and insert on the hyoid. The infrahyoid muscles insert on the sternum, scapula, and thyroid cartilage with the origin on the hyoid apparatus.
**Diagnosis and Treatment**

Motion palpation of both of TMJ and Hyoid apparatus can aid in diagnosis of muscle spasm or joint restriction. In addition, when significant motion restriction is recorded then additional imaging should be pursued. Treatment of dysfunction should be aimed at anti-inflammatory affects and restoration of joint motion.

**References**

Introduction to Holistic Veterinary Medicine: The Wave of The Future
Douglas Knueven, DVM, CVA, CAC, CVCH

Objectives
- Learn terminology associated with holistic veterinary medicine
- Learn the basic philosophy underlying holistic medicine
- Learn why holistic medicine is gaining in popularity

“He who joyfully marches to music rank and file has already earned my contempt. He has been given a large brain by mistake, since for him the spinal cord would surely suffice.” -Albert Einstein

Introduction
This lecture looks at why more and more pet owners and veterinarians are attracted to holistic methods. We will look at research showing that holistic therapies are increasing in popularity. We will explore the subtle differences in terminology associated with holistic medicine and give a summary of the holistic philosophy.

Why Take Notice?
2001 Harvard Medical School Study¹
- 67.6% of US adults have used CAM therapies at some time in their lives.
- “The trend of increased CAM therapy use across all cohorts since 1950, coupled with the strong persistence of use, suggests a continuing increased demand for CAM therapies that will affect all facets of health care delivery over the next 25 years.”

WHO, 2002²
- Populations in developed countries who have used complementary and alternative medicine at least once in their lifetime:
  - Canada 70%
  - France 49%
  - Australia 48%
  - USA 42%
  - Belgium 31%

National Center for Health Statistics, 2007³
- 38% of US adults and 12% of children use some form of CAM in past 12 mos.

Increasing CAM Use - 14% increase in the use of CAM from 2002-2007⁴

USA Today – Sept 15, 2008⁵
- AHA
  - 2005 – 25% offer CAM
  - 2007 – 37% offer CAM
  - 71% pay out of pocket

CAM use in USA increases with education⁶
Medical Student Survey 2009

- 77% agreed that patients whose doctors know about CAM in addition to conventional medicine, benefit more than those whose doctors are only familiar with Western medicine.
- 74% agreed that a system of medicine that integrates therapies of conventional and CAM would be more effective than either type of medicine provided independently.
- 84% agreed that CAM contains beliefs, ideas, and therapies from which conventional medicine could benefit.
- 60% favored more education related to CAM during their time in medical school.
- ½ of all U.S. medical schools currently offer some type of CAM course.

Colorado State University 2006

- Owners with dogs and cats with cancer
- 76% of surveyed owners reporting some use of CAVM
- 50% of pets over 10-y-o will die of cancer

Millennials

- > 1/3 of pet owners
- > ½ of Millennials will try natural and holistic remedies before conventional treatments
- 7/10 prefer pet food with natural ingredients
- Have broader sense of health than “lack of illness”

Veterinary Economics Survey Aug, 2006

- 71% “Our team doesn’t offer alternative therapies.”
- 36% “We don’t refer for alternative therapies.”

“Alternative medicine for pets may not be as widespread or publicized as the human variety, but it’s growing faster than a sprig of St. John’s wort.”

Time Magazine, November 3, 1997

Why Clients Seek CAVM

- Personal experience, Referrals, Standard care has failed, Less invasive, Less dangerous
- 5% hospitalized due to drugs/ 30% experience reaction in hospital

What is the Third Leading Cause of Death in the USA?

- Iatrogenic!!! (Conservative Estimates)
  - Medication Errors in Hospitals ------7,000/year
  - Medical Errors in Hospitals -------20,000/year
  - Unnecessary Surgery --------------12,000/year
  - Drug Adverse Events ----------106,000/year

Hospital Error Detection

“Our findings indicate that two methods commonly used by most care delivery organizations ... fail to detect more than 90 percent of the adverse events that occur among hospitalized patients.”
Adverse events occurred in one-third of hospital admissions, even in hospitals that had instituted advanced patient safety programs

**Why Vets Seek CAVM**
- Frustration, Clients, Questions, Interactions, Informed consent
- What’s best for the patient?

**What Is Holistic Medicine?**
An alternative approach to health care and prevention of disease which integrates the body as a whole, including mind and spirit, rather than separate systems. - *Saunders Comprehensive Veterinary Dictionary*

**Holistic Health** - Holistic Health is an approach to life. Rather than focusing on illness or specific parts of the body, this ancient approach to health considers the whole person and how he or she interacts with his or her environment. It emphasizes the connection of mind, body, and spirit. - *AHHA President, Suzan Walte*

**Complementary and Alternative Veterinary Medicine** - A heterogeneous group of preventive, diagnostic, and therapeutic philosophies and practices. The theoretical bases and techniques of CAVM may diverge from veterinary medicine routinely taught in North American veterinary medical schools or may differ from current scientific knowledge, or both. - *AVMA Guidelines 2001*

**Terms**
- Allopathic
- Alternative
- Complimentary
- Conventional
- Eastern
- Holistic
- Homeopathic
- Integrative
- Natural
- Traditional
- Western

**Holistic Philosophy**
- Whole > Parts
- Illness - dysfunction of the whole patient, not an isolated event
- Strengthen body vs. Fight disease
- Treat the patient, not the disease
- What kind of patient has a disease vs. what kind of disease a patient has?
- Treating the underlying causes of disease vs. treating symptoms alone
- Body = Pharmacy
Placebo Response

- Placebo almost as effective against pain as morphine and for depression as antidepressants\textsuperscript{16,17}
- Mr. Wright\textsuperscript{18}
  - Advanced Lymphoma
  - Given new drug – krebiozen
    - Gained wt/tumors shrank
  - Newspaper report – krebiozen not as good as 1\textsuperscript{st} thought
    - Lost wt/tumors grew
  - Dr.s gave glorified placebo injections “new improved batch”
    - Gained wt/tumors shrank
  - Newspaper report – “AMA reports that krebiozen is worthless against cancer.”
    - Tumors grew and he died shortly thereafter
- Dr. Wolf – 1940’s\textsuperscript{19}
  - Measured/graphed stomach muscle contraction
  - Placebo ipecac – disturbed wave pattern
  - Placebo atropine – calmed wave pattern
  - “Tom” – nauseated from atropine and soothed by ipecac
- Placebo - Up to 75% affected, average 35% – 45%
- Placebo – the body can heal itself if the conditions are right
- Holistic Medicine – create the right conditions for the body to heal itself
- Wellness = Dynamic balance
- Homeostasis
- Optimal health > Absence of sickness
- Prevention is preferable to treatment
- Energy system

Pseudo-science?
Tip of the EBM Pyramid\textsuperscript{20}
- 49 most cited research articles
- 45 claimed to have uncovered effective interventions
- 34 retested
- 14 = 41% wrong or exaggerated

JAVMA Study
“… in only 11% of reports were both randomization of the group allocation process and concealment of the allocation sequence described…It is known from empiric investigations that clinical trials that report inadequate or unclear allocation concealment may exaggerate the effects of the treatment being studied by up to 40%.”\textsuperscript{21}

“The AVMA believes that all veterinary medicine, including CAVM, should be held to the same standards. Claims for safety and effectiveness ultimately should be proven by the scientific method.” - \textit{AVMA Guidelines 2001}
Psuedo-scientific? – “Yearly” Vaccines

- AVMA Council on Biologic and Therapeutic Agents (two-year study)
- “The one-year revaccination frequency recommendation found on many vaccine labels is based on historic precedent and USDA regulation, not scientific data.” - *JAVMA*, June 1, 2001
- “Results - The percentage of cats that had titers at or above the threshold values or responded to revaccination with a ≥ 4-fold increase in titer was 96.7% for FPV, 97.8% for FCV, and 88.2% for FHV.
- Conclusion - In most cats, vaccination induced a response that lasted up to and beyond 48 months for all 3 antigens.”

- AVMA Council on Biologic and Therapeutic Agents (two-year study)
- “Results - The percentage of dogs that had titers at or greater than the threshold values or responded to revaccination with a ≥ 4-fold increase in titer was 98.1% for CDV, 98.4% for CAV-1, 99.0% for CAV-2, 100% for CPIV, and 98.1% for CPV.
- Conclusion - In most dogs, vaccination induced a response that lasted up to and beyond 48 months for all five antigens.”

Controlled Retrospective Study

- Dogs are 2X more likely to develop IMHA within 1 month of vaccination.

Vaccines

- Reduce lymphocyte numbers and responsiveness
- Cause thymic depletion

Vaccine-Associated Adverse Events within 3 Days of Vaccination of Dogs

- Retrospective cohort study
- 1,226,159 dogs vaccinated at 360 veterinary hospitals
- VAAE - 38.2/10,000 dogs vaccinated
- Risk increased as weight decreased
- Risk increased as number of vaccines increased

Small Dogs – Lower Dose

- 13 dogs ages 3-9, 12 lbs. or less
- At least 3 years since last vaccine
- ½ dose Distemper/Parvo vaccine given
- Pre- and Post-vaccine titers
- Protective immunity achieved/maintained

Evidence-Based DA2PP Vaccination

- Offer titers
- 3-4-year intervals
- Separate vaccines (alternate years)
- ½ dose to dogs under 12 lbs.

East Meets West

- Holistic/Integrative case study
“A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it". -Maxwell Planck

Books
- Complementary and Alternative Veterinary Medicine Principles and Practice. Allen M. Schoen & Susan G. Wynn (Mosby)
- Manual of Natural Veterinary Medicine Science and Tradition. Susan G. Wynn & Steve Marsden (Mosby)

American Holistic Veterinary Medical Association (AHVMA) www.ahvma.org

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An Introduction to Nutraceuticals: Evidence-Based Nutritional Therapies
Douglas Knueven, DVM, CVA, CVC, CVCH

Objectives
- Learn the oversight mechanisms for veterinary supplements
- Learn how to choose a supplement company/product for their patients

Introduction
According to the National Research Council (NRC) an Animal Dietary Supplement is a substance for oral consumption by horses, dogs, or cats, whether in/on feed or offered separately, intended for specific benefit to the animal by means other than provision of nutrients recognized as essential, or provision of essential nutrients for intended effect on the animal beyond normal nutritional needs, but not including legally defined drugs. The term Nutraceutical has no official definition but has been defined as a dietary supplement that is intended for health benefits beyond prevention of essential nutrient deficiencies.

The use of animal dietary supplements is widespread. Surveys show that 10% - 33% of US dogs, cats, and horses receive a daily supplement and 90% of US vets dispense supplements. Because I will be giving a lecture about herbal supplements, I will limit this presentation to non-herbal, nutritional supplements.

Animal Supplement Oversight
Human and animal supplements are not subject to the same regulations or regulators. At the federal level, animal supplements are regulated by the Food & Drug Administration, Center for Veterinary Medicine (CVM). The CVM may recognize them as either a food or a drug depending on the intended use of the product as established by the labeling claims. The difference in CVM status is determined by how the supplement company presents the product. If the animal supplement is bought to the market as a food, there are no registration or pre-market clearance requirements by the CVM, provided the product contains ingredients recognized for the approved nutritional purpose. In this scenario, suspicious ingredients must be brought to the attention of the CVM for approval. At the state level these supplements are usually overseen by the state’s agriculture department (often adopting AAFCO standards). Interpretation and enforcement of regulations differs by state. Such a supplement must be registered with the state, or the company licensed in the state, prior to product distribution. This usually involves the submission of labels to the state (every state) or registration of the company.

Alternatively, an animal supplement, for a health purpose, may be labeled similarly to an animal drug. Such supplements are still subject to CVM oversight and that of states with animal remedy laws. These supplements that cannot meet the FDA drug approval requirements may be allowed to be marketed as “unapproved drugs of low regulatory priority” by the CVM. (The CVM has enforcement discretion to allow marketing of products for which there are reasonable assurances that the company is acting responsibly. This discretionary enforcement may also apply to topical meds, those equivalent to OTC human drugs, and petroleum-containing cat laxatives.) These
supplements must conform to CVM labeling requirements. Furthermore, the company should register as a drug manufacturer with the FDA, “drug list” the product, and follow GMPs.\(^4\)

Given all this official oversight of supplements you would think that those available must be safe and effective, right? The truth is that the regulations for pet products are not well defined, thus it is easy for poor quality manufacturers to sell their pet products. Furthermore, the lack of federal and state resources results in ineffective monitoring and control of what is on the market leaving the impression that supplements are unregulated.

**Supplement Security**

We all want to be sure to dispense safe and effective therapeutics. Unfortunately, with little regulatory enforcement there is a high potential for ineffective, or even unsafe, supplements making fraudulent claims to be readily available to our clients. When you add to this the recent, vast proliferation of nutritional supplements coupled with their promotion and availability on the internet, the veterinarian is left in a difficult position. How do we choose supplements that we can trust and dispense?

The first thing to do is to evaluate the supplement company. We need to ask such questions as:

1. How long have they been in business? (Generally, the longer the better)
2. What is the company’s track record/reputation? (Colleagues/VIN Alt Med message board)
3. Contact the company with questions. (How responsive are they?)
4. Who is involved with formulating the products? (Nutritional experts/veterinarians are best)
5. What kinds of claims are being made? (If unbelievable, don’t believe it)
6. Is there specific safety/efficacy research on this product?
7. Is there a guaranteed analysis?
8. Is there a lot # and expiration date?
9. National Animal Supplement Council (NASC) - www.NASC.cc

NASC is a non-profit industry trade association and animal advocacy group. Their members are subject to ongoing quality review and monitoring including:

1. Verification of Raw Materials
2. Verification of Manufacturing Processes
3. Proper Labeling & Claims Review
4. Adverse Event Reporting (Over 1 Billion Bytes of Data)
5. Independent & Comprehensive Quality Audits
6. Product Testing for Label Claim from Certified Labs
7. Required Continuing Education

The NASC seal does not mean the company or individual supplement is perfect, but it does mean someone has checked them out. There are good products that do not have the NASC seal, but I do not trust an unknown company without it.
Prescribing Supplements

The next step in prescribing a supplement is to assess the need for it. This requires an accurate diagnosis of the pet’s condition. Then, research on the proposed supplement itself. Looking at research provided by the manufacturer is a place to start. Additionally, a literature search may be helpful. Check out PubMed, Google Scholar, and National Institutes of Health Office of Dietary Supplements (ODS) - https://ods.od.nih.gov/Research/resourcesforresearchers.sec.aspx

Ultimately, the final step in prescribing a supplement is to assess outcomes. This requires keeping searchable records and periodically evaluating the supplement’s effectiveness.

Supplements for Healthy Pets

Commercial Pet Diet Processing - Destroys Nutrients

Cooking (112° F – 117° F) reduces potency of almost all nutrients and destroys others including Thiamine, Folic Acid, Vitamin C, Vitamin A, Niacin, and Pantothetic Acid.5-11

While pet food manufacturers add back nutrients to balance the diets, they proceed based on incomplete knowledge. Even the experts agree that the AAFCO standards are lacking.

According to Dr. David A. Dzanis, “The formulation method does not account for … availability of nutrients. Yet a feeding trial can miss some chronic deficiencies or toxicities.”12

Dr. Quinton Rogers stated, “Although the AAFCO profiles are better than nothing, they provide a false security... Some foods that pass the feeding trials still won’t support animals over the long term.”12

Dr. Tony Buffington stated, ”The recommendation to feed one food for the life of an animal gives nutritionists more credit than we deserve.”12

Finally, Dr. Richard Hill said that it is a myth to think that “The minimum and maximum amount of essential nutrients that should be included in the diet is known for most nutrients in normal dogs and cats.”13

Besides the 40 or so nutrients that AAFCO recognizes, research shows that there are over 8,000 phytochemicals present in whole (unprocessed) foods and that these nutrients work together synergistically to create health.14 Furthermore, many of these natural compounds have biological effects that make them equally essential for life as vitamins.15

The bottom line is that healthy pets that are eating a “complete and balanced” diet may benefit from nutritional supplements.

Supplements for Sick Pets

No matter what the etiology, disease leads to compromised cells. Damaged cells require increased metabolic activity to remove debris and rebuild cell structures. Up-regulation of metabolic pathways leads to an increased nutrient demand. Without proper nutritional support, healing can be delayed or incomplete. So, every case has a nutritional component and may benefit from nutritional supplements.
Specific Supplements

**Whole-Food Multivitamin** – As described above, processed pet foods lack the thousands of micro-nutrients found in whole foods. Compounding this is the fact that most pet caregivers feed less food than the label calls for because the high energy-density causes weight gain. (The pet food’s nutrient profile is based on the pet getting the prescribed volume of food.) In my opinion, every pet benefits from a whole-food multivitamin.

**Probiotics/Prebiotics** – Probiotics are supplements that provide the gut with the beneficial bacteria needed for health. Prebiotics are the nutrients the probiotics need to survive in the intestines. Dogs and cats did not evolve eating sterile diets. The freshly killed and not-so-freshly killed animals they consumed were teeming with bacteria. Is it any wonder that so much research demonstrates the benefits of probiotic supplementation for pets?

There are 10 times more bacterial cells in the body than body cells themselves. From a cellular standpoint, we are more bacterial than we are human. The complex internal ecology within the body and the associated genetic fingerprint is called the intestinal microbiome – micro for microscopic and biome for a naturally occurring community of flora occupying a large habitat. We interact with the bacteria and their genes. The gut microbiome may be considered and organ just as vital to health as the liver, heart, or brain.

The beneficial bacteria in the intestine help to further break down foods to liberate the nutrients. They also manufacture several vitamins. Probiotic bacteria competitively inhibit pathogenic bacteria. They nourish the enterocytes with short-chain fatty acids and help to maintain the integrity of the intestinal lining, protecting the entire body from the inflammation caused by leaky gut syndrome.

Furthermore, the Gut Associated Lymphoid Tissue (GALT) makes up 70% - 80% of the immune system. Research shows that the balance of intestinal bacteria affects the systemic immune system. In fact, probiotic supplements have a profound effect on immune function.

In one study, puppies given a probiotic supplement produced a higher titer to vaccines. Another study showed that puppies that were given a probiotic supplement before six months of age were less likely to develop immune system changes associated with atopic dermatitis.

There is also a close link between the intestinal microbiome and the brain. Seventy to eighty percent of the body’s serotonin is made by the GI neurons. The intestinal nervous system is considered by some to be the body’s second brain. There is bidirectional communication between the intestinal microbiome and the brain via the Vegas Nerve.

One study showed that chronic administration of probiotics to mice reduced levels of anxiety and depression-like behavior and induced changes in GABAergic system in regions of the brain known to involve these behaviors. Vegotomy prevented the effects of the probiotic.

**Omega-Three Fatty Acids** – Another nutrient group that is vital for pet health is omega-three fatty acids. The meats used in most pet foods are lower in omega-three fatty acids than the ancestral diet of pets. Most farm animals are fed grains which are high in omega-six fatty acids.
This leads to meat high in omega-sixes and low in omega-threes. The wild prey of ancient dogs and cats ate mostly grasses which are high in omega-three fatty acids, which increases the omega-three to omega-six ratio. Omega-six fatty acids are pro-inflammatory while omega-three fatty acids are anti-inflammatory. It is important to balance the body’s system toward less inflammation.

Omega-three fatty acids, specifically docosahexaenoic acid (DHA) are also very important in proper neurological development and function. That is not surprising when you consider that DHA makes up 50% of the weight of a neuron’s membrane. I previously mentioned the 2003 study that indicated that a high DHA diet fed to pregnant bitches and their puppies led to an improvement in trainability.19 Another study found that aggressive dogs had lower serum DHA levels than non-aggressive dogs indicating the possible beneficial effect on temperament of DHA supplementation.20

Supplementation of omega-3 fatty acids has been shown to improve survival times of dogs with lymphoma.21 Such supplementation also helps dogs with atopic dermatitis.22, 23 Omega-threes help dogs with hyperlipidemia.24, 25 They have been shown to help with cardiomyopathy and chronic valvular disease.26, 27 Supplementation with omega-three fatty acids also aids the treatment of chronic kidney disease28, 29 and osteoarthritis in dogs,30-33 as well as IBD34 and asthma35 in cats.

**Glucosamine/Chondroitin** – Joint supplements such as glucosamine and chondroitin provide nutrients that improve the health of the body’s articulations. Many studies have been published that show that the supplementation of glucosamine and chondroitin, especially in the form of perna muscle, can decrease pain and improve mobility for dogs with osteoarthritis.36-39

Recent research demonstrated that a supplement containing glucosamine and chondroitin prevented the development of osteoarthritis in dogs.40 In the study, 105 healthy Labrador Retrievers were randomly divided into treatment and control groups. In the control group, 33.3% of the dogs developed radiographic evidence of elbow dysplasia compared to 18.5% in the treated group. Symptoms of dysplasia at 12 months differed between the treated (12.5%) and control (61.5%) animals.

**Conclusion**
Both diseased and healthy animals benefit from certain nutritional supplements. In my opinion, the fact that supplementation with these nutrients can help with so many problems indicates that our current diets are deficient and thus predispose pets to these diseases.

**References**


Introduction to Veterinary Chiropractic: Not Just “Animal Crackers”
Douglas Knueven, DVM, CVA, CAC, CVCH

Objectives
- To learn about animal chiropractic practice

Introduction
According to the American Chiropractic Association, chiropractic is the science and art which utilizes the inherent recuperative powers of the body and deals with the relationship between the nervous system and the spinal column, including its immediate articulations, and the role of this relationship in the restoration and maintenance of health.

History
The concepts of chiropractic can be traced back to 2700 BCE, when in China people used bamboo poles used for self adjustment. In the West around 400 BCE the father of medicine, Hippocrates wrote, “Look well to the spine for many diseases have their origins in the dislocation of the vertebral column.” Meanwhile, Egyptian manuscripts and hieroglyphs dating back to 200 BCE document the use of spinal manipulations. More recently, in the 1600’s English “bonesetting,” a form of musculoskeletal manipulation, was quite popular.

The modern practice of chiropractic began in the late 1800’s with an American healer named DD Palmer. He developed the basic principles of chiropractic by combining vitalism (the belief that there is a non-physical aspect to life), the rudimentary understanding of the nervous system at the time, and manipulation. Early chiropractors adjusted animals as well as people, but they soon abandoned the treatment of animals due to criticism by mainstream medicine.

The current practice of animal chiropractic was pioneered by Sharon L. Willoughby, DVM, DC. Her leadership led to a formal, post-graduate, animal chiropractic educational program for veterinarians and chiropractors in 1985. From this nucleus was formed the American Veterinary Chiropractic Association in 1989, a professional and certifying body. Today there are over 1,100 certified animal chiropractors and several other animal chiropractic courses.

Chiropractic has struggled for recognition in the world of modern medicine. One reason that chiropractic had such a hard time is that it was under constant attack from mainstream medicine. In fact, after a 15-year long law suit a group of chiropractors finally set the record straight. They sued the AMA and won in 1991. A federal Distric Court found the AMA guilty of conspiracy. The judge found that “…the AMA’s self-proclaimed and described ‘mission’ was to contain and eliminate the chiropractic profession.” It is interesting that after this decision in the 1990’s the popularity of chiropractic began to skyrocket.

Chiropractic Research
Let’s look at pertinent research on chiropractic. While studies on animals are lacking, there is much published human research. One study looked at 183 Patients with neck pain. This randomized, controlled trial compared the effectiveness of Manual therapy (spinal mobilization), Physiotherapy (mainly exercise) and General practitioner care (counseling, education and analgesics). The study published in the British Medical Journal concluded that, “Manual therapy
(spinal mobilization) is more effective and less costly for treating neck pain than physiotherapy or care by a general practitioner.

Another randomized, controlled trial\(^2\) looking at neck pain also compared Manual therapy, Physiotherapy, General practitioner care. They found that “Manual therapy scored consistently better than the other two interventions on most outcome measures.” They concluded that “In daily practice, manual therapy is a favorable treatment option for patients with neck pain compared with physical therapy or continued care by a general practitioner.”

A prospective, observational, community-based feasibility study\(^3\) involving chiropractors and family medicine physicians looked at chronic low-back pain. This study concluded that “Patients with chronic low-back pain treated by chiropractors show greater improvement and satisfaction at 1 month than patients treated by family physicians.” Another study\(^4\) of low back pain found that, “Acute and chronic chiropractic patients experienced better outcomes in pain, functional disability, and patient satisfaction (P < .01).”

A study\(^5\) of patient satisfaction found that, “The mean satisfaction score for chiropractic patients was greater than the score for medical patients…” In 1993, a study\(^6\) commissioned by the government of Ontario found that “…for the management of low-back pain, chiropractic care is the most effective treatment, and it should be fully integrated into the government’s health care system.”

You no doubt will hear of the supposed dangers of chiropractic. There have been cases where chiropractic adjustments, usually of the neck, have resulted in serious circulatory issues. However, the risk of such an occurrence has been overblown. In fact, the chance that a chiropractic cervical manipulation will result in a serious reaction in adult patients is remote, ranging from 1 in 1 million to 1 in 5.85 million manipulations.\(^7,8\) Compare that to the risk of even the most innocuous medication causing harm.

How Does It Work?
There are four basic concepts of chiropractic

1. Innate Intelligence – natural ability of the body to heal
2. The nervous system is supreme
3. Subluxation > Altered Nerve Transmission > Altered Physiology > Pathology
4. Adjustment of the spine can correct subluxations

Wait a minute! Did I just say that chiropractic can correct subluxations of the spine? The concept of the subluxation is where chiropractic often gets misunderstood by conventional veterinarians. According to Stedman’s Medical Dictionary, a subluxation is “an incomplete luxation or dislocation.” Such a condition would surely not be easily corrected.

However, the chiropractic definition of subluxation is more like “…lessened motion of the joints, by slight change in the position of the articulating facets…”\(^9\) and “A disrelationship of a vertebral segment in association with contiguous vertebrae resulting in a disturbance of normal biomechanical and neurological function”\(^9\) To help avoid confusion, modern chiropractic has coined the terms Vertebral Subluxation Complex (VSC) and Segmental Dysfunction (SDF) to replace subluxation. Joint Complex Dysfunction is defined as the process involving joint hypomobility, muscle tightening, and myofascial trigger points.\(^10\)
Subluxation Theories
There are a couple of theories about how VSCs cause problems. First there is the idea of nerve compression. If a spinal zygapohyseal joint is even slightly out of position it can result in intervertebral foramen encroachment or nerve root traction. Those can lead to ischemia and edema which can put pressure on spinal nerve roots which alters nerve transmissions. One study\(^\text{11}\) found that as little as 10 mm of pressure (equivalent to the weight of a dime) on spinal nerve caused changes in firing within 24 hours.

A second aspect of VSCs is the idea of fixation. This is when the vertebra is in normal position but there is an abnormal range of motion. Whenever a spinal segment is malfunctioning in this way, the result is dysafferentation. Afferentation refers to the transmission of afferent nerve impulses and deafferentation means the lack of afferent nerve impulses. So, dysafferenation refers to an imbalance in afferent nerve impulses, where there is increased nociceptor input (pain) and reduced mechanoreceptor (lack of motion) input.\(^\text{12}\) Research from different fields have verified that joint complex dysfunction alters afferent input in this way.\(^\text{13-17}\)

In order to understand the ramifications of dysaferentation, let’s start by looking at the affected receptors. There are two categories of somatic receptors – nociceptors and mechanoreceptors (the term “proprioceptor” is obsolete term). There are three types of nociceptors:

1. Mechanical nociceptors (which respond to noxious mechanical stimulation),
2. Mechanothermal nociceptors which respond to noxious thermal stimulation
3. Polymodal nociceptors (which respond to mechanical and thermal stimulation plus chemical mediators from injured tissue)\(^\text{18}\)

Spinal tissue nociceptors can be found in the associated skin, blood vessel walls, adipose tissue, joint capsules, ligaments, periosteum, and dura-mater. According to research, nociceptors consist of "a continuous tri-dimensional plexus of unmyelinated nerve fibers that weaves (like chicken-wire) in all directions throughout the tissue."\(^\text{19}\) Paraspinal nociceptors far exceed mechanoreceptors\(^\text{20}\) and they have high threshold – light tough and normal motion will not cause firing.\(^\text{21}\) At spinal cord level mechanoreceptor input (joint movement) can inhibit nociceptor input. It is theorized that reduced mechanoreceptor input (decreased joint range of motion) can enhance nociceptive sensitivity.\(^\text{22}\)

Furthermore, a physiological environment containing chemical mediators of tissue injury such as prostaglandin E-2, leukotriene B-4, bradykinin, histamine, and 5-hydroxytryptamine, reduce the nociceptive threshold, causing a condition called peripheral sensitization.\(^\text{23}\) In fact, local inflammation can cause up to a 100-fold increase in afferent firing.\(^\text{24}\) Peripheral sensitization can lead to central sensitization, which is characterized by increased excitability of nociceptive neurons in CNS (due to reduced thresholds, spontaneous activity, and increased responsiveness).\(^\text{25}\) One study found that just 20 seconds of nociceptive C-fiber stimulation can lead to 90 minutes of spinal cord excitation.\(^\text{26}\)
Nociceptive input reaches the hypothalamus, which means it could trigger neuro-endocrine symptoms.\(^{27}\) And, subcortical responses to nociception input can happen with or without pain, which is referred to as an asymptomatic neuro-endocrine response.\(^{28}\) In one study,\(^{29}\) hypertonic saline injected into the interspinous tissue and paraspinal muscles of normal volunteers. This resulted in pain plus pallor, sweating, bradycardia, decreased BP, “faintness”, and nausea. However, the less pain that was experienced, the more autonomic more symptoms. The researcher concluded that "this is an example of the ability of deep noxious stimulation to activate generalized autonomic responses independently of the relay of pain to conscious levels."

The bottom line is that spinal adjustments can improve spinal joint mobility, recalibrate mechanoreceptors, and bring CNS back to a normal state

**Animal Chiropractic Issues**

Common causes of VSCs include trauma (often minor, repetitive trauma, conformation, the birthing process, confinement, performance injuries, equipment (tugging on the collar), age, and even grooming (Long toenails throws off the biomechanics of the leg which translates to the spine). Symptoms of VSCs include “puppy sitting” (rear legs out to one side), behavior change (perhaps related to pain), evasiveness (sensitive to touch, failure to perform), abnormal posture (lordosis/kyphosis), abnormal gait (lame, ataxic, stiff), lick granulomas, and urinary incontinence.

In chiropractic we speak of the “motor unit” which consists of two adjacent vertebrae, the intervertebral disk, articular facets, ligaments, tendons, muscles, nerves and blood vessels that combine two vertebrae into a movable unit. It is also interesting to note that the boundaries of the intervertebral foramen includes the vertebral notches, intervertebral disk, ligamentum flavum, and the joint capsule of the articular facet. The contents of the intervertebral foramen include the spinal nerve, recurrent meningeal nerve, dural extension, CSF, intervertebral veins, spinal artery, connective tissue, and lymphatic vessels.

Before doing a chiropractic adjustment, typically we do a complete physical exam and appropriate diagnostics. Then the doctor does a chiropractic exam which includes patient observation (analyzing the patient’s posture and gait), static palpation (feeling the vertebral processes and paraspinal musculature), and then motion palpation (feeling how the spinal joints move).

The chiropractic adjustment is a “…carefully regulated thrust or force delivered with controlled speed, depth and magnitude to articulations at or near the end of the passive or physiological range of motion.”\(^{11}\) It is a specific force applied in a specific direction to a specific vertebra. This is a short-lever/high-velocity force along the plane of the zygapophyseal joint.

There are several training options for veterinarians who what to learn this technique.

- Options for Animals - www.Animalchiro.com
- Healing Oasis Wellness Center - www.thehealingoasis.com
- Parker College of Chiropractic - www.parkercc.edu/continuing/index.asp
AVCA certification requires a minimum of 180 hours of instruction including lecture and lab. After completing the course there is a written and practical exam. Then the candidate must submit case reports from their own experience. In order to maintain certification, the animal chiropractor must complete 30 hours of approved CE every 3 years.

It is important to know that laws regarding animal chiropractic vary by state. In some states human chiropractors can adjust animals and in others there are stipulations. Also, the use of the term “chiropractic” is tricky for veterinarians. By definition, chiropractic refers to work on the human spine. I cannot legally say that I am an “animal chiropractor.” I can say that I’m certified by the American Veterinary Chiropractic Association or that I do spinal manipulations.

References
Pathophysiology of Skin Disease
Steve Marsden, DVM, ND, MSOM Lac. Dipl.CH CVA

Objectives
- To identify the six phases of Chinese Medical Theory.
- To understand the role of the gut microbiome in driving skin disease.

Introduction
Dermatological problems in dogs and cats are among the most common and frustrating cases that veterinarians see. Successfully resolving these issues involves understanding new models of skin disease, and the roles that diet, herbs and the microbiome can play in their resolution.

Current Conventional Treatment Approaches
Apart from Omega 3 fatty acids influencing cytokine production, the current use of diet to manage skin inflammation involves the avoidance of antigenic food molecules, particularly proteins. Antigenic proteins are believed to be absorbed intact through the gut mucosa and viewed as foreign by immune cells residing in the lamina propria. Sensitized Helper T cells circulate to the skin, stimulating immune cells residing there to incite inflammation. In short, these animals are understood to be suffering a Type IV hypersensitivity mediated by T cell activation.

Typical strategies to address this problem include wholesale suppression of the immune system using pharmaceuticals; and using extruded diets in which molecular sizes are too small to incite a response. Novel protein diets are also used to avoid antigens to which the system has been previously sensitized. No conventional treatments are used to address the increased porosity of the digestive tract that allows entry of antigenic molecules; or the ability of circulating immune cells to enter the interstitium of the skin. Some of the perceived efficacy of natural therapies in dermatitis appears to be due to a targeting of these aspects of pathogenesis.

Despite conventional therapy, success is often inconsistent, even where a link between skin disease and diet appears to be present. In many cases, inflammation continues unabated when the animal is on extruded diets. New food allergies commonly develop, necessitating a parade of diets featuring ever more exotic protein sources. Immune suppression with drugs often has immediate dose-dependent side effects, as well as delayed side effects like predisposition to infections and tumors. It is for these reasons that owners seek out alternative perspectives and treatments for their pets’ skin diseases.

New Models of Skin Disease
Ironically, one can start with current medical research when looking for a new context in which to view small animal dermatitis cases. The knowledge that gave rise to the therapeutic approaches noted above has been added to significantly to create a schema that embraces this pre-existing model; but also goes well beyond this to suggest many new potential avenues for managing dermatitis. These new directions in research provide support for, and help explain the utility of, alternative therapies such as “real food” (e.g. homemade or raw) as well as various supplements and herbs.
Two broad models are emerging of the main mechanisms by which dermatitis arises. While lacking any official designations, for the purposes of discussion, they can be referred to as Inflammation Dysregulation and Immune Dysregulation. We’ll take a closer look at each of the below.

**Inflammation Dysregulation**

*The Role of Insulin Resistance*

Inflammation Dysregulation is secondary to the metabolic consequences of feeding processed diets. Any excess caloric intake can produce insulin resistance in cats and dogs, including an excess of carbohydrate. The energy surplus produces mitochondria over-activation resulting in an excess of ATP production. Remaining calories are then stored as fat under the influence of AMPK, undermining the ability of insulin to drive calories into cells for further energy production. Cells become less responsive to insulin, but its secretion continues anyway because of the continued caloric surplus, explaining the strong correlation observed between circulating insulin levels and the tendency for weight gains.

Simply gaining some weight might not be a problem, were this anabolic state not associated with inflammation. As body score increases, so do fasting plasma levels of inflammatory mediators like interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1). As feeding of energy-rich easily digested foods continues, cats and dogs enter a state of chronic inflammation. The situation only worsens as they eventually become obese.

Modern research has clarified that this added health risk is due to the elaboration of inflammatory cytokines and adipokines by body fat stores. Leptin, resistin, tumor necrosis factor-α, IL-1β, IL-6 and C-reactive protein all increase in obese dogs and cats, resulting in a persistent, low-grade inflammatory state. This inflammatory state has been shown to play a causal role in chronic diseases such as osteoarthritis, cardiovascular disease, diabetes mellitus and many others, including chronic dermatitis. The oxidative stress that results from chronic inflammatory states serves as an additional aggravating factor, predisposing the animal to tissue damage and tumor formation.

While weight gain is associated with the development of chronic inflammation in dogs and cats, weight loss produces reductions in circulating inflammatory cytokines. In one study of the effects of weight loss in 26 cases of naturally occurring obesity in a range of breeds, body fat mass before weight loss was positively correlated with both plasma insulin concentrations and serum insulin to glucose ratios. Both these parameters decreased after weight loss, confirming the presence of insulin resistance. As weight loss progressed, notable decreases in plasma tumor necrosis factor-alpha (TNF-alpha), haptoglobin and C-reactive protein concentrations were observed.

**Rethinking Current Approaches**

Food processing is widely known to raise the glycemic index of foods, allowing their more rapid absorption and causing an energy glut that, in turn, raises circulating insulin levels and increases the tendency to gain weight. Use of extruded diets, which represent the most extensively processed diets used by veterinary medicine, are thus contraindicated in these patients, behooving clinicians to ensure their patients do not have Inflammation Dysregulation before
prescribing them. Certainly, they should be used only as a last resort in patients carrying excess body weight.

Note, too, that the use of corticosteroids to instead suppress the immune systems of these patients is contraindicated, given their tendency to promote over-consumption, hyperglycemia, and increased insulin secretion.

It’s important to note that in all respects, the link between diet, insulin, body fat, and inflammation in dogs and cats is identical to that demonstrated in humans, to the point that dogs and cats have served as the animal models for researching these phenomena in humans. Since obesity with its secondary inflammatory effects in humans has been repeatedly and consistently linked with the consumption of processed foods, it is thus entirely reasonable to postulate the same is true for dogs and cats. More importantly, it is unreasonable to expect that it is not true.

The Role of the Microbiome

Weight loss is a primary goal in overweight animals suffering chronic inflammation. Weight loss with its attendant reduction in inflammation is achieved in association with, and even because of, shifts in the biome. For example, gut flora has been shown to play a crucial role in influencing metabolism, predisposition to weight gain, and blood lipid levels. Changing the microbiota by altering the diet may eliminate its role in creating a pro-inflammatory metabolism.

Raw and real food diets are being fed on an increasing basis to reduce body weight and tendencies to inflammation. Commercial high protein and high fiber diets produce weight loss with associated characteristic shifts in the microbiome that are identical to what real food diets achieve, suggesting they may work in a similar manner.

A crossover study was performed to examine the effect of raw diets and their functional opposites (namely, highly processed extruded diets) on the microbiome. Raw diet effects included:

- Reduced fatty acid synthesis
- Increased balance and diversity of the microbiome
- A shift in microbiome metabolites towards those associated with a healthy gut
- Increased lactic acid and pH of the stool
- The deleterious and opposite effect on the microbiome to what is needed to reduce body weight and inflammation is one more reason why extruded diets may make the Inflammation Dysregulation patient worse.

Other studies have shown the beneficial effects on the microbiome of real food diets. In one study, the improvements seen when dogs were fed a minced beef diet were reversed when the diet was replaced with commercial kibble.

The notion of processed foods contributing to small animal disease and fostering an obesity epidemic has been understandably unpopular among veterinarians, given the reliance of the profession on these foods for the management of medical conditions, as well as routine feeding. Nevertheless, to make meaningful progress in patients suffering from Inflammation Dysregulation, job one is the institution of a less processed diet. In tandem with the appropriate
insulin-sensitizing herbs, animals with dermatitis arising from Inflammation Dysregulation can be handily cured.

**Immune Dysregulation**

While the microbiome likely plays a key role in inflammation due to weight gain, its role in immune dysregulation is probably even more central. Gut microflora are important drivers of host immunity, help protect against invading enteropathogens, and provide nutritional benefits to the host. Their role when things go awry is still being unraveled, but so far, the discoveries for dogs and cats parallel what has been discovered for humans.

Specifically, shifts in the microbiome can:

- Cause synthesis of metabolites that have an epigenetic role in immune dysregulation
- Increase gut permeability, causing sensitization to antigens within the gut lumen that then propagates to the skin
- Stimulate ongoing inflammation in the gut wall (i.e. inflammatory bowel disease or IBD) to create persistent permeability increases

Cell-mediated immune reactions result from the latter two mechanisms. Helper T cells stimulated into action at gut level through excess exposure to microflora then circulate, eventually prompting Effector T cells in the skin to secrete interleukins that prod macrophages and neutrophils to ramp up their inflammatory response to local skin irritants. In other words, inflammation from a shift in microflora in the gut ramps up the inflammatory response to entirely different antigens in the skin. If both the ‘leaky gut’ and the exposure to the skin are ongoing, inflammatory responses in the skin persist or continue to grow. Conventional treatment with anti-inflammatory and immune-suppressive therapies often provides relief by suppressing the cell-mediated immune reaction in the skin, but may potentiate increased permeability and dysbiosis by impairing local immunity at the gut wall. Once the drugs are removed, then, the dermatitis often fully recurs or even worsens, since the inciting cause of dysbiosis has not been addressed.

Stress can amplify the role of the gut in inducing skin inflammation. It acts through the “brain-gut-skin axis” to suppress gut immunity through increased secretion of cortisol, promoting dysbiosis. Only after enteropathogens have proliferated is the immune system once again incited into activity, producing a cell-mediated inflammatory response that damages the gut wall and leads to secondary skin inflammation.

**Dietary Treatment of Immune Dysregulation**

Clinical experience suggests that if a less processed low glycemic index meat-based diet does not materially improve the condition, then immune dysregulation may be more likely to be present. This may be explained by the plunge in Lactobacillus numbers in stools of dogs fed both high-protein-high-fiber and raw meat diets. Lactobacillus is a major synthesizer of propionic acid in the gut. Propionic acid effects in humans include an immune suppressing and insulin sensitizing effect. It may be that reduction in Lactobacillus numbers following a shift to a raw or real food diet allows immune reactions to increase, or hypersensitivity reactions to be at least maintained.
In these patients, support of Lactobacillus numbers is likely a key directive. Lactobacillus growth is fostered by the presence of fermentable carbohydrates, food stuffs that are notably lacking in low carbohydrate meat-based diets as well as high protein high fiber weight loss diets. Fermentable carbohydrates include both ‘bad guys’ like sugars as well as relatively good guys, like the fructans of various fruits and vegetables; the galactans of various seaweeds; and polyols of various fruits, vegetables and mushrooms. Beet pulp is commonly used to support Lactobacillus populations in pet food. For these animals, any diet on which they experience a consistent subsidence of symptoms is probably the best one to start with and serves as a jumping off point for testing tolerance of diets that are still insulin sensitizing but contain fermentable carbohydrates.

Increasing butyrate levels within the gut should be another prime consideration in the quest for the ideal diet for the Immune Dysregulation patient. More than any other short chain fatty acid, butyrate is credited with enhancing gut wall integrity, tighten the junctions between gut mucosal epithelial cells, thereby reducing the priming of the immune system by lumen contents. Fecal IgA is also increased, helping to bind and inhibit the activities of enteropathogens. Butyrate is synthesized by intestinal bacteria from soluble fiber and resistant starches sources such as beans and potatoes. Other prebiotics that support bacterial populations in their production of butyrate include oats, asparagus, and sweet potatoes. Probiotic plant foods that deliver live, butyrate-producing bacteria to the gut include sauerkraut, kimchi, kombucha, non-dairy yogurts, and tempeh. These fermented foods tend to be rich in lactate, which has a modulating effect on inflammatory processes within the body.

All these plant-based foods are candidates for inclusion in the diet of an Immune Dysregulation patient. Exactly which ones will help a given patient the most has to be determined through trial-and-error. When feeding a carnivore with Immune Dysregulation, inclusion of more whole plant-based foods should not be done at the expense of meat content, however. Higher-protein diets promote greater stomach acidity, reducing the predisposition to small intestinal bacterial overgrowth and deleterious shifts in the microbiome.

Probiotics should also be considered for the Immune Dysregulation patient in the hopes they change flora composition and activity to improve host health. Probiotic benefits include:

- Inhibition of pathogen adherence
- Sealing of the intestinal barrier
- Killing pathogens through bacteriocins produced by commensal flora
- Increasing immunity and the intestinal barrier by stimulating IgA production
- Downregulation of cytokine secretion.

As reviewed by Craig, probiotics have been effective in clinical trials of human atopy, and early exposure to probiotics reduces the intensity of symptoms in models of canine atopy. As reviewed by Miraglia del Guidice and De Luca, many clinical trials have shown that probiotics have the ability to alleviate allergic inflammation, as evidenced by both the control of clinical symptoms and a reduction of local and systemic inflammatory markers.
When the microbiome is suspected as being operative in an animal’s inflammatory condition, certain pharmaceuticals, including antacids and antimicrobials, should be used only with great care to avoid perpetuating or worsening the problem.

At times, antimicrobials may be necessary to correct a dysbiosis, though efficacy is inconsistent. More popular among veterinarians recently has been the use of fecal microbiota transplantation (FMT) to restore normal gut flora populations. Transplants are usually used to address enteritis but should be considered for the allergic patient, given the apparent importance of the microbiome in Immune Dysregulation.

**The Perspective of Traditional Medical Systems**

Each of these contexts suggests new directions to move in - new physiological targets for potentially helpful herbal therapies, drugs, diets and supplements, but which of these is likely to work in a clinically meaningful way, and in what combination? Research will ultimately provide the answers but is time and resource intensive. Meanwhile, the diagnoses and treatments within traditional medical systems that correlate with either Inflammation or Immune Dysregulation provide a time-tested jumping off point for veterinarians to start helping their patients immediately while also providing an initial focus for research efforts.

There are many traditional medical systems to choose from. We will focus here on Chinese medicine, which has a track record of success measured in millennia, along with a very nuanced paradigm, thus increasing the odds of identifying within its disease patterns and diagnoses that correlate to the models described above.

**Damp Heat**

The Damp Heat diagnosis of Chinese medicine correlates perfectly with the western diagnosis of Inflammation Dysregulation. Affected patients are commonly overweight and are commonly afflicted with inflammation (i.e. Heat) in any number of locales – inflammation which is believed caused by the overconsumption of rich or sweet foods. The frequent manifestation of exudates, the carrying of excess body weight, and the worsening of the patient in hot damp weather and climates were the inspiration for the name.

In the Chinese medical model, Dampness is a pathological substance accumulating in the body as a result of faulty digestion. The digestive tract, known as the Spleen, is tasked with converting raw materials into substances that can be used by the body. All these substances are at least partly liquid, including even the various types of Qi; Blood; and the ‘thin fluids’ that lubricate the joints and digestive tract. If the Spleen becomes weakened because of excessive demands (especially due to overconsumption), the conversion of raw materials to healthful fluids is incomplete, and an unusable fluid known as Dampness accumulates instead.

Because it has no utility, Dampness just accumulates in the body. It accumulates anywhere that normal fluids go, including the joint spaces, bladder, and even in the blood vessels. Any pathological tissue accumulation can be a manifestation of Dampness, including benign tumors, lipomas, and especially adipose within the abdomen.
Within the vessels, Dampness is imagined to slowly encroach upon and obstruct the flow of Blood, releasing the Yang energy that impels it as a sort of heat of friction. This is the process by which Dampness accumulations begin to elaborate and become associated with Heat. If the process continues, the Blood stops moving altogether, leading to Blood Stasis and compromised circulation to the associated tissue. Dietary recommendations regardless of the stage of disease are the same – limit the consumption of high starch or high fat foods; and stop overconsumption of all types of food.

Regarding herbs, different treatment approaches are applicable at different stages of the disease’s progression. In the earlier stages, gentle herbs that strengthen the Spleen and drain Damp are more appropriate. As Heat accumulates, more bitter antimicrobial and anti-inflammatory herbs must be used to address the symptoms, while still maintaining Spleen support and draining and drying Damp. The main formula used for this stage, which is the stage of acute cutaneous inflammation, is Si Miao San (Four Marvels Combination). The pulse of these patients and is felt most strongly with only the slightest digital pressure.

As symptoms progress even further, and the pulse becomes deeper and more toned to the touch (i.e. vasoconstricted), herbs that restore peripheral circulation are called for – the so-called Damp dispellers, or even Blood movers. One commonly used formula for this stage is Chu Shi Wei Ling Tang (Eliminate Damp with Poria Five Herb Combination). If the main issue is impaired peripheral circulation, the herb may be used on its own. If there is a lingering Heat of inflammation, then it is paired with Si Miao San (Four Marvels Combination).

These are just commonly used examples of herbs used to manage Inflammation Dysregulation. They are widely available from various vendors although versions manufactured by Kan Essentials and Natural Path Herb Company are designed specifically to treat small animal skin disorders.

Herbs used in the early stages are warming and are thus contraindicated once the patient is in the Heat stage. Careful discernment of the state the patient is in is called for to have maximum clinical benefit without the risk of side effects. These formulas and their precise indications and uses will be examined in detail in the lecture entitled Herbs for Metabolism and Inflammation. Formulas used throughout the disease process tend to have insulin-sensitizing effects.

**Shao Yang Disharmony**
Shao Yang disharmony is the Chinese medical diagnosis that correlates most closely to immune mediated skin disease. These patients exhibit many of the traits associated with immune-mediated disease, including:

- Distinct seasonality to their flare-ups
- Tendency to gastrointestinal inflammation (predisposed by dysbiosis)
- Tendency to concomitant otitis externa, pododermatitis and even periocular dermatitis
- An often-good response to immune suppressant medications that wears off when they are discontinued
- A predisposition to severe excitability or anxiety, which can be associated with an aggravation of skin symptoms (in other words, inflammation that is heightened by an interaction along the brain-gut-skin axis)
All phenomena in the body are considered in Chinese medicine to be derived from Yin, Yang, and the nature of their interaction. Even Damp Heat is essentially considered an extreme accumulation of fluid or Yin (also termed a Tai Yin excess).

Yin and Yang are not static in the body but move inwards and back outwards to stay in step with changes in the environment, such that they can be sequestered away from unfavourable ambient conditions. Yang, which is essentially energy, hides from cool and moist conditions and is thus internalized during the early morning hours and the winter. Yin, which is essentially matter or moisture, hides from hot and dry conditions, and is thus externalized during the morning, and is in some stage of internalization over pretty much the rest of the day. Similarly, it is most evident in spring to early summer, before being sequestered away.

A pump network exists in the body for each of Yang and Yin. “Shao” means lower, so there is a Shao Yin network that lowers or internalizes Yin; and a “Shao Yang” network that lowers or internalizes Yang. Since Yin is heavy, it tends to sink inwards quite readily. Yang, on the other hand, is energy and does not like to be contained. Of the two pumps, then, it is the Shao Yang pump that most often malfunctions. Sometimes it traps Yang in the body interior, which most commonly occurs in the spring months. Sometimes it traps Yang in the exterior, which most commonly occurs in the fall months. Either state can be associated with broad scale skin inflammation.

As a form of energy and an active principle, Yang is a driver of circulation. When it moves outwards from the body core in response to warm weather, it pushes Blood before it. When it is internalizing from the cold, likewise, it pushes Blood before it. The result is something we’ve all experienced – reddening of the face and increased peripheral blood flow on hot days; and the pain of circulatory impairment associated with frostbite or even Raynaud’s disease. Just as with Damp Heat, then, circulatory impairment is a common feature of Shao Yang disharmony. The main formula to treat a broken Shao Yang pump is Minor Bupleurum Combination (Xiao Chai Hu Tang). In skin disease, it is often paired with Four Materials Combination (Si Wu Tang), a Blood tonic and mover, to better regulate the flow of blood.

**Endothelial Dysfunction**

Besides giving us specific ways to assess and treat our Inflammation and Immune Dysregulation patients, both Chinese medical models direct our attention to something that would otherwise never be factored into the biomedical assessment and treatment of the patient with skin disease – their circulatory state. This lack of emphasis notwithstanding, the role of disturbed microcirculation in propagating chronic inflammation has been thoroughly investigated in medical research. Those three decades of work resulted in virtually no drugs to address what turns out to be a ubiquitous problem, and if there are no drugs to treat something, western clinicians are generally taught precious little about it.

In degenerative and chronic inflammatory processes there is too little circulation, due to a phenomenon known as “endothelial dysfunction.” Until recently, medicine believed that inflammatory processes simply burned themselves out, resolving once all antigens that sparked the fire were eliminated. Recent research has confirmed, however, that inflammation does not naturally just fizzle, but must be “actively resolved” through compounds known appropriately as
resolvins, protectins, and lipoxins. These compounds are produced by the same inflammatory cascades that produce pro-inflammatory cytokines and work simultaneously to end the inflammatory process that those same cytokines start. If these compounds are not produced, then the inflammatory process ironically continues to smoulder.

Resolvins and lipoxins don’t throw water on the fire of inflammation themselves, but act through another compound called endothelial nitric oxide (NO). When nitric oxide is not produced in the vessels, this is when ‘endothelial dysfunction’ occurs.

NO is critical to the regulation of vascular responses. Specifically, it regulates:
- Vascular tone
- Regional blood flow
- Leukocyte-endothelial interactions
- Platelet adhesion and aggregation
- Vascular smooth muscle cell proliferation
- Those first four phenomena are crucial in facilitating tissue repair, draining off free radicals and edema, and in ending the ingress of lymphocytes and neutrophils into tissues that drives inflammation.

Specifically, adequate levels of NO:
- Limit further chemotaxis of neutrophils into the inflamed region
- Promote neutrophil clearance from the area via the lymphatic system
- Increase macrophage activity in clearing inflammatory debris
- Reduce excessive vascular permeability
- Promote development of new vasculature
- Vasodilate existing vasculature
- Heighten interstitial antimicrobial defenses

Specific examples of endothelial dysfunction (ED) include many common problems confronting veterinarians, including chronic hepatitis and its attendant portal hypertension with microvascular shunts; inflammatory bowel disease; congestive heart failure; and hypothyroidism. Degenerative joint disease, up until now believed to be due to “wear and tear,” has recently been shown to possess the same circulatory changes that characterize ED. Renal disease and failure, and even mood disorders like depression are yet more manifestations of endothelial dysfunction and impaired microcirculation.

Endothelial dysfunction is so common a disorder that the list is probably far shorter for degenerative and inflammatory conditions that don’t manifest it. Why is the condition so pervasive? Tissue perfusion impairments are very common in patients with insulin resistance, with high circulating insulin levels directly driving development of the condition. Feeding of processed foods is thus a major contributing factor to ED since it is the main cause of insulin resistance in dogs and cats.

As with Inflammation and Immune Dysregulation, we do have plants that counter endothelial dysfunction, including Damp dispellers and Blood movers. The exact plants used in tandem with
the formulas described above to actively resolve chronic skin inflammation is discussed in the lectures on Herbs for Immune Dysregulation and Herbs for Metabolism and Inflammation.

**Conclusion**

Advances in understanding of skin pathophysiology continue despite the relative dearth of new pharmaceutical approaches for the management of dermatitis. Two broad and reasonably mutually exclusive mechanisms funnel into the development of dermatitis, namely Immune Dysregulation and Inflammation Dysregulation.

The mechanisms involved in manifesting each are much more elaborate than the focus by the pharmaceutical industry on itch and wholesale immune suppression would suggest. Many opportunities exist for much more targeted approaches that are both minimally disruptive to the system and much more likely to be curative.

Diet change, various supplements and herbal medicines are the only approaches that currently exist for taking advantage of these opportunities. Traditional healing symptoms help greatly in identifying effective therapies for dermatitis, with anti-Damp treatments working on Inflammation Dysregulation; and Shao Yang approaches addressing Immune Dysregulation. Blood moving and tonifying herbs can be used in tandem or following both approaches to actively resolve residual skin inflammation and counter endothelial dysfunction. See the other lectures in this series for more details on some of these treatments as well as how to determine which of these mechanisms is most operative in your patient.

**References**


Interpreting Findings in Skin Disease
Steve Marsden, DVM, ND, MSOM Lac. Dipl.Ch, CVA

Objectives
- To identify potential causes of skin disease according to the time of year they are aggravated.
- To understand the importance of lesion type and location in identifying the cause of an animal's skin disease.

Introduction
In an earlier lecture, we provided an update on the pathophysiology of chronic or recurrent skin disease, identifying three main mechanisms that underlie it: Immune Dysregulation, Inflammation Dysregulation, and Endothelial Dysfunction. The latter is a feature of most chronic inflammation in most systems in most animals. It is a state of vascular impairment brought about by the failure of inflammation to actively resolve. Either arm of pathophysiology, whether Inflammatory or Immune in nature, can incite the inflammatory responses that then stall out in their resolution as a result of Endothelial Dysfunction. In addition, dermatitis that is “appropriate” such as when due to a skin infection, can also become persistent as a result of Endothelial Dysfunction. Where not associated with Immune or Inflammation Dysregulation, we refer to these cases in this article as “Blood deficient.” Each of these problems is associated with some common clinical findings that we will review here.

Additionally, that earlier article explored the correlations of Inflammation and Immune Dysregulation to diagnoses in Chinese medicine, in order to provide a shortcut to identifying likely effective herbal strategies to neutralize these two disease states. Those diagnoses come with their own diagnostic criteria that we can include with the ones noted above to help clarify where the problem lies with our patient – the regulation of inflammation, or the regulation of their immune responses?

As we review the lists, it is important to remember that diagnosis in holistic medicine is not a deductive process but rather an inductive one. Rather than ruling a diagnosis in our out based on the presence or absence of one finding, such as a lab test, inductive logic involves exploring what is true for a patient, and then asking which diagnosis is most consistent with that set of findings. The more the salient symptoms of a patient are all characteristic of a diagnosis, the greater the likelihood that diagnosis is correct, resulting in a better prognosis for the case when it is treated on that basis. The more that the patient’s salient symptoms cannot all be explained by that diagnosis, the more likely that it is at most only partially correct, and that positive outcomes will accrue more slowly, involving more visits until a single diagnosis finally does emerge.

Diet Impact
Preeminent in our discussion should be the response of the patient to diet change, meaning that it should be the first step that is instituted in the management of these patients. These explorations can be made before the patient even presents to the clinic for their first in-person holistic evaluation, saving valuable time and money in figuring out how to proceed with additional care.
The type of diet change we are referring to is not the switch from one novel-protein kibble to another, but rather a switch to a high protein low starch real food diet, whether raw, freeze-dried, dehydrate or homemade. Probably about the only type of kibble whose influence would illumine for us which pathway of disease is operative in our patient is some sort of high protein high fiber diet. If the animal improves on that diet, or did so in the past, they either have a pure endothelial dysfunction, or they have one that is complicated by Inflammation Dysregulation. Note that if an animal initially improves but then later suffers a relapse while on such a diet, this counts as a non-response to diet change.

The benefits of such a diet change are on lowering insulin resistance and shifting the microbiome towards species favouring weight loss. Dermatitis arising from weight gains and insulin resistance is at the core of Inflammation Dysregulation. Likewise, the chief cause of endothelial dysfunction in animals is insulin resistance stemming for the feeding of processed diets. Higher protein diets also can help restore circulating blood volume, allowing those patients to have sufficient cutaneous circulation to fend off infections and actively resolve inflammation.

One reason a patient might not improve or may get worse on such a seemingly healthy diet is due to a drop in Lactobacilli numbers within the microbiome in response to the diet change noted above. Propionate levels in the gut and circulation would also be expected to fall as a result. Propionate likely has significant immune suppressive effects, such that a major drop in its levels in the gut or bloodstream would be expected to cause any cell mediated hypersensitivity reactions (i.e. Immune Dysfunction) to get worse.

Although not strictly a diet change per se, improvements following just the introduction of omega three fatty acids into the diet tends to suggest the patient has Blood deficiency – that is, deficient cutaneous circulation. These fatty acids increase circulation to epithelial surfaces independent of their effects on inflammation. If the patient improves, they likely had mild endothelial dysfunction in their skin. If the patient worsens then they either have acute skin inflammation that increased blood flow has aggravated; or they have insulin resistance leading Inflammation Dysregulation, which the added fat intake has further aggravated.

Feeding of raw diets to animals with poor digestive capacity can cause gastrointestinal signs or inappetence. These tend to be Inflammation Dysregulation patients in their very early or late stages; or else immune deficiency cases. The latter patients may be presumed to have experienced unfavourable changes in their gut flora in response to the raw diet. Raw diets have been associated in a minority of studies with a greater tendency to enteropathogens in the microbiome.

Response to Previous Treatments
Immune Suppressants
Animals suffering from Immune Dysregulation tend to respond well to immune suppression but will usually relapse once the medications are lowered in dose or discontinued.

Immune dysregulation is often a double-edged sword, with the dermatitis being driven by a cell-mediated hypersensitivity affecting the systemic immune system but weakened local immunity at the epithelial surfaces themselves. Indeed, it is weakened immunity at the mucosal surface of the
gut that drives the systemic hypersensitivity reaction. Thus, continued use of immune suppressants can eventually cause the patient to relapse even while off the drug. This is especially true for powerful drugs like oclacitinib (Apoquel). Local immune stimulant herbs like Bu Zhong Yi Qi Tang (Ginseng and Astragalus Combination) are needed at that point to restore local immunity, potentially followed by formulas to treat the systemic hypersensitivity reaction. If even very low doses of corticosteroids or cyclosporine eradicate symptoms, the patient likely has Blood deficiency, or localized endothelial dysfunction. Blood tonics, a higher protein diet and omega three fatty acids can replace the need for immune suppressants in these cases. If corticosteroids aggravate tendencies to heat intolerance, polyphagia and weight gain, Inflammation Dysregulation should be ruled out.

**Antibiotics**

Inflammation Dysregulation is an excessive but appropriate inflammatory response to probably what should have been relatively mild infections. The problem is not the immune response, but the excesses of the inflammatory response that result. As such, Inflammation Dysregulation is improved by antibiotic administration, as are local cutaneous infections, whether from impaired peripheral blood flow or overuse of immune suppressant medications.

If skin symptoms worsen with the use of antibiotics, then a primary role of dysbiosis (i.e. Immune Dysregulation) in driving the pathology is more likely. Gastrointestinal symptoms arising from antibiotic use are more common in Immune Dysregulation or the latest stages of dermatitis from Inflammation Dysregulation. Use other signs to differentiate these cases.

**Vaccinations**

Vaccines often have a short-term immune depressing effect that can aggravate Immune Dysregulation cases. Once that period has passed, vaccines can also still aggravate Immune Dysregulation, as their adjuvants ramp up existing hypersensitivity reactions. The timeframe following vaccination in which Immune Dysregulation cases typically worsen is within two to three weeks of administration.

**Bathing**

In the model we’ve presented, Inflammation Dysregulation is a normal immune response that results in an excessive inflammatory response. As such, bathing can help reduce the tendency slightly for its propagation in an otherwise untreated animal but doesn’t have a great effect except in the mildest cases. The same is true of Immune Dysregulation, where the real problem, like with Inflammation, is systemic.

Bathing is much more likely to materially benefit those animals with dermatitis arising without a lot of systemic involvement, such as in reduced cutaneous immunity and blood circulation (i.e. Blood deficiency or pure endothelial dysfunction).

**Season of Onset or Aggravation**

The months of onset or aggravation listed below for the various types of skin pathology are for the northern hemisphere. Add about six months to get the approximate months of onset or worsening in the southern hemisphere.
Reduced cutaneous immunity (usually in response to drug therapy) typically worsens for a couple of months on either side of the winter solstice, during the same months that pure endothelial dysfunction or reduced cutaneous blood flow also worsens. Worsening during March and April in dry windy conditions may also be seen for either of these two conditions. Immune Dysregulation cases also worsen in spring, fall, or both. Generally, fall aggravations begin as early as late July and can extend through to just before December. Spring aggravations begin earlier as early as late January or February but are generally gone by late April.

Acute Inflammation Dysregulation cases often appear like clockwork for a few weeks on either side of the summer solstice, when skin circulation is maximal. Chronic cases, where circulation to the body exterior is obstructed, often worsen in the few weeks on either side of the winter solstice. Subacute cases may be worse at both solstices.

Table 1 - Seasons of improvement and aggravation. Pink months are when the associated diagnosis commonly worsens; and green months when it may improve

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**Time of Onset or Aggravation**
Most skin patients will be itchier when they first get up in the morning. Inflammation Dysregulation cases, especially if acute, will continue to be itchy until the early afternoon. Pure immune and circulatory deficiency cases will improve as the morning progresses into afternoon. Immune Dysregulation can be worse again in the evenings and all the way through to the wee hours of the next morning, whereas acute Inflammation Dysregulation cases often subside over that same timeframe, unless they are physically active. Nocturnal itching is most often associated with Immune Dysregulation, pure immune deficiency (such as from immune suppressant drug overuse), and pure endothelial dysfunction.

**Behavior**
Given the importance of the Brain-Gut-Skin axis in their pathophysiology, Immune Dysregulation cases will often tend to extreme behavior abnormalities, whether excitability, anxiety or aggression. Symptoms will generally be very pronounced, so much so that they are of equal concern to the owner as the skin complaints.
Inflammation Dysregulation cases are generally congenial but can be excitable, in the manner of your average Labrador Retriever.

Immune and circulatory deficiency cases may exhibit anxiety or fear aggression as well, but with the intensity of an incidental finding rather than a primary health concern.

**Lesion Location and Appearance**

Lesions characterized strictly by small fine powdery or tiny translucent flakes of dander affecting the dorsolateral surfaces signal Blood deficiency – that is, a pure endothelial dysfunction issue. Large or discolored dander flakes indicate Damp Heat (or Inflammation Dysregulation) as do the moist tacky lesions of Surface Pyoderma. Acute Damp Heat lesions are most prevalent on ventral surfaces.

Superficial pyoderma is associated with Blood deficiency if they are dry, flaky and dorsally located. If the lesions are oilier and dorsally located, then the problem is chronic Damp Heat. Both the dry and moist lesions described above can occur in Shao Yang disharmony (Immune Dysregulation). Immune Dysregulation cases often have concomitant otitis externa, periocular rashes, eye redness and pododermatitis. Severely erythematous lesions of the ventral neck are pathognomonic for Immune Dysregulation, although the redness may involve the entire ventral abdomen.

Lesions associated with bacterial overgrowth and weak superficial immunity can occur anywhere on the body, but especially in hairless areas and on the dorsolateral surfaces. If due to overuse of immune suppressive drugs, deep pyoderma can result. Mild lesions and symptoms tend to be associated with very chronic low-grade Inflammation Dysregulation, immune deficiency, and Blood deficiency. Failures of hair to re-grow following clipping, or general tendencies to hair loss not associated with active skin inflammation, are most often caused by Blood deficiency.

**Laboratory Findings**

- Anemia
- Normocytic normochromic nonregenerative anemia suggests Blood deficiency
- Liver Enzyme Elevations
- Mild to moderate elevations suggest Liver Blood deficiency.
- Moderate to high elevations are most often associated with either Immune or Inflammation Dysregulation. Rarely, Blood deficient cases can manifest this way, too.
- Depressed Liver Function
- Low levels of the products of liver metabolism, including one or more of BUN, albumin, ALP, ALT and cholesterol are almost invariably indicative of Liver Blood deficiency
- Eosinophilia

This is usually associated with Shao Yang disharmony

**Imaging Studies**

- Interpretation of imaging studies is self-explanatory
- Splenomegaly almost invariably indicates Shao Yang disharmony (because of the ongoing stimulation of the entire systemic immune system).
- Muco-coeles indicate either Immune or Inflammation Dysregulation.
- A small liver indicates Blood deficiency, particularly if Doppler ultrasound identifies vessel attenuation. Portal and cutaneous blood flow vary in tandem.

**Appetite and Thirst**
- One elevated and one depressed
- This is suggestive of Dampness and Damp Heat.
- Low appetite in the mornings
- A low appetite in the mornings only can be indicative of either Inflammation or Immune Dysregulation.

**Thirst**
- As manifestations of Shao Yang disharmony, Immune Dysregulation patients particularly seek out ice cold snow or water to drink
- Concomitant Respiratory Symptoms
- Reverse sneezing and snoring usually comes from Dampness accumulation. Collapsing trachea is almost invariably due to a Shao Yang disharmony disrupting the normal descent if Qi down the Triple Burner
Herbs for Metabolism and Inflammation
Steve Marsden, DVM, ND, MSOM, LAC. Dipl.CH CVA

Objectives
- To be able to list at least one Damp Heat formula and how it works both biomedically and in Chinese medical terms to resolve skin diseases presentations.
- To be able to name at least one formula addressing blood deficiency and how it works in biomedical and Chinese medical terms to resolve skin disease.

Introduction
Previous articles in this series have developed a more current understanding of the pathophysiology of dermatitis and discussed the primary importance of diet change in their management. This paper provides some herbal medicine recommendations to accelerate and make more improvements in affected animals, while waiting for diet change to eventually exert its effect.

The two main pathophysiologic mechanisms driving skin disease are Inflammation Dysregulation and Immune Dysregulation. This paper deals with the herbal management of Inflammation Dysregulation as well as the Endothelial Dysfunction that accompanies chronic dermatitis arising from both mechanisms.

The paper will discuss the general principles driving herb choice so that veterinarians can begin to assess the utility of the products already existing on their shelves. Additionally, specific Chinese herbal formulas that incorporate these principles are recommended. These formulas were developed over many centuries, resulting in increased safety and efficacy. They are available from a variety of vendors.

The recommendations below most specifically apply to versions of these formulas that are available through both Natural Path Herb Company and the Kan Herb Veterinary Essentials line. Both product lines are available in the USA from A Time to Heal Herbs (https://atimetohealherbs.com) and in Canada through the Natural Path Herb Company website (https://nphc.ca)

The following table provides the author’s starting dose recommendations for liquid, tablet and granular extracts for the formulas discussed in this paper:

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<th>BID Dose (tsp granular extracts)***</th>
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*At the present time, only Kan Veterinary Essentials provides the formulas in liquid form
**Tablets available from Kan Veterinary Essentials
***Required dose of granules from Natural Path Herb Company may be as little as half these amounts, due
to their higher purity and lack of excipients

**Endothelial Dysfunction**

Endothelial dysfunction is a perturbation of the local blood supply that hinders the active resolution of chronic inflammation. It is a feature of dermatitis arising from both Inflammation Dysregulation (Damp Heat) and Immune Dysregulation (Shao Yang disharmony), but milder forms also exist where a reduced circulating blood volume (Blood deficiency) is the major aggravating factor.

The condition often improves with the introduction of higher protein real food diets. In mild, so-called Blood deficient cases, the extra nourishment provides the raw materials needed to synthesize more blood and increase the volume delivered to the skin. Inflammation Dysregulation or Damp Heat cases also improve because these diets reduce insulin, which is an important driver of endothelial dysfunction.

One manifestation of reduced cutaneous blood flow is a predisposition to exogenous cutaneous infection, because of an associated dearth in the interstitium of macrophages and histiocytes. Specific examples include:

- Localized demodex infestations
- Localized dermatophyte infection
- Superficial pyoderma
- Seborrhea sicca and alopecia are common manifestation of cutaneous hypoperfusion arising from Blood deficient endothelial dysfunction. Co-morbidities that may respond to treatment of Blood deficient endothelial dysfunction of the skin include KCS (keratoconjunctivitis sicca) and lymphocytic thyroiditis.

**Treatment Principles**

Endothelial dysfunction is characterized by:

- Vasoconstriction and vessel attenuation
- Gaps between endothelial cells that allow microscopic formation of edema
- Reduced endothelial budding that perpetuates the poor vascularity and impedes healing
- Increased adhesion of neutrophils and pro-inflammatory cells to the lining of blood vessels, facilitating their accumulation and degranulation in tissues
- Reduced macrophage presence, raising vulnerability to infection

Herbs used to treat endothelial dysfunction should counter one or more of these features. A prime example is Rehmannia glutinosa.

As a single herb, Rehmannia has been shown to significantly reduce dermatitis scores, ear thickness, and serum histamine levels in laboratory animal models of atopic dermatitis. Histological analysis demonstrated decreased thickening of the dermis and epidermis, along with reduced dermal infiltration by inflammatory cells. Much of the credit for this effect stems from Rehmannia’s ability to inhibit not just inflammatory cytokines like IL-4 and TNF-α, but also VCAM-1 and ICAM-1.¹
The latter two compounds are cell adhesion molecules that facilitate entry of white blood cells into the interstitium. White cell ingress requires they must first be ‘tethered’ to the endothelium as they flow past. Leukocytes are then activated by chemo-attractants on the endothelium. As adhesion becomes even more firm, leukocytes can eventually undergo trans-endothelial migration into the dermis. While ‘selectins’ are responsible for initial tethering, adhesion is governed by β2 integrin (ICAM-1) and α4 integrin (VCAM-1), and it is these two compounds that Rehmannia inhibits.

Many other plants have been shown to ameliorate different aspects of endothelial dysfunction in the skin and should probably figure prominently in any effective formula for the condition. Uncomplicated Endothelial Dysfunction (Blood deficiency)

For our discussion of a specifically recommend formula for endothelial dysfunction, we will focus particularly on those cases due to Blood deficiency. The enhancement of peripheral circulation in Damp Heat cases will be covered in the next section.

In pure Blood deficiency, the skin appears dry and flaky and may even exhibit alopecia. The coat feels coarse, the tongue is often pale or a washed-out lavender color, and the pulse at the femoral artery proximal to the knee feels relatively attenuated.

Since half the problem in this form of endothelial dysfunction is reduced circulating blood volume, any one lesion incited in response to a cutaneous pathogen eventually produces enough acute inflammation that the lack of localized blood flow is overridden. Unfortunately, since there is not enough blood to go around, this leaves another area vulnerable. The net effect, then, is a shifting of location of skin lesions, none of which are particularly severe.

When circulating blood volume is reduced, peripheral circulation to the dorsum and extremities is particularly reduced. Symptoms of Blood deficiency, then, include a preponderance of lesions on the dorsal and dorso-lateral skin surfaces, while the extremities including the paws and ears become cool to the touch. The ear margins may become chronically inflamed, resulting in ear margin dermatosis. The pulse feels thin and weak, reflecting the low blood volume and reduced peripheral circulation. Lesions on these surfaces are particularly apt to worsen during the winter months but may even be seen in early to mid-spring.

Omega three fatty acids are commonly used by veterinarians in managing dermatitis since they provide the raw materials that will shift cytokine production from those of a pro-inflammatory nature to those that actively resolve inflammation. This shift takes time, but the compounds also act immediately as peripheral vasodilators. An immediate response of dermatitis to omega three fatty acid supplementation is thus pathognomonic for cutaneous Blood deficiency.

**Si Wu Xiao Feng Yin (Four Materials Eliminate Wind Powder)**
The formula to treat this disorder in dogs (for it rarely occurs in cats) is Si Wu Xiao Feng Yin (Four Materials Eliminate Wind Powder, Natural Path Herb Company; Dry Derma Relief, Kan Herb).
In addition to the effects noted above for Rehmannia, the formula achieves its benefits by stimulating the bone marrow to produce more red blood cells, through the actions of Dang Gui and Rehmannia. The formula also contains ample aromatic herbs, the volatile oils of which mobilize circulation to the periphery and act as broad-spectrum antimicrobials.

**Case Management**

Adverse effects may be seen with this formula and other ‘Blood tonics’ if the inflammatory response turns out to be more acute than originally appreciated, which is especially likely to occur in animals that actually have Inflammation Dysregulation. Stronger anti-inflammatory formulas may be needed, such as Si Miao San (Four Marvels Combination) or Chu Shi Wei Ling Tang (Eliminate Damp with Poria Harmonize the Stomach Combination). These two formulas are discussed in the next section. Fortunately, the intensity of any adverse events will be mild and limited to the appearance of seborrhoea oleosa, pruritis and an increase in erythema, while exudates may become moister.

**Inflammation Dysregulation**

A hallmark of patients with Inflammation Dysregulation is their tendency to chronic or recurrent inflammation at multiple epithelial surfaces over time, including often the gastrointestinal tract. These patients appear to have a heightened inflammatory response to an irritant or stimulus, driven chiefly by insulin resistance arising from the long term feeding of a processed diet. The animal is often overweight, and their medical record becomes peppered over time with instances of otitis externa, colitis, dermatitis, conjunctivitis and cystitis as though inflammation is roving around the body.

The most important intervention for these patients is a real food diet that can lower insulin levels, induce weight loss and create favourable shifts in the microbiome. High protein high fiber commercial weight loss diets may create some of the same benefits. Diets that are rapidly digestible, particularly if carbohydrate-based, increase insulin secretion which, in turn, reinforces current inflammatory tendencies. This link between diet and inflammation has been established in many species including humans, horses, and laboratory animal models. While waiting for these diet changes to undermine the process of Inflammation Dysregulation and dermatitis, herbs and formulas for the Chinese medical diagnosis of Damp Heat can be used to further expedite improvement. Bitter ‘cold’ anti-inflammatory and antimicrobial herbs are
indicated for more acute cases of inflammation, while more ‘warming’ and aromatic herbs are used to improve peripheral circulation and actively resolve chronic cutaneous inflammation. Formulas for both strategies, whether for acute or chronic inflammation, have insulin-sensitizing effects.

**Acute Inflammation**

Acute inflammation in Inflammation Dysregulation (or Damp Heat), although ultimately diet driven, may be triggered by just about any irritant. The inflammatory response is more exuberant than necessary and may be exacerbated in the mid-summer (May and June) when peripheral circulation is maximal.

The acute nature of the inflammation can be confirmed by palpating the pulse. While chronic inflammation is characterized by deeper firm pulses, acute inflammation is characterized by more superficially felt pulses, which vary from bounding to toneless.

Lesions in acute inflammation from Damp Heat tend to be especially prominent on the ventro-medial surfaces of the torso and limbs. Alopecia may occur because of the severity of the inflammation.

In addition, there may be systemic inflammatory tendencies affecting also the pancreas, intestinal tract, bladder, colon, bile ducts and ears. The patient (usually a dog and especially a Retriever) can manifest other problems typical of metabolic syndrome, such as obesity and hyperadrenocorticism.

An occasional tendency to seizures is not uncommon, as is osteoarthritis, particularly in the stifle or lumbosacral joints. Pain at the lumbosacral region can be severe.

The patient commonly exhibits increased appetite or thirst (or both, in some cases). The paws and ears feel warm. The animal may be heat intolerant and exhibit a red or even dark red discoloration on the underside of its tongue.

**Treatment Principles**

The goal of treatment of acute inflammation arising from so-called Damp Heat, or Inflammation Dysregulation, is to provide an ice pack effect on the skin while at the same time reducing insulin resistance and the metabolic events that are responsible for the exuberance of the inflammatory process. Coix is an important herb in small animal Chinese herbal medicine that exhibits both these effects. Its ability to inhibit nitric oxide synthesis, as well as superoxide production and release by macrophages, confers an anti-inflammatory effect while at the same time, Coix fosters insulin sensitization. The ultimate goal in many Inflammation Dysregulation cases is weight loss, and Coix has been shown to assist with that, too.²

**Si Miao San (Four Marvels Combination)**

An excellent example of an acute-acting anti-inflammatory formula for the treatment of Inflammation Dysregulation is Four Marvels Combination. It is the most commonly used Chinese herbal formula in small animal veterinary medicine, testifying to the frequency with which veterinarians treat acute inflammation.
Figure 2. Four Marvels Combination

<table>
<thead>
<tr>
<th>Herb</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cang Zhu</td>
<td>Atractylodes rhizome</td>
</tr>
<tr>
<td>Huai Niu Xi</td>
<td>Achryanthus root</td>
</tr>
<tr>
<td>Yi Yi Ren</td>
<td>Coix seed</td>
</tr>
<tr>
<td>Huang Bai</td>
<td>Phellodendron bark</td>
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Several herbs enhance the effects of Coix in Si Miao San. Phellodendron has demonstrated antioxidant activity in numerous studies and has an anti-inflammatory effect through its inhibition of the production of inflammatory cytokines and nitric oxide. It inhibits expression of the gene for iNOS, as well as tumor necrosis factor (TNF-alpha).

Si Miao San as a formula has been shown to improve insulin sensitization and signalling. Berberine, a plant compound extracted from Phellodendron in Si Miao San, has been shown through a systematic review of clinical trials to improve multiple aspects of Type II diabetes and insulin resistance, including blood glucose markers such as HbA1c, hyperlipidemia and hypertension. Phellodendron as a whole has been shown to directly combat the central mechanism by which insulin resistance is generated, by reversing the inhibition by AMPK of glucose and lipid oxidation, facilitating the removal of adipose stored in hepatocytes. Si Miao San also contains Atractylodes, which has been shown to improve several metrics in diabetic patients.

Case Management

Si Miao San can significantly lower the dose of prednisone required to control cutaneous inflammation, while helping prevent the insulin resistance and metabolic syndrome-related side effects that corticosteroids tend to foster. In any case that is reliant on corticosteroids for adequate symptom control, consideration should be given for its concomitant use.

When the peripheral circulation is more attenuated, as evidenced by a weak deep pulse, Si Miao San is less likely to benefit the patient, and due to its strong “ice pack” effect on the skin, may precipitate skin dryness. If the formula otherwise appeared beneficial, then rather than using Si Wu Xiao Feng Yin described in the last section, the single herb known as Dang Gui (Chinese Angelica) may be added to help restore and normalize skin circulation, about 20g of granular extract per 100g of Si Miao San granular extract.

If dryness is not present, but the circulation has internalized with Si Miao San’s use, a second formula known as Chu Shi Wei Ling Tang (Eliminate Damp with Poria Harmonize the Stomach Combination) may be introduced. At this point, the patient’s dermatitis should appear milder, and more subacute to chronic.

Chronic Inflammation

In chronic inflammation due to Inflammation Dysregulation, the peripheral circulation is reduced, with the pulse palpating often as deep and firm. On occasion, it will still be superficial, but will now feel feeble and forceless.
As with endothelial dysfunction, the goal now is to improve peripheral circulation, while still addressing the underlying concern of insulin resistance and metabolic predisposition to inflammation.

A major formula that accomplishes both of those goals is Chu Shi Wei Ling Tang (Eliminate Damp with Poria Harmonize the Stomach Combination).

| Chu Shi Wei Ling Tang (Eliminate Damp with Poria Harmonize the Stomach Combination) |
|---------------------------------|-----------------|
| Bai Zhu                         | Atractylodes rhizome |
| Cang Zhu                        | Atractylodes rhizome |
| Chen Pi                         | Citrus peel      |
| Fu Ling                         | Poria            |
| Hou Po                          | Magnolia bark    |
| Ze Xie                          | Alisma tuber     |
| Tong Cao                        | Rice Paper pith  |
| Gan Cao                         | Licorice root    |
| Sheng Jiang                     | Ginger rhizome   |
| Da Zao                          | Jujube           |
| Rou Gui                         | Cinnamon bark    |
| Hua Shi                         | Talc             |
| Fang Feng                       | Ledebourriella root |
| Zhi Zi                          | Gardenia fruit   |
| Deng Xin Cao                    | Rush pith        |
| Di Fu Zi                        | Kochia fruit     |

Figure 3. Chu Shi Wei Ling Tang (Eliminate Damp with Poria Harmonize the Stomach Combination)

Chu Shi Wei Ling Tang was originally developed to treat shingles in humans. It is anti-inflammatory, but not anywhere near as strongly as Si Miao San. The formula is derived from Wei Ling Tang (Harmonize the Stomach with Five Herbs and Poria Combination), which is most commonly used to address subacute inflammation of the pancreas, liver, stomach and small intestine. Both Gardenia and Atractylodes are anti-inflammatory while Kochia fruit contains significant amounts of vitamin A to promote epithelial integrity. The formula’s aromatic herbs help resolve inflammation both in the skin and the GI mucosa. Normalization of epithelial circulation results in the gut and skin inflammation healing simultaneously.

The specific clinical presentation calling for Chu Shi Wei Ling Tang includes:
- Toned pulses
- A pale or slightly purplish tongue
- Chronic tendencies to soft stool or small bowel diarrhea, but not colitis
- Rashes that are often mild in appearance and shifting in location
- Predominantly ventro-medial lesion distribution, although superficial pyoderma may appear in winter
- An aggravation of GI and potentially even skin complaints by antibiotics
An aggravation of GI complaints by anti-inflammatory drugs.

Chu Shi Wei Ling Tang tends to be more effective than any other formula for animals with severe and extensive lichenification. Chronic endothelial dysfunction can produce both the profound thickening of the dermis from continued chronic inflammation and the reduced immune surveillance that allows bacteria and yeast to overgrow and continue propagating the inflammation. These animals may exhibit a clear benefit from shampooing and oral antimicrobials. Use of Chu Shi Wei Ling Tang in these cases may help minimize any adverse effects of the antimicrobials on GI function and boost cutaneous circulation through its content of powerful aromatic compounds.

The warm circulation enhancing effects of the formula can worsen skin symptoms if the inflammation was more acute or subacute than anticipated. If this happens, use Si Miao San (Four Marvels Combination), simultaneously or instead, until the acute inflammatory response has subsided. Use of the two formulas together can also be continued until all skin symptoms have resolved.

References

7. Seo WG et al. Inhibitory effects of methanol extract of seeds of Job’s Tears on nitric oxide and superoxide production in RAW 264.7 macrophages. Immunopharmacol Immunotoxicol 2000 Aug;22(3):545-54
Herbs for Immune Dysregulation
Steve Marsden, DVM, ND, MSOM, Lac. Dipl.CH CVA

Objectives

- To identify a formula that addresses Wei Qi deficiency and how it likely helps skin disease in biomedical term.
- To identify a Shao Yang disharmony formula and how it likely helps skin disease in biomedical terms.

Introduction

Previous articles in this series have developed a more current understanding of the pathophysiology of dermatitis. The two main pathophysiologic mechanisms driving skin disease are Inflammation Dysregulation and Immune Dysregulation. This paper deals with the herbal management of Immune Dysregulation.

The paper will discuss the general principles driving herb choice so that veterinarians can begin to assess the utility of the products already existing on their shelves. Additionally, specific Chinese herbal formulas that incorporate these principles are recommended. These formulas were developed over many centuries, resulting in increased safety and efficacy. They are available from a variety of vendors.

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*At the present time, only Kan Veterinary Essentials provides the formulas in liquid form

**Tablets available from Kan Veterinary Essentials
**Immune Dysregulation**

The term “dysregulation” is chosen here as the best description for the role of the immune system in generating allergic dermatitis, because the condition is not strictly due to an overactive immune system. It has both an immune deficient and hypersensitivity aspect, both of which must be successfully addressed for the animal to be cured of the condition. Immune suppressive drugs are thus not a complete solution, which is why the condition keeps returning when these drugs are discontinued and may even get more severe each time they are withdrawn. Effective treatment must include an effort to stimulate the local immunity of the gut in order to have any hope of stopping the condition, or at least delaying its recurrence.

The reason that the local immune response of the gut is so important is that it is one of the main factors in creating and preserving a healthy microbiome within the intestinal tract. Otherwise, “dysbiosis” or an imbalance in gut flora can arise that increases the predisposition of the patient to a so-called leaky gut.

One way that increased gut porosity, otherwise known as a leaky gut, can arise is if enteropathogens build up and incite an inflammatory response that affects gut wall integrity. In that event, the immune system within the lamina propria gets too good a look at lumen contents, with more antigens being presented than usual to the gut associated lymphoid tissue. The dendritic cells that process those antigens circulate in greater numbers, stimulating T Effector cells within the systemic immune system to a larger degree than normal. The T Effector cells, in turn, ramp up other immune reactions currently in process, which are most commonly located at other epithelial surfaces, including the skin.

This mechanism, known as cell-mediated hypersensitivity, is well known to veterinarians, such that the concomitant occurrence of gastroenteritis with dermatitis is considered highly indicative of food allergy hypersensitivity. What veterinarians may not realize is that this same mechanism can be invoked by non-pathogenic flora that still end up increasing gut wall porosity, but through different mechanisms.

One way flora can increase gut porosity is through their inactivity. Under normal circumstances, the microbiome converts soluble fiber into short-chained fatty acids (SFCAs) that maintain gut wall integrity. Diets lacking in sufficient soluble fiber for that particular patient and its microbiome can result in lower levels of butyrate being produced. This SCFA is the one most credited with maintaining gut wall integrity by keeping junctions between epithelial cells tight.

Other strains play more of an active role in increasing the leakiness of the gut. They metabolize dietary gluten to produce a compound that opens the gaps between intestinal epithelial cells.

Both of these reactions would not necessarily be accompanied by gastroenteritis, thus offering no indication the gut is involved in generating the animal’s skin complaints. The patient might still
respond, however, to diet change, providing the veterinarian with a clue that a food-mediated hypersensitivity is still somehow being produced.

Local immunity at the gut wall thus deserves more attention than veterinary medicine gives it in treating allergic dermatitis. For decades, the focus of treatment has been on providing novel proteins in the diet that are not yet antigenic to the patient and suppressing the cell-mediated reaction that is currently occurring. No drugs or treatments are deployed to boost mucosal immunity, and this crucial step in pathology remains unaddressed in western treatment protocols, allowing the animal to acquire new allergies, necessitating a parade of ever-increasingly exotic protein sources in the animal’s diet to maintain symptom control. Fortunately, while there are virtually no drugs to resort to in boosting gut immunity, there are many herbs and herbal formulas.

Another important factor in determining local gut immune response is stress. Animals highly prone to stress have increased circulating cortisol levels, which can have an immune suppressive effect at the level of the gut mucosa, allowing the wrong types of bacteria to proliferate and damage the gut wall. Providing calming herbs can likewise help in an indirect fashion in fostering the right kinds of species in the microbiome.

**Treatment Principles**

Based on the foregoing, there are three main ways an herbal medicine can address immune dysregulation manifesting as immune-mediated dermatitis.

- Support a normal local immune response within the gut to correct dysbiosis
- Modulate the cell-mediated immune reaction being propagated to the skin
- Reduce stress as a cause of immune suppression and secondary enteropathogen proliferation.

Astragalus-based formulas such as Ginseng and Astragalus Combination (Bu Zhong Yi Qi Tang) are used to support or restore normal and local immunity within the gut, while Minor Bupleurum (Xiao Chai Hu Tang) derivatives work through all three pathways (see Tables 1 and 2).

**Table 1. Bu Zhong Yi Qi Tang (Ginseng and Astragalus Combination)**

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<td>Chinese angelica root</td>
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<tr>
<td>Huang Qi</td>
<td>Astragalus root</td>
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<td>White atractylodes rhizome</td>
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<td>Chen Pi</td>
<td>Citrus peel</td>
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<tr>
<td>Gan Cao</td>
<td>Licorice root</td>
</tr>
<tr>
<td>Sheng Ma</td>
<td>Cimicifuga rhizome</td>
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Astragalus-based Formulas for Local Immunity

Several studies illuminate the role of astragalus (*A. membranaceus*) in the correction of dysbiosis. Polysaccharide extracts from the plant have been shown to alter gut microbiota and the SCFAs they synthesize in diabetic mice.\(^1\) Another study in broiler chickens showed a reduction of pathogenic gut flora and a concomitant increase in commensal and symbiotic species.\(^2\)

Indeed, astragalus (Huang Qi) is much studied for its ability to improve productivity in farm animals by correcting the microbiome. The plant was shown in pigs to reduce diarrhea secondary to dysbiosis, leading to enhanced growth rates and improved digestibility of food. Improved microbiota health was also indicated by an increase in species diversity and was likely due to an improved immune response against enteropathogens, as evidenced by increases in IL-2 and TNF-alpha.\(^3\) The same general impact was seen in a study on chicks, where the plant extract was used in tandem with probiotics to successfully combat pathogenic strains of E.coli.\(^4\)

Minor Bupleurum for the Systemic Immune Reaction

Minor Bupleurum consists of three key herbs: Bupleurum (Chai Hu), Scutellaria (Huang Qin) and Panax Ginseng (Ren Shen). It is an herbal powerhouse for the management of immune dysregulation caused by “leaky gut” with all three plants showing efficacy independent of each other in all three areas of correcting dysbiosis:

- Reducing predisposition to, and the adverse effects from, stress on microflora
- Modulating the immune system to support local immunity or reducing the intensity of cell-mediated immune reactions

Dysbiosis

With respect to dysbiosis, Bupleurum was shown in the context of another formula, Bupleurum Soothe the Liver Combination (*Chai Hu Shu Gan San*), to protect microflora from pathogenic overgrowth.\(^5\) Scutellaria (in the formula Huang Lian Jie Du Tang) has been shown to help restore normal gut flora in rats by reducing pathogens and increasing the presence of bacteria that do not incite inflammatory responses. SCFA synthesis increased accordingly.\(^6\) Many studies support the use of Ginseng for the correction of dysbiosis secondary to antibiotic use.\(^7\)

Brain-gut-skin axis
Ginseng is widely known as an adaptogenic herb that can normalize and optimize adrenal gland output of cortisol, lessening its secretion in times of repetitive stress, but increasing it when increased alertness is required. Normalization of cortisol secretion reduces immune suppression that otherwise allows enteropathogenic bacteria overgrowth. Scutellaria species likewise have research support for their long history of use in treating anxiety and other CNS organic and mood disorders. Bupleurum has likewise been shown to reduce depression and anxiety in animal models of repetitive stress.

**Immune Dysregulation**
Wogonin, found in Scutellaria, has been analyzed for its ability to support normal immunity and reduce inflammatory bowel changes in colitis in rats. Levels of protective IgA were increased, while IgE levels associated with hypersensitivity were maintained at low levels. The ability to induce local immunity in the gut was increased in rats given wogonin, but the intensity of the inflammatory response during colitis was reduced, making Scutellaria a true immune modulator.

A decrease in bowel wall integrity can increase exposure of the immune system to endotoxins (LPS), sparking an inflammatory response that can propagate to the skin. Administration of bupleurum tempers the pro-inflammatory effects of LPS exposure, while supporting phagocytosis and removal of the offending antigens. Bupleurum’s tempering effect of an immune response has been widely studied and demonstrated at other mucosal surfaces as well, including for the reduction of allergic responses at respiratory epithelia.

**Endothelial Dysfunction**
Despite a panoply of beneficial compounds and effects, Minor Bupleurum is seldom sufficient by itself to resolve allergic dermatitis. Ginseng and Astragalus Combination must often be used afterwards to help prevent recurrences of the condition, but to fully resolve the systemic hypersensitivity reaction, herbs must also be employed to actively resolve inflammation within the skin itself.

As with Inflammation Dysregulation, a certain degree of endothelial dysfunction characterizes the inflammatory response of the skin, allowing it to continue to smolder and not wind down to a conclusion. By combining one part Si Wu Tang (Four Materials Combination) with two parts Minor Bupleurum, the herbalist can avail themselves of the beneficial effects of Rehmannia in inhibiting white blood cell egress into the dermis; and of both Rehmannia and Chinese Angelica in boosting circulating blood volume to help the skin heal.

<table>
<thead>
<tr>
<th>Table 3. Si Wu Tang (Four Materials Combination)</th>
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<tbody>
<tr>
<td>Bai Shao Yao White Peony root</td>
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<tr>
<td>Chuan Xiong Ligusticum rhizome</td>
</tr>
<tr>
<td>Dang Gui Shen Chinese Angelica root</td>
</tr>
<tr>
<td>Shu Di Huang Prepared Rehmannia root</td>
</tr>
</tbody>
</table>
References

Essential Oils 101: An Introduction to the Basics
Jared Mitchell, DVM

Objectives
- To understand what essential oils are and how they work.
- To understand the basics of essential oil history, chemistry, how they are produced, and quality control measures.
- To understand how to select the highest quality, unadulterated essential oil.

Definitions
- Essential Oils: Aromatic, volatile liquids distilled from plants.
- Volatile: A substance that is readily vaporizable at relatively low temperatures.
- Hydrosols: The condensate water coproduced during aromatherapy.

What Are Essential Oils?
Essential Oils are the aromatic, volatile liquids distilled from certain parts of plants. This can include leaves, stems, barks, roots, flowers, and in the case of citrus oils, the rind. However, it is important to remember that not every plant can be utilized to harvest essential oils. While sources may vary on the exact number, scientists estimate that there are nearly 400,000 plant species on the planet with about 2,000 new plant species discovered or described each year, many of which are already on the verge of extinction. Estimates show that approximately 3,000 essential oils are known with about 300 commercially available.

A Brief History
Aromatic plants and essential oils have been used in some form for thousands of years. Their use in medicinal and ceremonial practices, such as with physical ailments, meditation, spiritual and prayer rituals, and behavior modification, are well documented throughout history. The Egyptians were among the first to use essential oils some 6,000 years ago. They were using them in virtually every aspect of life from medicinal benefits and beauty care to spiritual and ceremonial rituals.

Following the Egyptians, evidence for essential oil use in the ancient world can be noted among every major society. Rome, Greece, China, India, and Europe all advanced the study of aromatherapy. One of the most famous stories of aromatherapy in the ancient world which still resonates today is that of “grave robbers” who used a combination of essential oils and herbs to prevent illness during the Bubonic Plague of Europe.

The modern resurgence can be attributed to Rene-Maurice Gattefosse, a French chemist, during the early 1900s. In 1910, he suffered severely burned hands due to an accident at his lab. He dipped his arms into a vat of Lavender EO and felt immediate relief. The medicinal properties of Lavender aided his healing and provided for a more rapid healing time.

How Plants Store Essential Oils
Plants can carry essential oils in different locations within the plant. Some carry the oils so close to the surface that the simplest of movement or stimulation from wind or insects can stimulate the release of the vapors into the air. Other plants may require a more forceful stimulation such
as bruising or roughing the plant to release the oils that are found deeper inside the plant. Finally, there are some plants that require a large amount of disturbance, such as cutting the root, to release the stored essential oils.

In general, essential oils are found either outside or inside a plant’s structure.

<table>
<thead>
<tr>
<th>External secretory structures / cells</th>
<th>Internal secretory structures / cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Glandular trichomes</td>
<td>-Internal secretory structures are classified as either cavities or ducts</td>
</tr>
<tr>
<td>-Easily “burst” to release essential oils</td>
<td>-Depends on the plant and its purpose</td>
</tr>
<tr>
<td>-Act as both protectors and attractants</td>
<td>-They are held between cells and released when disturbed or when neighboring cells are damaged or disintegrates</td>
</tr>
</tbody>
</table>

How Plants Use Essential Oils

Because most plants are stationary. Instead they must rely on their surroundings, i.e. their environment. Plants use essential oils for a variety of reasons. These can include:

- **Nourishment** (nutrition, hormones, vitamins, minerals, energy reserves)
- **Protection** (anti-fungal, anti-bacterial, anti-septic, immune stimulating, antioxidant, repels insects and pests, protecting from cold and heat, and environmental damages),
- **Attraction** (communication with surrounding environment, aids in pollination), and
- **Regeneration** (oxygen rich, transporters, intra and extra cellular repair, DNA/RNA modulation, helps modulate dehydration).  

Essential Oil Chemistry

Essential oils are extremely complex. A single oil can contain hundreds of chemical compounds. Knowledge of the chemical composition and which chemical constituent predominates can give insight into how the oil will behave when used in a clinical setting.

The biochemical properties of essential oils fall into two main categories:

1. Terpenic Hydrocarbons
2. Phenylpropanes

Terpenoid compounds predominate. They are composed of the hydrocarbon building unit isoprene.

\[
\text{H}_3\text{C}\begin{array}{c}
\text{C} \\
\text{H}_2\text{C}
\end{array}\begin{array}{c}
\text{C} \\
\text{CH}_2
\end{array}
\]

Classes of terpenes are named according to how many isoprene units are present.

- Monoterpenes (C10) = two isoprene units
- Sesquiterpenes (C15) = Three isoprene units
- Diterpene (C20) = Four isoprene units
- Triterpenes (C30) = Six isoprene units
- Tetraterpenes (C40) = Eight isoprene units
Essential oils can consist of these plain hydrocarbon units or they may contain functional groups. These can include alcohols, aldehydes, esters, ethers, and phenols.

**Methods of Essential Oil Application**

Three main application techniques:
- 1. Inhalation
- 2. Topical
- 3. Oral/Ingestion

The physiology of how essential oils interact and influence the body, while appearing simple at first glance, is in fact a very complex and in-depth process that intertwines numerous mechanisms within the body to exert the desired effect.

When inhaled, essential oil molecules travel up along the nasal passages and interact with receptor sites that line the olfactory epithelium. These receptors send signals to the olfactory bulb, which transmits signals to the limbic system.\(^\text{11}\)

The limbic system is the part of the brain that is most connected to our “primitive” brain. This is where memory and emotions are housed. The limbic system is related to the Autonomic Nervous System (ANS) and functions as the automatic part of our brain. This is very important for our veterinary patients because most of the animal’s world is influenced or “seen” by smell. Topical application is another common method for applying essential oils. Remember, essential oils are lipophilic in nature (they like fatty substances) and therefore are readily absorbed through the skin and into the bloodstream.

Absorption is not hindered by the presence of hair in our animal friends. In fact, a large amount of absorption can occur along the hair shaft. The hairs can act as “wicks” and allows for an increase in the absorption of the topically applied essential oils.\(^\text{12}\)

Oral administration of certain essential oils has been utilized and documented for various conditions. Caution should be used and proper training, experience, and safety guidelines using unadulterated, pure quality essential oils must be considered and followed.

Overlapping benefits can be achieved when using these methods. For example, when an oil is inhaled, it can interact with the olfactory aspects of the body but can also be absorbed by the mucus membranes and thus enter the bloodstream as well. Likewise, when applying an oil topically, the oil will directly affect the body systems by direct absorption, but also the pet, which has a heightened sense of smell, will benefit from the inhaled features of the oil as well.

**How Essential Oils Are Produced**

There are two main methods for producing essential oils. The first, and most common, is by steam distillation. The second method, cold pressing, applies to the production and extracting of citrus oils.

1. **Steam distillation**: The most common method for extracting essential oils. This method uses the application of heat applied to the part of the plant being distilled. The steam
causes the plant’s cell wall to breakdown and release the essential oils. The steam containing the vaporized essential oils passes through a condensing chamber. Here the mixture is cooled and reforms into a liquid. Because essential oils do not mix with water, they will float on the top and thus can be separated and collected.\textsuperscript{13}

2. \textit{Cold Pressing}: This method is used exclusively with the citrus oils and is considered a mechanical process. No heat is required for the process to work while producing the oils. Lemon, orange, lime, and grapefruit are examples of citrus oils produced from cold pressing.

- \textit{Carbon dioxide extraction}: This is a newer process which can be used for extracting essential oils. Carbon Dioxide has a unique property and can transform into a supercritical state which means it can be both a gas and a liquid. The gas must be kept at a constant temperature and a high pressure. The result is a gentler process. However, it is a much more expensive process when compared to steam distillation.\textsuperscript{14}

\section*{Purity and Quality Control}

Purity and quality are two of the most important attributes to consider when choosing essential oils.

With the growing interest in essential oils, both as therapeutic aids and everyday home décor, research into these amazing products is growing. To fulfill these increased demands, scientific research and testing methods continue to advance making it easier to analyze and determine the purity and quality of essential oils.\textsuperscript{15}

Purity and quality are not just what is in the bottle. It begins with the environment and land used to grow the plants. It should be clean and free of chemicals that could leach into the plants as they grow. Seed selection is also of great importance. Choosing wisely and using the most organic, non-GMO (genetically modified) seeds that have not been treated with any form of chemicals furthers the quality of the oils produced. The process continues through the growing and harvesting process with no chemical use and truly knowing how to grow, harvest and distill the plants to produce the purest and most therapeutic essential oils. A great deal goes into producing an unadulterated, pure quality essential oil. It is truly an art as well as a science.

Here are some questions to ask an oil company when choosing an essential oil.\textsuperscript{16}

Do they grow their own plants, or do they use outside suppliers? Are the techniques and procedures used at all their supplier’s farms uniform and consistent? Is the company checking each step of the process to make sure no synthetic chemicals are being used? Do they visit their supplier’s farms? Can you visit their farms? Do they know the complexity of harvesting at peak times, and how to distill the oils properly with the use of low pressures and temperatures? Are the distillation cookers made of the correct material to prevent chemical reactivity between the oils and the metal? Is each batch tested with five different chemical analyses? Are the oils tested by outside / independent laboratories? Do the oils smell and feel like true essential oils, or do they feel synthetic or chemical in nature? Is the botanical info provided by the company listed correctly on the bottle? In other words, does it list the complete scientific name down to chemotype?
**Gas Chromatography (GC) and Mass Spectrometry (MS)**
These are two scientific tests that can be performed in laboratories to help determine the quality and purity of essential oils. Gas Chromatography is a technique used to separate volatile compounds into their individual components. An essential oil sample is vaporized and carried through and absorbent column, where the components separate. When they exit the column, a signal is generated. The results produce a chromatogram with varying peaks. This is proportional to the concentration of the corresponding substance. Combined with the Mass Spectrometry, which allows us to look at the molecular mass spectrum of each chemical, these tests are known as Gas Chromatography-Mass Spectrometry (GC-MS).\(^\text{17}\)

![Gas chromatogram from the GC-MS analysis of the lemon essential oil](image)

**Proper labeling**: Even though we have mentioned proper labeling before, it is important enough to spend some time focusing on its importance. Adulteration is very common within the modern essential oil world. It is important to know and trust that what is in the bottle is really what is in the bottle. That is why the bottle should include the proper labeling information. This should include the complete scientific name all the way to the chemotypes.

**Essential Oil Safety**\(^\text{18}\)
When working with essential oils, just as with other all natural or pharmaceutical treatments, safety is an import aspect to consider, especially when prescribing essential oils for our clients to use with their pets. It is also critically important to adhere to safety guidelines and protocols when working with our animal patients due to their size and increased senses.

1. Utilize an unadulterated, pure quality essential oil from a company you trust that can produce quality testing reports.
2. The essential oils should be clear in appearance with no chemical or offensive (rancid) smell. *A few exceptions in color can appear.
3. Use and store oils in airtight, amber, glass bottles and avoid direct sunlight.
4. Keep stored in appropriate locations and out of reach of children and pets.
5. When diffusing essential oils:
a. Allow for an “escape” route so the animal can move to an area without essential oil exposure
b. Do not run diffusers for extremely long time periods
   i. Start slowly with no more than 10 to 15 minutes at a time.
c. Although essential oils are used for treating medical conditions, when possible alternate oils that are being diffused.
6. When topically applying oils use dilution guidelines and patch test.
7. Avoid using essential oils directly in the eyes and ears.
8. Avoid or use with extreme caution in pets who are pregnant or debilitated with medical conditions such as seizures. Also avoid or use extreme caution with oral administration.
9. Avoid exposure to sunlight for 48 hours with oils that are photosensitive:
   a. Orange, Lemon, Tangerine, and other citrus oils
10. If essential oils get into pet or human eyes
    a. DO NOT USE WATER
       i. Water will spread essential oils
    b. Carrier oils (coconut oil) have been used in the past
    c. Flush with saline solution
11. If skin reaction occurs wash with soap (unperfumed) and water for at least 10 minutes

It is important to note that most reported toxic exposures that are reported in humans and animals come from improper storage or usage of essential oils. These are very concentrated and very little is needed.

As we expand our knowledge of essential oils, safety guidelines will continue to be revised. Staying up to date is important. Dr. Robert Tisserand provides updated safety info through the Tisserand Institute and can be accessed at [www.tisserandinstitute.org](http://www.tisserandinstitute.org).

**Dilution Guidelines**

Essential oils are very concentrated and very powerful. One of the hardest concepts to understand is how little is required when using EOs. Due to animal’s heightened senses, a small drop of undiluted oil can be very overpowering to our pets. That is not to say that in emergency situations and in certain advanced conditions, with the proper training, EOs could be applied “neat” (undiluted). However, dilution is recommended.19

In an essential oil bottle:
- 5ml bottle contains approx. 150 drops
- 10 ml bottle contains approx. 300 drops
- 15 ml bottle contains approx. 450 drops

Common dilutions used in veterinary medicine:17
- Diffuser: 1-4 drops essential oil with 50 ml (1/4 cup) - 100 ml (1/2 cup) water
- Topical:
  - To 30 ml (1 ounce) distilled or spring water, add this many drops essential oil:
    - 1% dilution = 5-7 drops (cat or small dog)
    - 2% dilution = 10-15 drops (medium or large dog)
    - 5% dilution = 25 - 30 drops (small farm animal)
    - 10% dilution = 50-60 drops (horse)
References

Adding Essential Oils into Everyday Practice
Jared Mitchell, DVM

Objectives
- To understand how to introduce unadulterated, pure essential oils into a veterinary practice.
- To identify areas within a practice where essential oils could be utilized.
- To become familiar with select essential oils that are well known, easy to work with, and a great starting point to introduce essential oils into practice.

Introduction
I am often asked how to incorporate essential oils into everyday clinical practice. My colleagues often want to know how their clients or fellow veterinarians will react. The truth is there are no easy answers to these questions. Nothing is “cookie cutter.” There is no “one size fits all” and no “one way” to incorporate essential oils into everyday practice. You, as the veterinarian, know your clients and your colleagues better than anyone. You will be the best advocate to find areas and opportunities to educate and incorporate the use of essential oils within your practice and the community.

One important point to remember: integrating essential oils into practice cannot be forced, it must be introduced and embraced in its own time. And don’t be surprised if there are some instances where no amount of education or exposure will convince clients or colleagues about the amazing world of essential oil use. Sometimes they must experience it for themselves.

Understanding Essential Oils
Essential Oils are the aromatic, volatile liquids distilled from certain parts of plants. This can include leaves, stems, barks, roots, flowers, and in the case of citrus oils, the rind. When discussing essential oils, remember, volatile refers to a substance that is readily vaporizable at relatively low temperatures.1

Essential oils are produced in 2 main methods. Steam distillation is the most common method used. Cold pressing is the other method used and is exclusively dedicated to the production of citrus oils.2 Producing the highest quality pure essential oils is a very specific and labor-intensive process. Assuring purity and quality is one of the most important aspects of introducing essential oils into practice. Clients, staff, and colleagues must know that they are safe and effective.

Essential Oil Safety
Safety is an important issue no matter how familiar someone is with essential oils. From novices to aromatherapy experts, guidelines and protocols for safe use of essential oils should be reviewed often as new research and scientific data emerge.

Safety is key when introducing essential oils into a veterinary practice. These are public settings with many different variables to consider. While most clients are receptive and enjoy the use of essential oils in practice, some may not. If this is the case, we must respect our clients and their concerns. We can create notes in our practice software and when a particular client is in the clinic, we can discontinue the use of the essential oils and put them in an exam room that does not have a diffuser.
It is important to discuss essential oil safety with clients when prescribing any take home regimen as a treatment plan that the clients will be administering. It is a good idea to have a typed-up plan in hard copy form to send with clients as a take home handout for them to refer to as needed. Here are a few safety recommendations:\(^3\)

1. Utilize a pure quality essential oil
   a. Find a company that you trust that produces pure quality oils and that can produce quality testing reports.
2. The essential oils should be clear in appearance with no chemical or offensive (rancid) smell.
   a. A few exceptions in color can appear
3. Use and store oils in airtight, amber, glass bottles and avoid direct sunlight.
4. Keep stored in appropriate locations and out of reach of children and pets.
5. When diffusing essential oils
   a. Allow for an “escape” route so the animal can move to an area without essential oil exposure
   b. Do not run diffusers for extremely long time periods
      i. Start slowly with no more than 10 to 15 minutes at a time.
   c. Although essential oils are used for treating medical conditions, when possible alternate oils that are being diffused.
6. When topically applying oils use dilution guidelines and patch test.
7. Before beginning a treatment protocol with essential oils, it is recommended to perform baseline tests such as bloodwork (CBC, Chemistry panel) and routinely monitor as needed.
8. Avoid using essential oils directly in the eyes and ears.
9. Avoid or use with extreme caution in pets who are pregnant or debilitated with medical conditions such as seizures. Also avoid or use extreme caution with oral administration.
10. Avoid exposure to sunlight for 48 hours with oils that are photosensitive:
    a. Orange, Lemon, Tangerine, and other citrus oils
11. If essential oils get into pet or human eyes
    a. DO NOT USE WATER
       i. Water will spread essential oils
    b. Carrier oils (coconut oil) have been used in the past
    c. Flush with saline solution
12. If skin reaction occurs wash with soap (unperfumed) soap and water for at least 10 minutes

How My Journey with Oils Began
As with most, my journey with essential oils came about through personal experience. You could say it all started with my wife and a turtle. Each played an important role in the addition of essential oils within my life and within my practice.

My wife was the first to introduce me to essential oils. She had torn the tendon in her foot and everyday tasks were painful and difficult. We had consulted with all the traditional physicians that were available. She saw her general practitioner, podiatrist, and even an orthopedic
specialist. They tried different pain medications, anti-inflammatories, boots, casts, and even the mention of surgery that would carry a success rate of 50% and may require additional procedures as she aged. Nothing gave her the relief she was looking for until she experienced essential oils firsthand. They gave her the relief she needed in an all-natural form without the side effects of pharmaceutical medications.

After seeing my wife’s experience and her results firsthand, I began to research the science and art of aromatherapy and essential oils. I was amazed at what I learned. And the more I learned, the more I wanted to know. I decided that I wanted to incorporate the essential oils into my veterinary practice, but I was not sure where to start or how they would be received. This is where the turtle comes in.

Amelia, as she would come to be known, was a wild box turtle who was attacked by a dog and suffered severe trauma and a broken carapace. The turtle was stabilized, and the shell was surgically repaired using a wiring technique. Post-operative treatment included antibiotics and pain medications. Amelia responded well postoperatively and began healing very well. However, there was a piece of the carapace that had been torn off and was not able to be attached. This left an open wound. I decided that this would be the perfect case to begin utilizing essential oils.

I applied 1 drop of Lavender mixed with a carrier oil to the wound twice daily. Within the first week, I noticed healing beginning. As I continued, I noticed more and more healing. I was amazed. As I continued to research I found a study that showed that lavender oil has the potential to promote wound healing in the early phase by acceleration of formation of granulation tissue, tissue remodeling by collagen replacement and wound contraction through up-regulation of TGF-β. This sold me on incorporating essential oils into my everyday practice.

**Where to Start?**
A clinic’s support staff can be the lifeline of the veterinary practice. From receptionists, to technicians (veterinary nurses), and kennel staff, they are the first people most clients interact with when coming into your practice. Working with your staff and getting them on board with incorporating essential oils is a must. Consider holding educational staff meetings and allowing the staff to try the oils. Once the staff experiences the benefits of the oils and become more comfortable with them, they will be advocates to help clients better understand how to safely use essential oils with their pets. This helps send a uniform message from everyone in the clinic.

Another way to help introduce clients to essential oils is through client education materials. You can create your own, or you can find some from the essential oil company that you choose to use. Displays can also help to open the conversation on essential oils. These can be placed in the reception area or in the exam rooms. The clients can look at the display and ask questions if they are interested. This way they do not feel pressured. It also highlights the particular brand that you use and recommend. When setting up a display, I recommend using empty bottles of essential oils. This will prevent any from accidently “wondering off” or “spilling” if a bottle is dropped and broken.

Diffusers placed throughout the clinic, especially in the reception/waiting area or the exam rooms help start conversations with clients as well. The key is to remember important safety
features and choose an oil or a blend that is not too overpowering but creates an uplifting atmosphere within the clinic. Switch your oils and do not always diffuse the same over and over. You can use a mini dry erase board or a small chalk board to list the oils you are diffusing for the day in a manner similar to the “daily special” signs of restaurants.

Specific Uses for Essential Oils Within a Clinic

Air Purification: As we all know veterinary facilities have a multitude of smells. Some can be pleasant and others not so much. Essential oils can aid in keeping a pleasant and uplifting aroma within the clinic. However, they do much more than that. They can aid in purifying the air and the environment. Certain essential oils have been shown to have antimicrobial and antifungal effects when diffused. This can keep odors and infectious agents from spreading throughout the clinic. Still others have been shown to have a calming effect on pets and their owners. Animals can sense the fear and the negative emotions in an environment. Diffusing essential oils known for their calming effects can be very beneficial for nervous pets who usually will not cooperate and have unpleasant veterinary visits.

Improving Healing Ability for Wounds and Post Operatively: From the routine, elective surgeries performed daily to the more advanced soft tissue and orthopedic procedures, surgeries are common in most veterinary practices. Essential oils can be incorporated into the post-operative treatment plan to help manage pain and inflammation as well as helping with tissue healing.

Because essential oils are lipophilic, they are stored in the fat cells. Other chemicals such as petrochemicals, cleansers, and creams also have an affinity for fat cells. In some cases, essential oils can facilitate the absorption of certain topical medications and chemicals. Care should be taken when using products together and consultation with a trained veterinary aromatherapist is recommended.

Halitosis and Dental Problems: Halitosis is a very common complaint among clients at their wellness visits. However, there are many other dental problems that can afflict our patients. Common clinical signs of dental problems can include bad breath (halitosis), broken or loose teeth, abnormal or excessive drooling, abnormal or difficult chewing, unusual or unpleasant smells, discharges, bleeding, pain, and swelling. It is reported that periodontal disease is the most common dental condition affecting dogs and cats. While proper dental care and routine dental cleanings are often needed, essential oils can help reduce dental problems including halitosis and inflammation within the mouth.

Emergency Visits: Essential oils can be utilized in emergency situations as well. One important difference from day to day use for chronic medical issues, is that most of the time the oils are applied undiluted or “neat” during emergency situations. This allows for the most potent effects from the oils. Care should still be taken and once the pet is stabilized a more routine treatment plan with properly diluted essential oils can begin.

When using essential oils in emergency situations one must consider the patient’s temperature and hydration status as these can affect how quickly the oils will be absorbed and utilized by the body. They can be used as a standalone treatment or combined with other medications and
treatment modalities. As you begin to incorporate essential oils into practice, it is a good idea to have an emergency oil kit just as we have our standard emergency kits and crash carts for traditional medicine.

Behavior: Behavior problems are some of the most common problems seen in veterinary practices. They can also be some of the most challenging to treat, frustrating both owners and veterinarians alike.

Essential oils can be very helpful at addressing behavior problems. They can also provide a safer option as direct contact is not always needed. Techniques such as diffusing, misting the pet or environment, as well as applying essential oils directly to oneself as a natural diffuser are easy starting points and generally much safer when trying to gain the pet’s trust.

In my clinic, it has been my experience that both clients and pets appear to be more relaxed and gain more from the visit when we are diffusing essential oils in the reception / waiting area as well as the exam rooms. We couple this with other techniques to help calm the pets and make them as comfortable as possible. This in turn relaxes the client which further relaxes the pet. While not openly included in the “Fear Free” certification, essential oils, when used properly can easily fit into the fear free philosophy and can readily be utilized in a practice already practicing the fear free method.

With the help of essential oils, a veterinary clinic can produce an environment with reduced anxiety, stress, and fear. A less anxious pet is a calmer pet. And a calm pet makes for a calm vet. As you incorporate essential oils into behavior modification it is important to remember the importance of imprinting. Aromas are very powerful and can lock in memories. So, when an animal experiences an oil for the first time they could lock in the emotion that is occurring with the olfactory experience. These can be good or bad emotional responses. Veterinarians and clients should be aware of this and try to introduce essential oils when pets are at their calmest and allow them to associate the aromas with positive experiences. This allows for a much better response from the pet when the oils are needed in times of sickness or stress.

Utilizing Essential Oils and Other Holistic Modalities
If you are new to holistic veterinary medicine or you’re just looking to add a new modality to your practice essential oils are a great starting point. They can often be used as stand-alone treatments or combined with western medical practices as well as other holistic modalities to synergistically improve overall health and well-being. Laser therapy, acupuncture, chiropractic, animal massage, energy medicine, TCVM modalities, and nutrition are some areas where combining essential oils can be helpful.

Laser therapy has become a well-known and viable non-pharmacological method to reduce pain and inflammation as well as promote faster wound healing. Essential oils can be added to the treatment protocol, and the use of the laser can help drive the oils deeper into the tissues, allowing for a more synergistic form of healing. While I have never experienced any problems, it should be noted that some aromatherapists recommend using caution when using essential oils and lasers so as not to create a photosensitive reaction. Knowledge of laser therapy, essential oil
use, and which brand of laser and oils is an important learning process before using essential oils with lasers.

Essential oils can be utilized in acupuncture and traditional Chinese veterinary medicine (TCVM). They are often classified using criteria similar to Chinese herbal medicine, via the law of signatures, five elemental associations, nature or temperature, taste as well as aroma, and channel affiliation.15

**Multi Species Advantage for Clinics**

Essential oils give clinics an advantage at treating multiple species. The oils can be strong enough to fight off infections, yet gentle enough to use on exotics. Dilution is extremely important when adding essential oils to the treatment protocol of an exotic.16

**A Few Basic Oils to Begin**

**Lavender (** *Lavandula angustifolia***)

Lavender is probably the most well-known essential oil. Much research has been conducted throughout the years. Many consider Lavender to be the “Swiss army knife” or the “universal oil” when studying aromatherapy. Lavender’s properties are many and include antiseptic, antifungal, analgesic, relaxing, anti-inflammatory, and antitumoral.

The Anti-inflammatory mechanisms are thought to exhibit effects through the inhibition of lipoxygenase, prevention of leukotriene synthesis, inhibition of the cyclooxygenase-2 enzyme, inhibition of pro-inflammatory cytokines, and repression of pro-inflammatory genes.17 Lavender is well known for its ability to balance the autonomic nervous system and reduce stress and anxiety. In 1 study it was concluded that the scent of lavender oil and its active component, linalool, affects autonomic neurotransmission and reduces blood pressure through the central histaminergic nervous system and the suprachiasmatic nucleus.18

**Frankincense (** *Boswellia carterii***)

Frankincense is considered the “holy anointing oil” in the Middle East. During ancient times it was considered more valuable than gold. Over the ages, it has been used to treat every variation of illness known. It has properties known for being anti-inflammatory, anti-infective, tissue healing, immuno-stimulating, and antitumoral.19

**Helichrisum (** *Helichrysum italicum***)

This essential oil is also known as Immortelle or Everlasting. It is often used to help prevent or lessen bruising, help with tissue healing, and helps to stop bleeding. Reported medical properties include antioxidant properties, antispasmodic, chelates chemicals and toxins, and helps with neurologic issues by regenerating nerves.20

**Copaiba (** *Copaifera officinalis***)

Produced from the gum resin of specific neotropical trees. It has powerful anti-inflammatory properties as well as neuroprotective, anxiolytic, and antimicrobial properties. β –caryophylline, a sesquiterpene hydrocarbon, is the main chemical component with anti-inflammatory effects. It acts much like an NSAID by blocking the oxidation of 5-lipoxygenace, a major player in the inflammatory cascade, thus reducing pain and inflammation.21
**Peppermint (**Mentha piperita**)**  
Peppermint is one of the oldest and most highly regarded herbs for soothing digestion. Medical properties include anti-inflammatory, antibacterial, antiviral, antifungal, and digestive stimulant. Its fragrant influence has been known to be purifying and stimulating to the conscious mind. This makes it a great choice to use as a “smelling salt.”

**Vetiver (**Vetiveria zizanoides**)**  
Vetiver is very useful for “grounding” or bringing patients back into reality and back into themselves. It is well known for its anti-inflammatory properties as well as its relaxant, antiseptic, and antispasmodic properties.

The chemical composition of vetiver can be very complex, containing upwards of 100 sesquiterpene-type compounds and their derivatives, which are thought to produce the calming effects noted when using this oil.

**References**


Essential Oils and Cancer
Jared Mitchell, DVM

Objectives
- To introduce basic terminology, concepts, and pathophysiology of cancer.
- To introduce the basic premise of essential oil use in cancer.
- To introduce and have a working knowledge of a few basic essential oils and their uses in cancer treatment.

Introduction
“Growths” or “masses” are non-descriptive terms used to describe the physical appearance of any lump or bump. A malignant tumor (or neoplasia) is one that can be severe in nature and spreads from the area of origin to another area within the body. A benign tumor is one that does not spread but may be locally invasive.

In general, when we hear the term cancer used today, it is most often referring to a neoplastic tumor. Once a diagnosis is made, the treatment options can be physically and psychologically challenging to the patient. Essential oils are a great integrative option to help balance the body’s homeostatic mechanisms and allow for a stronger immune system when battling cancer.

What is Cancer
The Merriam-Webster dictionary defines cancer as a serious disease caused by cells that are not normal, proliferate in an uncontrolled way, and can spread to one or many parts of the body.\(^1\) While the definition may seem straightforward and easy to comprehend, cancer is a much more complex pathological disease entity.

Cancer can originate anywhere in the body. In a normal animal, the cells grow and divide to form new cells as they are needed. As the cells become old or become damaged, they die, and new ones take their place. This cycle of cell growth, death, and replacement is a very tightly regulated process. When cancer develops the orderly process is disrupted. As cells become more and more abnormal the old or damaged cells survive. New cells continue to form when they are not needed.\(^2\)

Cancer Statistics
Humans\(^3\)
An article focusing on 2018 cancer statistics was published by the American Cancer Society in the journal *CA: A Cancer Journal for Clinicians*. The article provides a status report on the global burden of cancer worldwide using the GLOBOCAN 2018 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer, with focus on geographic variability across 20 world regions.
- 18.1 million new cancer cases
- 9.6 million cancer deaths
- In both sexes combined, Lung cancer is the most commonly diagnosed cancer (11.6%)
- Lung cancer is the leading cause of death (18.4% total cancer deaths)
- Female breast cancer (11.6%)
- Prostate cancer (7.1%)
- Colorectal cancer (6.1%) for incidence
- Colorectal cancer (9.2%),
- Stomach cancer (8.2%)
- Liver cancer (8.2%) for mortality

Animals
- Approximately 1 in 4 dogs will, at some stage in their life, develop neoplasia.
- Almost half of dogs over the age of 10 will develop cancer.
- Dogs get cancer at roughly the same rate as humans
- Half of all breast neoplasms in dogs and greater than 85% of all breast neoplasms in cats are malignant

Work done by the ATR of Genoa, Italy, between 1985 and 2002 showed that all cancer incidence was 3 times higher in female than in male dogs, a difference explained by the high rate of mammary cancer observed in female dogs.

Causes of Cancer
Cancer is a disease that alters genetic control of cell functions, especially how they grow and divide. While this can be considered a genetic disease because of how it affects the genes, it should be noted, however, that inheritability is different. Estimates show that only 5% of cancers are inherited. This means all other cancers come from some form of environmental exposure or stress to the body’s natural homeostatic mechanisms.

Inflammation’s Role in Cancer
Inflammation in simplest terms is the reaction of tissues to an irritant. This is by far an oversimplification of a very complex and dynamic process. Inflammatory responses play decisive roles at different stages of tumor development, including initiation, promotion, malignant conversion, invasion, and metastasis. Inflammation also affects immune surveillance and responses to therapy. In recent studies, the cytokine IL-6, a major mediator of inflammation and activator of signal transducer and activator of transcription 3, serves to block apoptosis in cells during the inflammatory process, keeping them alive in very toxic environments. Unfortunately, these same pathways serve to maintain cells progressing towards neoplastic growth, protecting them from cellular apoptotic deletion and chemotherapeutic drugs.

Other Environmental Considerations in Cancer
Environmental factors can also affect the formation and progression of neoplastic cancers. Environments where pets are under constant stress weakens the immune system, promotes chronic inflammation, and allows proliferation of neoplastic cells.

Toxic environments allow for the production and proliferation of cancers. These toxicities can include physically contaminated environments such as those containing multiple chemicals like scented plug ins and cleaning products, but also psychological contamination with negative energies and emotions.

General Treatment Options for Cancer
a. Medical Management
Many forms of treatments exist in today’s modern medicine. These can include oral tablets and capsules, injectables, and topical forms. Some can be administered easily, while others require the direct administration or supervision of a trained oncologist. The mainstays of modern cancer treatment are radiation and chemotherapy. These are not without side effects such as weakness, lethargy, nausea and vomiting, as well as neuropathies, and alopecia along with other skin disorders.

b. Holistic management
Complementary and alternative treatment modalities can be of great benefit when battling a disease entity such as cancer. In some cases, they can be used as a stand-alone treatment or they can be used synergistically with standard prescribed treatments such as chemotherapy and radiation.
Holistic management looks at more than just the disease and its symptoms. It focuses on the entire pet, both physically and emotionally, as well as nutrition and environment.

Early Research with Essential Oils and Cancer
In the 1990s academic research was conducted on the antitumor activity of terpenoid essential oil components. Perillyl alcohol, a terpene alcohol closely related to limonene, was tested in clinical trials for its efficacy against mammary cancer.

Proposed Mechanisms by which Essential Oils Affect Cancer
Essential oils can affect cancers in numerous ways: From preventing secondary infections to reducing patient anxiety as well as inhibiting tumor growth in certain cancers. Elson and Peffley investigated the HMG CoA reductase. They observed that HMG CoA reductase of tumor cells differs from that of healthy cells but resembles that of fungi. Fungal organisms usually experience an explosive growth rate. In turn, they are able to switch off the synthesis of the membrane stabilizing steroids. So, the HMG CoA reductase does not switch off like it is supposed to in the presence of excess steroid molecules. However, plants have learned how to switch this enzyme off. Plant terpenes are able to fight fungal infections by shutting down their steroid synthesis, which thereby inhibits fungal growth. By observing that the sterol insensitive HMG CoA reductase of tumor cells resembled that of fungi, they concluded that the reproduction of the cancer cells might be inhibited with essential oils.

Essential Oils and Their Role in a Cancer Treatment Protocol
Dr. Anne-Marie Giraud-Robert is a French physician who has contributed groundbreaking clinical studies in the field of aromatherapy and its use with cancer. She concludes that essential oil treatments improve quality of life in cancer patients. This can occur by reducing the side effects of traditional cancer treatments and cancer drugs as well as stimulating the natural defenses and draining toxins from liver and kidneys. Within her studies, Dr Giraud-Robert also noted that with essential oil treatments an increased efficacy of conventional treatments was noted leading to an improved chance of patient survival.

Dr. Giraud-Robert states that aromatherapy and essential oils are beneficial in the following stages of cancer:

- Pre- or postoperative
During and after chemotherapy
- During radiation therapy
- During immunotherapy treatment
- During hormonotherapy treatment
- During comfort care

Before we discuss specific essential oils that can be beneficial for adding to a cancer treatment protocol, we must remember one important aspect: most essential oils have multiple beneficial effects. They can help prevent infections and thereby help prevent secondary and opportunistic infections during cancer treatments when immune systems are weakened. They can also help with pain control, sedation, congestion, tissue healing, and scar reduction, and appetite stimulation. The oils can also work as gentle antidepressants, helping to calm and relieve anxiety.\textsuperscript{17} An example of how one oil can have multiple effects is Lavender (\textit{Lavandula angustifolia}). It has properties such as antiseptic, antifungal, antitumoral, anti-inflammatory, calming.

\textbf{Common Essential Oils Used in Cancer Treatment}

\textbf{Frankincense} (\textit{Boswellia carterii})

In recent years, Frankincense is probably one of the most thought of and well-known essential oils used in the treatment of cancer. The chief constituents include Alpha-Pinene (30-65\%) and Limonene (8-20\%). The medicinal properties include anti-tumoral, immuno-stimulant, anti-depressant, and muscle relaxant.\textsuperscript{18} One of the main components of frankincense oil is boswellic acid, a component known to have anti-neoplastic properties.\textsuperscript{19}

\textbf{Copaiba} (\textit{Copaifera officinalis})

The oleoresin of Copaiba has been widely used as a traditional medicine for thousands of years in the neotropical regions from which it originated. It is produced from the resin of trees most notably from Brazil. The primary medical properties include: powerful anti-inflammatory actions, neuroprotective effects, anti-microbial, anxiolytic, anti-ulcer, and antineoplastic actions.\textsuperscript{20} \textit{β}-caryophylline, a sesquiterpene hydrocarbon, is the main chemical component with anti-inflammatory effects. It acts much like an NSAID by blocking the oxidation of 5-lipoxygenase, a major player in the inflammatory cascade, thus reducing pain and inflammation.\textsuperscript{21} As cancer can arise from chronic inflammation, the better it is controlled, the better chance of preventing or lessening cancers caused by inflammation.

\textbf{Lavender} (\textit{Lavandula angustifolia})

Lavender is one of the most well-known essential oils used in aromatherapy. Its uses are many and is considered by most as the “universal” essential oil. This EO has powerful anti-inflammatory and analgesic properties and the ability to provide calming and relaxing effects on behavior. It can be used to treat both physical and psychological manifestations of disease. The Medical properties can be antiseptic, antifungal, analgesic, anti-inflammatory, relaxant, and anti-tumoral. Anti-inflammatory mechanisms are thought to exhibit effects through the inhibition of lipoxygenase, prevention of leukotriene synthesis, inhibition of the cyclooxygenase-2 enzyme, inhibition of pro-
inflammatory cytokines, and repression of pro-inflammatory genes. Lavender is well known for its ability to balance the autonomic nervous system and reduce stress and anxiety. In 1 study it was concluded that the scent of lavender oil and its active component, linalool, affects autonomic neurotransmission and reduces blood pressure through the central histaminergic nervous system and the suprachiasmatic nucleus.

Helichrysum (*Helichrysum angustifolia*)
In the literature, Helichrysum is also known by the names Everlasting and Immortelle. It has known Medical properties such as anticoagulant, anesthetic, antioxidant, antispasmodic, chelates chemicals and toxins, and regenerates nerves. It can be extremely useful following surgery by helping with clotting, reducing hematomas, improving healing, helping reduce scarring, and reducing lymphatic edema. Psychologically it can also be helpful by soothing the soul’s “bruises” and helping with emotional shocks.

Myrrh (*Commiphora myrrha*)
Medical properties are as follows: Powerful antioxidant, antitumoral, anti-inflammatory, antibacterial, and analgesic / anesthetic actions. Myrrh is also known to drain toxins from the kidneys during and after chemotherapy. It can also stimulate the nervous system, has antidepressant properties, and can induce cellular apoptosis. The induction of cellular apoptosis is important when preventing and fighting cancer.

Grapefruit (*Citrus paradise*)
The medical properties of grapefruit include its ability to be: Antitumoral, Metabolic stimulant, Detoxifying, Diuretic, Fat-dissolving, antidepressant, and cleansing for kidneys, lymphatic, and vascular system. Grapefruit is very rich in Limonene and has been exclusively studied in over 50 clinical studies for its ability to combat tumor growth.

<table>
<thead>
<tr>
<th>Essential Oils for Use With Specific Areas During Cancer Treatment</th>
<th>Essential Oil Examples</th>
<th>Desired Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detoxification (Environment)</td>
<td>Citronella, Rosemary, Lemongrass, Tea Tree, Lavandin, Myrtle</td>
<td>Helps promote detoxification of the environment, rids the area of certain infectious agents, helps remove or decrease odors and air borne toxins</td>
</tr>
<tr>
<td>Detoxification (body)</td>
<td>Lemon,</td>
<td>Helps promote detox of liver and major organs due to decreased or damaged function directly from the cancer or due to the chemotherapy and radiation treatments</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>Copaiba, Northern Lights Black Spruce, Lavender</td>
<td>Helps reduce inflammation</td>
</tr>
<tr>
<td>Anti-Infective</td>
<td>Lavender, Myrrh, Clove, Lemon, Cinnamon, Eucalyptus Radiata, Rosemary</td>
<td>Helps prevent or lessen infections</td>
</tr>
<tr>
<td>Wound care</td>
<td>Frankincense, Lavender, Helichrysum, German Chamomile</td>
<td>Help with healing, reduce bruising, reduce chance of wound infections</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Peppermint, Spearmint, Fennel, Ginger, Tarragon</td>
<td>Ease GI pain, ease nausea, and promote appetite stimulation</td>
</tr>
<tr>
<td>Neurotoxicity / Neurological</td>
<td>Helichrysum, Galbanum</td>
<td>Reduce neurological issues as a result of cancer treatment</td>
</tr>
<tr>
<td>Anxiety / Behavioral</td>
<td>Vetiver, Lavender, Marjoram, Orange</td>
<td>Reduction of stress and anxiety and improve behavior issues to help facilitate a calmer environment to improve treatment outcomes</td>
</tr>
<tr>
<td>Pain Control</td>
<td>German Chamomile, Copaiba, Lavender</td>
<td>Manage pain directly from the cancer or from treatment such as post-op or radiation and chemotherapy</td>
</tr>
<tr>
<td>End of Life Care / Euthanasia</td>
<td>Vetiver, Lavender, Sandalwood, Frankincense</td>
<td>Create an environment of relaxation, calmness, and acceptance (pets and owners) to facilitate a peaceful transition</td>
</tr>
</tbody>
</table>
References


13. Henriques J. Holistic Vets Explain: Natural Treatment Of Cancer In Dogs. *Dogs Naturally*


Essential Oils and Seizures  
Jared Mitchell, DVM

Objectives
- To review the basic terminology and pathophysiology of seizures.
- To introduce and investigate the proposed mechanisms by which essential oils affect the neurologic system with emphasis on seizures and epilepsy.
- To introduce which essential oils are safe and beneficial for using with seizure disorders and which oils should be avoided.

Introduction
Neurological disturbances such as seizures can be very unsettling for owners, especially if they are unfamiliar with the clinical presentation. The loss of mentation, loss of bowel control, and the rigid limbs thrashing about can be an unforgettable physical and mental stressor not easily unseen or forgotten.

Statistics show that in 2015, 1.2% of the US population had active epilepsy. This is about 3.4 million people with epilepsy nationwide: 3 million adults and 470,000 children.¹ Epilepsy is the 4th most common neurological problem – only migraine, stroke, and Alzheimer’s disease occurs more frequently.² Epilepsy is the most common chronic neurological disorder in veterinary medicine, and is estimated to affect up to 1% of dogs and 2% of cats in the general population.³

Review of the Stages of Seizures⁴
Seizures have multiple stages the owner or veterinarian may recognize, and these may be beneficial when preparing for or treating a seizure disorder. There are 3 phases of seizures. These include the preictal, ictal, and postictal phases. The preictal phase occurs during the time before the seizure. It can result in unusual or altered behavior, and animals may appear nervous, seek out their owners for comfort, or hide to isolate themselves. As a side note, it can be important to try and help the owner learn to recognize this phase so they will be aware that a seizure is forthcoming.

The term “ictus” or “ictal phase” is referring to the actual seizure episode. This phase can last for 1 to 2 minutes; however, severity and time variations can occur. During this phase the pet may exhibit clinical signs such as, but not limited to: loss of consciousness or memory, changes in muscle tone or movement, changes in sensations and special senses (visual, auditory, olfactory), disturbance of the autonomic nervous system (salivation, urination, defecation), and severe mood and behavioral changes such as fear or rage.

The postictal phase occurs after the seizure. During this phase, the animal may return to normal in seconds to minutes, or the pet may exhibit a longer recovery phase that could last for minutes or hours. During this recovery time the animal may appear restless, lethargic, confused, disoriented, or blind.
Causes of seizures
It is important to remember that seizures are always a sign of abnormal brain function. With that fact established, the bigger diagnostic question which must be asked is what is causing the dysfunction. Is the problem a primary lesion in the brain or is it secondary to another disease process?

Seizures are the clinical manifestation of abnormal electrical activity in the brain occurring at a specific period, while epilepsy, on the other hand, refers to multiple seizures occurring over a longer period. With epilepsy the inciting cause may be idiopathic and inherited. The causes of non-epileptic seizures are numerous and include nutritional conditions, developmental anomalies, degenerative disorders, inflammatory brain conditions, traumatic head injuries, neoplastic conditions, organ failure, electrolyte imbalances, medications and medication withdrawals, toxic exposures, and hypersensitive encephalopathy.

Proposed Mechanism for How Essential Oils Treat Seizures
Normal brain function and CNS balance relies on the activation of the GABA receptor system and the blockage of sodium channels. Research is showing that EOs and their constituents can affect the GABAergic system and the neuronal voltage-gated sodium channels in CNS disorders.

GABA is an amino acid neurotransmitter which is widely distributed throughout the neuraxis. It is secreted by nerve terminals in the spinal cord, cerebellum, basal ganglia, and many areas of the cortex. Within the mammalian central nervous system, GABA, is the main inhibitory neurotransmitter.

Voltage-gated sodium channels are channels which open in response to voltage changes across the membrane and are largely responsible for the neuron’s ability to transmit information along their length and release neurotransmitters. Voltage-gated sodium channels are excitatory and play an essential role in the initiation and propagation of action potentials in neurons and other electrically excitable cells such as myocytes and endocrine cells.

Constituents Having Anti-Seizure Activity
Some of the most common chemical constituents reported to have anti-seizure activity in animal models of convulsions include: terpinen-4-ol, citral, β-myrcene, limonene, safranal, linalool, γ-decanolactone, α-terpineol, (-)-isopulegol, citronellol, thymoquinone, α,β-epoxycarvone, (S)-(+) -carvone, eugenol, methyleugenol, isoeugenol, estragole, trans-anethole, (-)-borneol, and carvacrol.

Common Essential Oils Used to Treat Seizures:

<table>
<thead>
<tr>
<th>Essential Oils</th>
<th>Chief Constituents</th>
<th>Actions Within Nervous System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copaiba (Copaifera officinalis)</td>
<td>β-caryophyllene</td>
<td>β-caryophyllene is a sesquiterpene classified as a phytocannabinoid with actions similar to cannabidiol.</td>
</tr>
</tbody>
</table>
It acts as an agonist for cannabinoid type 2 receptors with no psychotropic adverse effects."\textsuperscript{15}
It exhibits synergy with μ-opioid receptor-dependent pathways.\textsuperscript{15}
It also was found to be a potent antagonist of homomeric nicotinic acetylcholine receptors and devoid of effects mediated by serotonergic and GABAergic receptors.\textsuperscript{15}
A dose-dependent anxiolytic-like effect, similar to that produced by diazepam, was noted in a study conducted with male Wistar rats submitted to the elevated plus-maze model of anxiety using an ethnopharmacological analysis.\textsuperscript{16}

<table>
<thead>
<tr>
<th>Plant</th>
<th>Constituents</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cypress (\textit{Cupressus sempervirens})</td>
<td>α- and β-pinene</td>
<td>Cypress modulates GABA\textsubscript{A} by binding to benzodiazepine sites.\textsuperscript{17}</td>
</tr>
<tr>
<td>Frankincense (\textit{Boswellia carterii})</td>
<td>α-pinene, Limonene</td>
<td>α-pinene has anxiolytic and hypnotic effects by being a partial modulator of GABA\textsubscript{A} receptors and directly binding to the benzodiazepine-binding site of the GABA\textsubscript{A} receptor.\textsuperscript{17}</td>
</tr>
<tr>
<td>Helichrysum (\textit{Helichrysum italicum})</td>
<td>Neryl acetate, Gamma curcumene, α-pinene</td>
<td>α-pinene has anxiolytic and hypnotic effects by being a partial modulator of GABA\textsubscript{A} receptors and directly binding to the benzodiazepine-binding site of the GABA\textsubscript{A} receptor.\textsuperscript{17}</td>
</tr>
<tr>
<td>Idaho balsam fir (\textit{Abies balsamea})</td>
<td>α- and β-pinene</td>
<td>Idaho balsam fir modulates GABA\textsubscript{A} by binding to benzodiazepine sites.\textsuperscript{17}</td>
</tr>
<tr>
<td>Lavender (\textit{Lavandula angustifolia})</td>
<td>Linalool, 4TRP</td>
<td>Linalool has an antinociceptive effect by</td>
</tr>
</tbody>
</table>
blocking excitability by decreasing the voltage-dependent Na⁺ current in dorsal root ganglion neurons.18
4TRP has anticonvulsant effects due to the involvement of the GABAergic system and decreased Na⁺ current.19

<table>
<thead>
<tr>
<th>Hawaiian Sandalwood (Santalum paniculatum)</th>
<th>α- and β-santalol</th>
<th>Hawaiian Sandalwood displays neuroleptic activity resembling the pharmacological activities of chlorpromazine.20 Its fragrance can be grounding and stabilizing because the high levels of sesquiterpenes stimulate the pineal gland and the limbic system.21</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Valerian (Valeriana officinalis)</th>
<th>Valerenic acid</th>
<th>Researchers pinpointed the sesquiterpenes valerenic acid valerone as the active constituents that exert a calming effect on the CNS.22,23 Valerian delayed onset of PTZ-induced seizures in adult Danio rerio (zebrafish).24</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Valerone</td>
<td></td>
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<tr>
<td></td>
<td>Bornyl acetate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>α- and β-pinene</td>
<td></td>
</tr>
</tbody>
</table>

**Essential Oils to Avoid with Seizures**
While most EOs are considered safe and effective when diluted properly and used correctly, there are some which have been reported in the literature to avoid in cases of neurological disturbances such as seizures and epilepsy.

Camphor, thujone, pulegone, cineole, pinocamphone, fenchone, and sabinylacetate are oxygenated monoterpenes and are common constituents found in EOs known to have proconvulsant effects. The exact pathophysiology is still under investigation. However, one mechanism is believed to be their effect on the CNS by leading to loss of tissue gradient for Na⁺ and K⁺ producing and increase in cellular excitability.25,26
<table>
<thead>
<tr>
<th>Essential Oils</th>
<th>Main Constituents</th>
<th>Effects in the Nervous System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basil</td>
<td>Methylchavicol (estragol) Linalool 1,8-cineole (eucalyptol)</td>
<td>Basil has shown dose-dependent effects on the CNS. At lower doses, no effects were noted; however, at higher doses motor impairment was noted. 27 1,8-cineole can cause neuronal hyperexcitability and epileptiform activity by inhibiting potassium channels. 28,29</td>
</tr>
<tr>
<td>Camphor</td>
<td>1,8-cineole</td>
<td>Camphor can cause neuronal hyperexcitability and epileptiform activity by inhibiting potassium channels. 28,29</td>
</tr>
<tr>
<td>Cedar</td>
<td>Thujone</td>
<td>Thujone is a GABA receptor antagonist. 30</td>
</tr>
<tr>
<td>Fennel</td>
<td>Trans-anethole Fenchone Methylchavicol (estragol)</td>
<td>Anethole has been demonstrated to have pro-convulsive effects in humans; however, animal studies have yielded mixed dose-dependent results, leading some to speculate that other compounds may be the cause. 31 Fenchone could have narcotic effects and result in convulsions, hallucinations, and mental imbalance at high doses. The exact pathophysiology and mechanism of action are unknown at this time. 32</td>
</tr>
<tr>
<td>Hyssop</td>
<td>β-pinene Sabinene Isopinochamphone</td>
<td>Pinocamphones have a GABA antagonistic action. 33</td>
</tr>
<tr>
<td>Pennyroyal</td>
<td>Pulegone</td>
<td>Pennyroyal is a neurotoxin. 34 It can be hepatotoxic, leading to liver failure and epileptic encephalopathy. 34</td>
</tr>
<tr>
<td>Rosemary</td>
<td>Cineole Camphor</td>
<td>Rosemary can cause neuronal hyperexcitability and</td>
</tr>
<tr>
<td>Plant</td>
<td>Components</td>
<td>Effects</td>
</tr>
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<td>-----------------------------</td>
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<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Sage</strong> <em>(Salvia officinalis)</em></td>
<td>α-thujone, 1,8-cineole, Camphor</td>
<td>Thujone is a GABA receptor antagonist.28,29 Camphor and 1,8-cineole can cause neuronal hyperexcitability and epileptiform activity by inhibiting potassium channels.28,29</td>
</tr>
<tr>
<td><strong>Thuja</strong> <em>(Thuja plicata)</em></td>
<td>Thujone, Fenchone, Camphor</td>
<td>Thujone is a GABA receptor antagonist.30 Camphor can cause neuronal hyperexcitability and epileptiform activity by inhibiting potassium channels.28,29</td>
</tr>
<tr>
<td><strong>Wintergreen</strong> <em>(Gaultheria procumbens)</em></td>
<td>Methyl salicylate</td>
<td>Salicylates affect many aspects of the body, including direct stimulation of the CNS respiratory center, leading to respiratory alkalosis, uncouple oxidative phosphorylation, inhibition of the Krebs cycle, interference with hemostasis by damaging hepatocytes and interfering with prostaglandin synthesis, and ultimately progressing to altered mental status and seizures.35</td>
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**References**

How Tissues Heal and How We Can Help
Jo Moyes, LVMT, CVMRT

Objectives
- To examine the structure of and the way specific connective tissues heal and methods of ensuring optimal outcomes after injury.
- To understand how a specific type of tissue heals, it is useful to understand how it is structured looking primarily at connective tissue (specifically cartilage, ligaments, and tendons).

Introduction
Cartilage tissue is found, among other places, covering the ends of bones that come together to form a joint. It serves the vital function of cushioning the joint against impact and protecting the underlying bone from damage. It aids in allowing the joint to move smoothly as it goes through its normal range of motion. The main bulk of the cartilage is made up of extracellular matrix (ECM), which is the basic framework of the tissue. It contains very specialized cells, called chondrocytes, which are responsible for the maintenance of the cartilage, but they are sparsely distributed throughout the ECM. Instead, it is primarily composed of collagen, proteoglycans, and water, along with other nutrients and ions present in smaller amounts. These substances provide the support and strength to cartilage that is necessary for it to do its job. If there is any repair or remodeling that is required, the chondrocytes are responsible for performing those functions.

The articulating area of this cartilage (the areas that form the joint and oppose the opposite bone) do not have any nerves, blood vessels, or lymphatics of their own. Instead, it relies on the subchondral layers and the synovial membrane to diffuse nutrients and waste in and out of the ECM. Within the ECM, the water—which makes up about 80% of the net weight of the tissue—is primarily found in a gel, which moves throughout the tissue to distribute nutrients to the chondrocytes as pressure is applied. There is a significant amount of friction acting against this movement, which works in conjunction with the pressure of the fluid to contribute to the supportive function of the cartilage.

If there is damage to the cartilage, the chondrocytes work to repair it. This is usually a slow and very limited process, but there is some repair that happens. They also work to maintain the ECM, which in turn maintains the support provided by the cartilage tissue. In order to carry out these vital functions, the chondrocytes require nutrients coming into them and the proteoglycans they produce being transported to the areas where they are needed, all of which requires movement through the ECM. This is done when pressure that is applied to the tissue moves the gel-like fluid portion of the ECM from one area to the other. “Regular joint movement and dynamic load is important for the maintenance of healthy articular cartilage metabolism”1 because without it, there is limited to no movement of material to and from the chondrocytes. A joint that does not move cannot maintain its health, let alone heal an injury to its cartilage.

Ligaments and tendons have a similar structure, with fibroblasts taking the place of chondrocytes, maintaining the integrity of an ECM similar to that of cartilage. Once again, nutrients and wastes are transported in and out of the tissue through the matrix, necessitating the
movement of the tissues involved to apply pressure to the fluid to move it from one location to another.

Ligament injuries have become common in both pets and humans, and as a result, there have been numerous studies about how they heal and the best methods of improving long term outcomes. After an injury, ligaments undergo three stages of the healing process: hemorrhage with inflammation, matrix and cellular proliferation, and remodeling and maturation. This first stage involves an increase in vascularization and blood flow in the damaged area, which sets up the second stage, the matrix and cellular proliferation stage, where the scar tissue is formed that will serve as a replacement for the damaged ligament in the future. These scars are made up of different types of collagen (primarily type III as opposed to I, and different proportions of type V than the original ligament tissue), and the makeup of the tissue is disorganized at the outset. As it heals, it reorients itself along the stress lines of the ligament, so it can apply the maximum amount of support in the direction needed, and this process occurs through the application of stress to the tissue. Just as bone density increases when weight bearing stress is applied to the bone tissue, stress needs to be applied to the developing scar in the direction of its functionality to develop correctly.

Early movement is vital for ensuring the strongest tissue possible. Experiments involving ligaments that have been intentionally cut show that early mobilization is possibly the most important consideration in increasing ligament strength and function, more so that whether the tissue is surgically repaired versus being allowed to form a scar for stabilization. Early mobilization results in more type I collagen (the “normal” collagen in ligaments) than type III (which is typically associated with healing and does not possess the same strength and diameter as type I) in scar tissue, emphasizing the need for early movement in the development of functional scars around the joint.

In addition to the effects of the mechanical stress on connective tissues, there is evidence to suggest the body automatically initiates a repair cycles when it engages in activity. A study of orthopedically healthy Thoroughbreds measured the effect of exercise on serum levels of cartilage oligomeric matrix protein (COMP). This protein plays a key role in maintaining ECM, not only in cartilage as its name would imply, but in ligaments and tendons as well. The horses were entered into rigorous training workouts, during which the serum COMP was tested before and after exercises. The study found that the levels of COMP increased after exercise, and, as the intensity of the workouts increased over time, the level of COMP rose as well, indicating that movement and healing go hand in hand in these animals.

The flip side of this is that lack of movement correlates with a decrease in structural integrity. This has been demonstrated in numerous studies. When looking at the development of the superficial digital flexor tendon in foals, researchers found that foals raised with no or limited exercise had a smaller diameter of collagen fibrils in relation to pasture raised foals who got all the exercise they wanted. The force required to rupture the tendons of the pasture raised foals was considerably greater than that of the foals with restricted exercise. Another study showed that withholding exercise in foals had a negative effect on their capillary supply and oxidative capacity. This did not resolve after the foals were released from stall rest. Additionally, a study of large and giant breed puppies showed that off leash exercise was one of the factors that helped
protect against the likelihood of developing radiographic signs of hip dysplasia when they were checked at 12 months.\textsuperscript{8}

All of this leads us to conclude that one of the worst things we can do for our injured patients is to cage rest them, regardless of how popular this practice continues to be. Horses with no injury had one leg, casted and were stall rested for 7 weeks, followed by 8 weeks of increasing exercise to see how this affected the tissues of the limb. After their 8 weeks of exercise, the immobilized limb showed a decrease in bone density, joint range of motion, and peak force compared to the contralateral limb. Despite having no “injury” all the of the horses were lame after the cast was removed.\textsuperscript{9} Except for a non-stabilized fracture, as a general rule, cage rest does not help an injury heal. Restricted exercise does not help a young animal develop in a healthy, safe way. The body is not going to strengthen and reinforce tissue that it doesn't use when it could be shunting nutrients to a more active area or limb. Structural integrity of a joint requires that joint to be used to the full extent of its capabilities.

That is not to say that after an injury or surgery, the patient can just be turned loose to do whatever it wants. Just like you would imagine, they don't understand what they should and shouldn't do and typically do something stupid that causes greater injury. Therefore, it is important to have someone trained in how different movements and stresses affect the tissue so they can guide the owner in what to do. They need to be able to arrange a treatment protocol that provides enough stress and movement to drive healing while preventing further injury from being done. And just as importantly, they need to be able to communicate what needs to be done to owners. In my experience, handing the owner a print out of generic exercises is not effective because, number one, the owners need things demonstrated to them to in order to feel confident enough to do it correctly; number two, most owners are terrified of hurting their animal further, so they will often not do exercises if the pet shows the slightest dislike (and sometimes even if they don't); and number three, all animals do not heal at the same speed. It is unrealistic to believe that a three-year-old border collie and a geriatric mastiff are going to respond the same way to the same exercises. They need protocols that are designed for them, as individuals, that can be adjusted as needed to fit their personal needs.

The old ideas of rest and immobilization have been proven to be a less than optimal choice for the healing of wounds, either traumatic or surgical. If we want to provide the best medical care possible to our patients, we need to understand the importance of movement and stress on tissues during the healing process, so they can achieve the best possible long-term outcomes.

References


Why We Worry About Weight
Jo Moyes, LVMT, CVMRT

Objective

- To discuss the physiological damage done by excess adipose tissue and why it is so important to emphasize weight control in our client education, as well as steps to take to correct weight problems.

Weight concerns in pets, just like in humans, are a growing problem that are primarily viewed by a large portion of society as mostly an issue of aesthetics. Physiologically, though, it is much more serious than that. Excessive accumulation of adipose tissue contributes to a variety of health issues, both structural and metabolic, that can lead to disease, pain, and ultimately, a much shorter lifespan than the patient would have enjoyed had it been an appropriate weight.

An animal is generally considered “obese” if its weight is 20% over what it should be, which, when you consider the size of some of our patients, isn't a lot. A 10-pound chihuahua is obese at 12 pounds. A 50-pound pit bull is obese at 60 pounds. And the animal doesn't have to hit the “obese” marker before it becomes a potential health problem. Any excess weight can contribute to future struggles for our animals, and, considering the fact that well over half of America's pets qualify as overweight or obese, it's something that the veterinary community cannot afford to ignore.

Unfortunately, it's not a topic that a lot of people, even medical professionals, feel comfortable talking about. We use euphemisms, like “chunky” of “fluffy” to soften what feels like a severe judgment, which lessens the impact of what should be valid medical assessment. Fat shaming has become a serious taboo in our society (as it should be), and there has been a strong movement for being comfortable with all body sizes and shapes, no matter what they are. These are great and wonderful shifts in societal mindsets, but they should not distract medical professionals from recognizing the detrimental effects of excess adipose tissue in the bodies of our patients.

One of the more serious diseases linked to excess weight in veterinary patients is osteoarthritis, a condition that affects more than half of the dogs over 7 years of age in America. (It is not truly known how many cats have this disease, because they do not typically see veterinarians for pain issues and radiographs as often as their canine counterparts. This is commonly believed to be related to the tendency cats have to hide signs of illness or injury to a greater extent than dogs do.) A healthy joint requires adequate amounts of cartilage over the ends of articulating bones to provide cushion and support during normal, everyday movement. The cartilage absorbs the stress of impact and allows for smooth, friction-less movement through the joint's normal range of motion, and it is vital if the joint is going to function properly.

The first and most obvious issue for an overweight pet is the weight itself. The heavier an animal is, the more stress is being put on the joints, and therefore the cartilage within those joints, as the pet goes through its daily life. A study published in the American Journal of Veterinary Research showed greater ground force reaction during movement in obese dogs than in lean dogs,\(^1\) which leads to greater compressive forces within the joints of the animal. The damage caused by being too heavy is not something the tissue is designed to deal with, and that in itself can be enough to
start breaking down the cartilage, as there is repetitive, excess stress with literally every step the animal takes. Studies have shown that arthritis is strongly correlated with excess body weight, so weight control should be considered one of the most basic steps to keeping a pet healthy.

The stress from the extra pounds is not the only thing damaging the joint when a patient is overweight. The same study that looked at ground force reaction also looked at the range of motion in the joints of lean versus obese dogs while trotting at two different speeds. There was an increase in the range of motion in elbow, shoulder, hip, and tarsal joints in the obese animals, which means that every step these dogs were taking resulted in a degree of hyper-extension in these joints. The constant, repetitive stress can, over time, lead to the loss of elasticity in the tissues of the tendons and ligaments around the joints. Think of an elastic band that is repetitively stressed to beyond its normal anticipated load capacity. Eventually, that elastic will be permanently stretched out, and it will never return to its original shape and strength. This is roughly the same thing that can happen to the connective tissue around a joint. Constantly being stretched beyond what it is designed to do, as is happening in the joints of the obese dogs, will result in those connective tissues being stretched to the point that they are unable to return to their original configuration. This results in a loss of stability around the joints in question. Without the support of the tendons and ligaments, there is excess movement in the joint, which leads to abnormal wear on the cartilage. This leads to a breakdown of the tissue, resulting in progressive osteoarthritis.

What is probably more concerning than the mechanical results of the extra weight is the fact that adipose cells are not inert tissues simply exerting gravitational stress and storing energy for future use. Instead, over the last few decades, research has increasingly shown that adipose tissue produces and secretes a vast array of chemical substances that affect the entire body. It is, in fact, now believed that it may be the largest endocrine system in the body, exerting an influence on everything from metabolism to the immune system. Because this is a rehabilitation lecture, I will focus primarily on issues that relate to that field, but it is vital to know that excessive adipose cells have a complex effect on every aspect of health. Any veterinarian or owner approaching health from a whole-body mindset needs to understand that these cells play a big part in the overall chemical picture of the body.

One of the most important—for our purposes—effects of adipose chemicals is inflammation. “Obesity is now viewed as a state of systemic, chronic low-grade inflammation,” due to its production of pro-inflammatory cytokines. Small amounts of inflammation are normal and serve as vital components of wound healing, but if it goes on too long, the inflammatory process can begin to break down connective tissue, which can contribute to the cartilage damage already being done by the mechanical forces of the extra weight. Two cytokines in particular, IL-1β and TNF-α, that are known to be produced by adipose tissue in potentially excessive amounts, have been linked to the degradation of chondrocytes. As chondrocytes are responsible for the maintenance of the extracellular matrix of the cartilage, their loss or damage can only have a negative impact on the structure and function of the joint. There is no way to control the inflammation in a pet’s body without first getting control of its weight. Even in cases where there has been traumatic injury, adipose-induced inflammation can exacerbate the condition and make rehabilitation much harder, if not impossible.
There are other disease conditions that are being studied in correlation to obesity, such as calcium oxilate uroliths, intestinal permeability, and airway abnormalities, all of which can be just as harmful to health and overall quality of life. Issues of excess adipose tissue are not as fully understood as we would like, but we do have enough information to understand that they are not minor problems in our patients. These are serious concerns that can literally create life-or-death situations for the animals in our care. Mobility problems are one of the leading causes of euthanasia for dogs in our country, and, as has been shown, the animal's weight and body condition plays a huge part in this disease.

When it comes to controlling weight, prevention is the best practice to follow. Appropriate diets with the correct portion size and an active lifestyle from the time a pet is young is the best and safest way to go. Unfortunately, the best-case scenario is rarely what we see, so we're usually faced with a patient that is already overweight or obese. In this case, the same principals apply. The pet needs to consume less energy that it is expending. Diet is an important factor in this, but it is important to look at the actual calorie content of food rather than just the feeding guidelines when feeding a commercially prepared diet. A survey of different diets claiming to be designed for weight loss had a large range of calories contained in their recommendations for daily feeding, so it important to talk to owners about specific caloric intake that is appropriate to the individual instead of telling them to feed according to package recommendation. The appropriate number of calories is going to depend on several factors, such as age and activity level. On average, every 1,000 steps a pet takes results in an increase of 1 kcal/kg of increased energy burned. The more sedentary a pet is, the fewer calories they will need. But increased exercise is important for more than just burning more calories. Caloric restriction without exercise is more likely to result in the loss of lean muscle tissues as well as fat. The loss of this muscle can cause a decrease in the stability of the animal's joints, which leaves them more vulnerable to the very injuries we are trying to prevent.

The topic of weight control in our patients is not one that can be ignored, no matter how uncomfortable some people may find the topic. The health risks associated with being overweight can affect the entire body in ways that, until recently, were unknown to the medical community. Now that we have this information, it is unjustifiable not to address them with clients. Fear of treading into sensitive territory should never stop us from providing the best medical care possible for our patients.

References


Rehab in Action
Jo Moyes, LVMT, CVMRT

Objective
- To examine case studies and explore examples of how rehab can be performed.

Roxy
Roxy is an 8-year-old, spayed female Pomeranian who was four weeks post op after a medial patella luxation repair in the left stifle. She had been largely non weight baring on the limb for approximately one month before surgery. Patient presented as completely non weight baring on the affected limb. She had moderate muscle loss in the limb and, per the owner, had not used the leg at all since her surgery.

Patient was very treat motivated, which made working with her easier than otherwise, though she did not like to be handled by anyone other than her owner. We started with cookie stretches up, which caused her to toe touch on her LH leg. We did several of those, saying “foot” and treating every time her toes touched the ground. We did circles next, which resulted in a few toe touches with each rotation. Our last floor exercise that day was standing with her front feet elevated about two inches on a ramp, shifting weight to the back limbs, again resulting in toe touches. We also did a short swimming session, which resulted in her moving the affected limb through most of its normal range of motion. I demonstrated passive range of motion exercises with owner and did laser as well, to address any potential inflammation from osteoarthritis.

Over the course of her treatment, Roxy slowly began to use her leg more and more. Owner was discouraged when she did not immediately start using it right away but felt better when she understood that this was not something that was fixed overnight. The goal was to continue to see gradual improvements. The time to be concerned about the protocol was if she stopped improving. We gradually increased the intensity of her exercises, raising the elevation of her feet, adding army crawls, cavaletti poles, and balance exercises with an air mattress. By the time of her last appointment to date, Roxy was consistently using her leg when moving with toe touches at a stand.

Hendo
Hendo was an 8-month-old, male English Bulldog with bilateral hip dysplasia. The left hip was worse than the right, so his rDVM preformed a triple pelvic osteotomy on the left side and ordered 8 weeks of cage rest following the procedure. RDVM referred him to me at owner's request at the end of this 8-week period.

Patient presented with significant ataxia in both rear limbs and an almost constant toe drag. He had very poor muscle tone overall and pain response upon manipulation of both hip joints. Patient “puppy” sat consistently. He had full range of motion in both rear limbs.

We started with basic strengthening exercises and multiple short walks a day. Patient began with sit to stands, circles, weight shifting with front legs elevated, and low cavaletti poles. He had basically the personality of Godzilla when he was after a treat, so instead of going over the poles, he shoved them all together in a pile. He also had a tendency to throw himself around wildly to
get to the cookie, so we had to work on ways of slowing him down so he would use his back legs correctly. He was extremely brachycephalic, so care had to be taken to keep his walks and exercise sessions short. This is also why we didn't do any work in the pool. We also had to make sure he didn't get too crazy in his movements, because he still had a dysplasic hip on the right side, and after the prolonged cage rest, he had no muscle tone to support it. We did cold laser therapy and as much massage as he would sit still for.

Luckily, the patient was young and progressed readily. He moved on to army crawls, ramp then stair work, and balance work on an unstable surface. The biggest issue was compliance—on the dog's part, not the owners. We tried rear leg lifts, but he just sat down. We had to find ways to manipulate him into moving the way we wanted, instead of just throwing himself full speed ahead at whatever he wanted.

At the time of his last appointment, muscle tone had improved significantly, and he had much better control of his rear legs. He still had a toe drag at times, but it wasn't nearly as common as it had been. He had no pain response upon palpation or manipulation of rear limbs or hip joints. Owner left with an understanding of the importance of keeping Hendo active for the rest of his life, as physical activity is key for preventing lameness in dogs with hip dysplasia.2 This is especially important considering research that suggests that the TPO procedure does not stop the progression of arthritis.3 At that point, she did not feel the experience with the surgery had been a positive one, so she did not choose to proceed with a further surgery on the right hip, which she had originally planned to do. Instead, she chose to continue with rehab exercises at home and see how he progressed.

Peabody
Patient was a 6-month-old, female boxer, found abandoned in a house after the tenants moved out. She was severely emaciated (19 lbs.) and dehydrated, with advanced neurological symptoms. She was unable to stand in the back, had no superficial sensation in her back feet, and had a severe intention tremor (to the point that she was unable to eat by herself, because she could not keep her head in the bowl). She was hospitalized at an emergency center for a week to get her stabilized, then transferred to my care. Radiographs showed a broken rib, broken pelvis, and bilateral broken femoral heads. She had a scar from a previous wound on the top of her skull. Patient was fecal and urinary continent, but she had a very short time between signaling her need to urinate/defecate and when she would go. She was able to drag herself along the floor with her front legs, and back legs would kick while she did this.

RDVM made her feeding, herbal, and acupuncture treatment protocol. Original rehabilitation protocol began with passive range of motion in her back legs, restricted to her feet and hocks, because of the broken femoral heads. I also tickled her feet several times a day. I did this to gently stimulate sensory nerves in her back legs. Patient did cookie stretches several times a day to work on coordination and strengthening in core. We played games with treats where I would place one on the ground in front of her and she would have to control her head and aim to get it, working on cerebellar function. She went to work with me every day, and I kept her out of the kennel and engaged as much as possible. The more she moved, the more likely she was to heal her nerves and build muscles. Being out and engaged also stimulated her frontal cortex, which contains motor cortices. These cortices have a direct link to motor nuclei in the spine, which are
indicated in motor learning and sequencing. I also tried “grounding” or “earthing” with her, placing her in direct contact with the ground outside to access the available electrons. This has shown to have a positive impact on all the body systems, though it is a therapy that needs more research to fully understand. Additionally, patient spent as much time as possible playing with the other dog in the household. This worked on muscle control, strength, coordination, and frontal cortex stimulation. After about a week, she was able to eat on her own, though the tremor continued to be strong. Patient also received short massages daily and cold laser therapy several times a week.

After about 3 weeks, patient was considered healthy enough to undergo surgery, so a double FHO was performed to remove the broken femoral heads. During the initial surgical healing, I continued the same exercises as before with the addition of passive range of motion on her hip joints. After the incisions healed, patient continued to get seromas at the site, so I did Epsom salt poultices. Approximately three weeks after surgery, patient began to kick when her back feet were tickled. We added resistance exercises, pushing against the bottoms of her feet to encourage her to push back. This progressed to holding her in a standing position, supporting most of her weight but letting her take some of it in the back end. The tremor continued to decrease as she became stronger.

Patient stood on her own for the first time 3 months after beginning treatment. Within a few days, she was able to take several steps with the aid of a support harness. Within a week, she was walking around the yard after her canine brother. From there, we moved to the more common strength building exercises like circles, sit to stands, leg lifts, etc. to continue to strengthen her back legs.

Today (3 years out) she is healthy and happy. She runs—it looks a little weird, but it still counts—and is a bossy troublemaker. She still has a head tremor, but only when she is tired or excited. She is still uncoordinated and must have someone walk up and down full-sized staircases with her, so she does not fall. She falls a lot more than a regular dog and sometimes forgets where her feet are when she is excited, but for the most part, she can function as a normal canine. She is also a bed hog and a trash surfer, but those are probably unrelated issues.

**Touch**

Patient is a 6-year-old retired racing greyhound with intermittent front left limb lameness. Radiographs showed spondylosis in the mid-thoracic vertebrae. Physical exam showed mild (¼) lameness on the affected limb and trigger points in the left latissimus dorsi from just caudal to the shoulder blade to the mid thoracic vertebrae. Owner had hopes of doing agility training with the dog but only if it wouldn't harm her.

Patient began a standard protocol to strengthen and support the front limbs and thoracic trunk area. These included pushups, cookie stretches, circles, low cavalettis and ramp work. Patient was stubborn and would only work for cheese. She was also terrified of the floors in the clinic, because she had lived her entire life in a racing environment and didn't like walking on anything she didn't recognize. For the first appointment, she would do very little for me because she insisted on having at least one foot on the massage mat the entire time. We eventually had to cover the entire floor with blankets and rugs in order to get her to do anything for me.
Touch responded well to massage and traction, as well as her exercises. She refused to do circles but did well on the others. Owner did not restrict her running (because the dog loved it so much) but was compliant with other instructions to the best of her ability (she was an older lady with severe back and shoulder pain). By the end of the course of appointments, owner felt Touch was significantly more comfortable, though she still had an occasional limp. I told her this would be something that would have to be continued all her life, and that agility was probably not something she could ever safely do.

**Chester**

Chester is an approximately 4-year-old pit bull terrier at our local animal control. He was heartworm positive on admittance, so he had been on 6 weeks of kennel rest with leash walks only during his treatment. He came to me immediately upon being released from kennel rest by the shelter doctor. He had poor muscle tone overall and volunteers who had been working with him felt that his back was sore.

Chester had obviously come from a situation where he was not used to being touched. Per the volunteer who brought him, he had been very uncomfortable with physical contact when he came into the shelter, and new things were scary for him. They had been working with him during his heartworm treatment, so he was better, but not great about being handled by a stranger.

Patient's back was very reactive to gentle palpation. My first step with back pain is usually a good massage, but because of Chester's shyness, I was only able to work around his shoulders and cranial spinal region before he decided he was done and began displaying increased avoidance behavior. Instead we worked on exercises to stretch and strengthen his core muscles. These were cookie stretches, weight shift with front leg elevation, low cavaletti poles, and army crawl under a chair. We tried circles, be he was uncomfortable with these, so we didn't push him. Chester did well with his exercises at the shelter (volunteers worked with him). A lot of times, just getting a dog out of their kennel and moving again can help with some of their discomfort, especially back pain. I only saw him once before Coronavirus protocols made it impossible, but per his volunteer helpers, he was much more comfortable after a few weeks of exercises.

**References**

10 Reasons Adjusting the Atlas Will Help
William L. Ormston, DVM, DVetHom, Certified in Animal Chiropractic

Objective
- To learn the value of adjusting the atlas in every patient that is seen in their practice.

One of my good friends greets people with the question, “How’s your atlas?” instead of the usual “How are you?” True chiropractic is based on the spine and the central nervous system. The atlas is the first bone of the spine, located at the base of the skull or right behind your pet’s ears. A principled chiropractor will almost always adjust the atlas. This infuriates those who are not educated in the science of chiropractic. When we forget the whole and start to look at individual segments of the body, it is difficult to see how the atlas can be a problem no matter what the symptom is. When we begin to expect healing to occur due to outside intervention, it is difficult to understand how the atlas can help so many problems with so few side effects. Most doctors learn in their Introduction to Physiology classes how healing occurs, how the immune system works, and how the nervous system controls it all. They then forget how important these things are as they begin to learn and use pharmacological agents.

“Above-Down, Inside-Out” is a statement of chiropractic philosophy. What it means is that the brain is the control center of the body, it is the “Above.” The control of the body comes from above and then travels “Down” into the entire body on the “Inside” and finally flows to the “Outside.” It is a very simple phrase born at the turn of the previous century to express a very complex process. It refers to the functioning of the nervous system and all its manifestations. The more you know about the nervous system, the more you can appreciate the phrase. If we remember that healing comes from “Above-Down, Inside-Out,” the importance of the atlas becomes clear. The body was designed from Day 1 for the brain to be in control of everything from regulating movement to healing.

All but two nerves exit the brain at the back of the skull. Most of these go through the foramen magnum, which is the hole that communicates with the hole in the atlas. Lack of motion causes SHaRP, a phenomenon every student studying to become a doctor learns. SHaRP is an acronym that stands for Swelling, Heat, Redness, and Pain. Science has proven that the weight of a feather on a nerve decreases transmission by up to 50%, so any swelling in the area of the atlantooccipital junction may impact almost every nerve in the body. Inadequate motion will have a negative effect on the body in significant ways. Joints require movement through a full range of motion to maintain the health of cartilage and other structures within the joint. Full motion results in increased blood supply and nutrients to joint structures with increased quantity of synovial joint fluid (oil in the crank case).

The edema that comes from inflammation is affected by gravity, and it sinks down to the bottom of the joint. This puts the swelling next to the area of the animal’s spinal cord that controls the hind limbs. The first nerves affected by the swelling due to a lack of motion of the joint between the base of the skull and first cervical vertebra in the animals we examine are the ones that cause proper movement of the hind limbs. Animals with weakness in the back legs, dogs that slip when they go around corners, and even dogs with veterinary diagnoses like hip dysplasia and problems with their stifle joint probably have a restriction in movement of the upper cervical region.
For a four-legged animal to move correctly, it requires that every bone, muscle, ligament, tendon, and joint in its body move correctly. A human can move around easily without moving anything above the waist. This is not possible for an animal that walks on four legs. When your animal walks or runs, its head moves up and down in a bobbing motion. This helps shift weight to the correct end of the animal as limbs are picked up and put down. When there is a problem in a foot, this bobbing motion becomes exaggerated as the affected limb is placed or lifted. When there is a problem in the atlas, this motion will become reduced, increasing forces that the lower limbs are exposed to on every step, leading to problems in the lower limbs such as arthritis and tendon problems. Keeping the atlas moving properly will help keep the lower limbs healthier.

The ability for your animal to bend its head and neck around so that it can see behind itself is called lateral flexion. The motion begins at the junction between the occiput (base of the skull) and the atlas. There will be about 10 to 15 degrees of lateral flexion at this first joint. If that joint is subluxated, then the first motion occurs between the atlas and the axis (second cervical vertebra). The only motion that occurs at this second joint is rotation. When the first motion at the top of the neck is a rotation instead of a lateral flexion, it locks the neck out, causing the entire neck to be stiff and unable to bend properly.

When the atlas is out of alignment, it can put pressure and maybe a little torque on the brain stem. This puts direct pressure on the animal’s brain, disrupting the flow of messages through its central nervous system and affecting its body in a multitude of ways. The brain stem controls the flow of messages between the brain and the rest of the body, and it also controls basic body functions such as breathing, swallowing, heart rate, blood pressure, consciousness, vomiting, and whether one is awake or sleepy. Pressure on the brain stem can cause changes in behavior and the inability of the animal to perform at 100%. Parts of the brain stem have a role in maintaining homeostasis, the body’s ability to adapt and survive in the environment. There are nerve tracts in the brain stem that play a large role in maintaining tone, balance, and posture, especially during movement. They also relay eye and ear signals to the cerebellum so that visual, auditory, and vestibular stimuli can be integrated in motor coordination. There are centers located here that enable the eyes to track and fixate objects, and central pattern generators, which produce rhythmic signals to the muscles of breathing and swallowing.

We know that the central nervous system is constantly reorganizing in response to changes in sensory input. During every second of every day, animals’ brains monitor and integrate all incoming sensory information. This allows them to accurately formulate and execute the motor commands it requires based on what they choose to do at any one point in time. This integration of sensory information to perform movements accurately is known as sensorimotor integration. Throughout their lives, their activities, thoughts, and behaviors will lead to specific molecular, biochemical, electrophysiological, and structural changes in their brains and central nervous systems. These adaptations and changes are in fact the mechanisms for learning, memory, and recovery from injury. The results of research studies have indicated that vertebral subluxations (those dysfunctional spinal segments) lead to changes in the information that the spine sends to the brain. To start with, instead of the brain receiving information that the subluxated spinal segment is moving as it should, it may get information that the segment is moving way more than normal, not moving much at all, or just moving differently from normal. That seems obvious, but for now, remember that any change in information to the brain can lead to changes within the brain itself. When a spinal segment doesn’t move properly, it appears to influence
how the brain perceives and responds to all other sensory information. Spinal function seems to be one factor the brain uses as part of its processing and integration of all information. This may cause some animals to be afraid of shadows, lights, and noises that a subluxation-free animal would ignore. Spinal adjustments can restore normal movement patterns in these spinal segments and therefore restore a more natural pattern of input from the spine to the central nervous system. This in turn will allow the spinal cord, brain stem, and brain to process incoming information in a more coherent and meaningful way. Therefore, seemingly unrelated events are corrected by the animal that is under chiropractic care.

Veterinarians have learned about the mechanoreceptors in the neck. They are what allow the righting reflex to occur. They also allow us to safely keep a large animal lying down after a surgery or other procedure. These receptors are important because they communicate with the vestibular system in the ear canal to help all animals maintain balance and proper movement. A disruption in this communication will alter the animal’s ability to maintain balance while turning. This is a very important function in our athletic animals. It has been shown that the number of muscle sensors are remarkably high in the deep small upper neck muscles (those around the atlas and base of the skull). These deep upper neck muscles seem to act primarily as proprioceptive sensors in the body, rather than playing any significant role in actual movement of the head and neck. A New Zealand researcher has shown that chiropractic care, adjusting the spine to restore spinal function, changes the way the brain functions.1

The vagus nerve exits the skull at the base near the foramen magnum and travels down into the abdomen. The four key functions of the vagus nerve are sensory, taste, motor function for the muscles in the neck responsible for swallowing and speech, and parasympathetic functions that make it responsible for the digestive tract, respiration, and heart rate. Its functions can be broken down even further into seven categories. One of these is balancing the nervous system. The nervous system can be divided into two areas: sympathetic and parasympathetic. The sympathetic side increases alertness, energy, blood pressure, heart rate, and breathing rate. The parasympathetic side, which the vagus nerve is heavily involved in, decreases alertness, blood pressure, and heart rate and helps with calmness, relaxation, and digestion. As a result, the vagus nerve also helps with defecation, urination, and sexual arousal. The vagus nerve communicates with the diaphragm. With deep breaths, an animal feels more relaxed. The vagus nerve sends an anti-inflammatory signal to other parts of the body. If the vagus nerve is overactive, it can lead to the heart being unable to pump enough blood around the body. In some cases, excessive vagus nerve activity can cause loss of consciousness and organ damage. Proper vagal tone is important in lowering the heart rate and blood pressure. The vagus nerve sends information from the gut to the brain, which is linked to dealing with stress, anxiety, and fear. Heart rate variability (the evenness of the heart rate) has been shown to decrease with the chiropractic adjustment. Lower heart rate variability indicates a more relaxed individual.

An atlas subluxation will alter the shape of the vertebral canal at the base of the skull. This will alter the ability of cerebral spinal fluid (CSF) to flow properly. CSF is the nutrition and the sewer system for the brain and spinal cord. Its movement is imperative for the health of the nervous system. Without the flow of CSF, neurons become damaged. CO2, ketones, and metabolites (cellular waste products of the CSF) cause the nerve cells to dehydrate and then die. Movement is what drives CSF flow. Movement is what drives all fluid flow in the body except for blood.
When the spinal column is not moving, neither is CSF. CSF will drain to the lowest region of the cord or stagnate in the area of greatest expansion. The chiropractic adjustment is a force applied to the spinal segments to fire joint mechanoreceptors. Upon doing so, the reflex arch of each joint relaxes muscles surrounding that joint and allows for more uniform motion across the spinal segments. Because the force is very specific, high velocity, and low amplitude, the results are beneficial to the body. This force resets the Golgi tendon apparatus, removes muscle spasm, allows for joint fluid to refresh, and results in the improved flow of CSF along the cord.

The dura mater is a tough tissue that completely covers the brain and spinal cord like a glove; it serves to protect the spinal cord. It attaches in two places, the atlas and the sacrum. It monitors their relative positions and will activate muscles (tension along the spine and neck) when needed to protect and twist the skeletal frame if deviations are present. The cranial dural membranes act as stabilizers to the bones of the skull. Physical trauma (e.g., whiplash injuries, blows to the head, forceful tooth extraction, etc.) and dental malocclusions have the potential to disrupt dural membrane balance and normal cranial rhythm. Such changes can cause adverse neurological function throughout the body. The dural arrangement and attachments also protect and facilitate the smooth pumping of the cerebral spinal fluid by the brain and spinal cord. The dural attachments and the articular motion of the cranial bones, atlas, and sacrum are of paramount importance to the brain and spinal cord’s ability to move and replenish the CSF in and around the CNS. This ensures proper neuron firing. Disturbance or malfunction in the articular function of the cranial bones, atlas, or the sacrum results in dural torque (a twisting of the spine and pelvis). For normal neurological function to be restored, there must be compensation for the malfunction with a countertwisting occurring at a different level. At any spinal level, torqueing of the dura may result in paravertebral muscle weakness, spinous tippage with motor unit anteriority (muscle spasm or twitching), CSF pooling, and sensory overload to the associated organs and/or somatic structures. This causes all of the nerves that exit the spine to be affected. It will also cause a leg length inequality that is very easy to determine.

There are numerous ways to determine if your animals have a leg length inequality and we will look at a few of them in the next lecture. When the atlas has been cleared, everyone is able to see that the animal is clear of subluxations, free of interference to its nervous system. This will allow healing to occur as it should, Above-Down, Inside-Out.

References

Leg Length as an Indicator of Spinal Health
Wm. L. Ormston, DVM, DVetHom, Certified in Animal Chiropractic

Objective
To learn one “evidence based” and “patient centered” method to determine spinal health.

Leg length is an important aspect of the chiropractic examination of humans and is mentioned as a finding in the animal chiropractic examination. Reasons for inequality of leg length would include a difference in the length of the bones in the leg or a difference in the tone of the muscles in the leg. Veterinary textbooks state and veterinarians are trained that a short leg is usually due to an anatomical difference in the bones of the leg. The only way to truly diagnose this is via radiographic analysis of both limbs. A disparity of muscle tone from side to side is rarely considered and is not even mentioned in one standard equine lameness book. Research indicates that leg length inequality is a frequent, significant and reliable biomechanical finding that may contribute to back pain, hip pain, sciatica and accelerated degeneration of lower limbs.

A proposed mechanism is that the structural component affects the central facilitatory and inhibitory mechanism, causing an increased stimulus in the ascending cerebellar afferent fibers, which are then carried to the cerebellar/cortical system. The cerebellum and hypothalamus monitor and compare the actual state of the body with the value of body function maintained by the cortex. The structural subluxation interferes with this mechanism and allows an imbalance between the inhibitory and facilitatory nerve flow. The result of this aberration is an increased spinal stretch reflex, yielding muscle contracture which is demonstrated as a contractured short leg. In humans the leg imbalances that chiropractic care will help correct are those due to spastic contraction of the extensor muscles in the lower spine and pelvic girdle. Evidence based medicine proves that these leg length inequalities are also found and helped in the quadruped. Depending on the nature of the misalignment (cervical, pelvic, etc.) the contracted leg displays different characteristics, identified by both subjective and objective findings. Pelvic joint misalignments (SI joint subluxations) change the biomechanical locations of the coxofemoral joint relative to each other. This creates both a physiological and biomechanical long and short leg. Upper cervical subluxations create dural torque resulting in contraction of the muscles on one side causing a compensatory vertebral rotation, a sciotic pelvis, resulting in a shortening of one leg. The unequal leg length occurs when certain muscles are overstimulated. In the human the short leg should be called the contracted leg as this denotes the neuropathophysical relationship seen and emphasizes the origin of the neurological imbalance which appears as an innervational overload to the extensor muscles, causing unilateral spastic contraction. The leg length inequality is caused by the relative position of the coxofemoral joints to each other and not the movement of the sacroiliac joint. In the biped it is the superior rotation of the coxofemoral joint that occurs with the PI that results in the short leg; however, in the quadruped the anterior rotation of the coxofemoral joint that occurs with the PI will result in a long leg.

The dura mater is discussed in detail in human anatomy texts but barely mentioned in veterinary texts. The dura mater is the outermost, toughest, and most fibrous of all three membranes covering the brain and spinal cord. The dura mater and its attachments determine the functional capability of the cranial sacral respiratory mechanism. It has two layers in the cranium - the outer (endosteal layer) that attaches to all the ridges of the inner cranial vault and serves as the
covering of the inner surface of the cranial bones. It also acts as a cuff around the blood vessels that supply the cranial bones, forms the sheaths around the cranial nerves, and attaches to the rim of the foramen magnum (the hole at the base of the skull that the spinal cord passes through). The inner (meningeal layer) adheres tightly to the outer layer. The dura then extends downward after attaching to the foramen magnum, now becoming the spinal dura, it firmly attaches to the atlas, and like butterfly wings spreads out and attaches along the occipital ridge. It then forms a loose connection with the posterior longitudinal ligament. Moving downward, it attaches to the T-12 vertebra (in humans) and then down to the sacrum, making an attachment at the sacral foramen. The dura then becomes closely invested with the connective tissue of the filum terminale, the threadlike prolongation of the spinal cord. The two then continue downward and attach to the coccyx (tail bone). The dura has sensory innervation that allows it to determine when the spinal cord is threatened. The dura can trigger muscles enabling the spinal column and musculoskeletal system to protect the CNS resulting in compensatory twists and muscle spasms. In veterinary texts the dura is described as attaching to inner periosteum of the skull bones that splits at the foramen magnum to form a free tube separated from the wall of the vertebral canal by an epidural space. The spinal dura attaches to the first two cervical vertebra and the membranes of the atlanto-occipital joint cavity at the cranial end and the filum terminale which fuses with the upper surface of the caudal vertebra. The epidural space is occupied by fat, fluid and the internal vertebral venous plexus. The fat and vessels together cushion the spinal cord and allow it to adjust to the movements of the neck and back. To put this into simple English, the dura is a tough tissue that completely covers the brain and spinal cord like a glove; it serves to protect the spinal cord. It also attaches to several spinal vertebra, primarily to the atlas and the sacrum. It monitors their relative positions and will activate muscles (tension along the spine and neck) when needed to protect and twist the skeletal frame if deviations are present.

The cranial dural membranes act as stabilizers to the vault bones. Physical trauma (whiplash injuries, blows to the head, forceful tooth extraction, etc.) and dental malocclusions have the potential to disrupt dural membrane balance and normal cranial rhythm. Such changes can cause adverse neurological function throughout the body. The dural arrangement and attachments also protect and facilitate the smooth pumping of the cerebral spinal fluid by the brain and spinal cord. This is accomplished by a rhythmic contraction and relaxation of the neuroglia (glial cells, particularly the astrolites). The normal rhythm averages 14 times per minute. This delicately controlled action is termed the cranial sacral respiratory mechanism. The dural attachments and the articular motion of the cranial bones, atlas, and sacrum are of paramount importance to the brain and spinal cord's ability to move and replenish the cerebral spinal fluid (CSF) in and around the central nervous system (CNS). This insures proper neuron firing. Disturbance or malfunction in the articular function of the cranial bones, atlas, or the sacrum results in dural torque (a twisting of the spine and pelvis). There must be compensation for the malfunction or a neurologic deficit result. At any spinal level, torquing of the dura may result in paravertebral muscle weakness, spinous tippage with motor unit anteriority (muscle spasm or twitching), CSF pooling, and afferent nerve impulse bombardment to the associated organs and/or somatic structures.

Compensation is achieved by a return of efferent impulses to the spine, which ultimately results in contraction of the muscles causing compensatory vertebral rotation, a scoliotic pelvis, causing a shortening of one leg, tilted shoulders and head and; hopefully, resultant relief of CSF pooling.
If not corrected, it results in pain, disease, and pathology. The atlas subluxation generally causes a 5mm to 8mm anterior intrusion of the posterior arch into the spinal cord/brainstem area causing signals to be generated that over-stimulate the tone of muscles in the spine and through the pelvis causing a contractured leg that appears “short” (different length).

If we understand chiropractic body priorities and the implications of actions, it will allow us to better understand common compensations and reactions we see in our animal companions. The priorities of the nervous system in appropriate order are: 1) to minimize dural torque and tension (twisting of nerve tissues and their protective coverings) in order to keep the brain and nervous system uncompromised. 2) to evaluate gravity and balance. 3) to assess afferent inputs (input from the periphery of the body toward the brain) and the environment. 4) to handle pain/discomfort levels.

Minimizing dural torque is stating the obvious! This is the first priority of the body. One absolutely must have a functioning Central Nervous System in order to survive. All other functions of the body are dependent upon the CNS being kept alive and uncompromised. Evaluating gravity and balance becomes the second priority. Gravity/weight is a constant force for organizing function but can also be destructive if asymmetry is beyond critical limits. To maximize function and longevity, weight bearing should be as symmetrical possible. To distribute weight in stance and motion evenly, the body needs to be balanced. Being symmetrical and balanced helps achieve Priority #1, which is to minimize dural torque and tensions and Priority #2, to effectively balance against gravity.

Assessing afferent input and the environment is the third priority and is in constant flux. Afferent input includes incoming information to the CNS from the body and the senses. The normal function of the central facilitatory mechanism is to increase the normal spinal stretch reflex, while the inhibitory mechanism decreases the reflex. These two systems constantly react to proprioceptive input to the cerebral cortex, cerebellum and brain stem to maintain postural balance. The cortex stores previous values of body function, while the actual state of the body is monitored and compared to the cortical data by the cerebellum and hypothalamus. Structural imbalances (subluxation or articular joint fixation) become displayed in the cerebellar/cortical system as increased input from the ascending cerebellar afferent fibers. Environmental input includes terrain, predators and general environmental conditions that affect the body. This includes weather conditions, visual cues, internal sensations, sounds and smells.

Posture and walking are maintained by a unique neurological chain of reacting events. Every action, conscious or unconscious, is coordinated and is orchestrated through the neurological system. The nervous system applies constant checks and balances; this occurs through the feedback of mechanoreceptors when the animal is preparing to access and during the accessing of a biomechanical joint.³ Mechanoreceptors, nociceptors and proprioceptors communicate to the nervous system a stream of information from the muscles, ligaments, tendons, discs, cartilage, articular cartilage, synovial pressure, blood vessels, bones, and the myofascial connective tissue webbing system, thereby coordinating the joints for just the right amount of mobility while stability for the action is maintained. This feedback loop, which is used to coordinate intended movements, considers the anticipated speed of movement and anticipated resistance.⁴
Stability and mobility must occur in the correct proportions if a healthy joint is to be maintained. A joint that is dysfunctional because of hypomobility or hypermobility causes problems and results in changes to the integrity and health of all related structures. The repetition of abnormal movement has compensating consequences and may result in disc degeneration, osteophyte formation, tightening of the ligaments and muscles, or overstretching of tendons, ligaments and muscles as well as myofacial adhesions. Abnormal neurobiomechanics outside of the neutral zone creates an overall weakening of the joint making it more susceptible to further injury and accelerating degeneration. A cascade of consequences is noted for joints associated with the malfunctioning joint and learned patterns of neurological adaptation become imbedded in the nervous system. Even after correction of abnormal movement and the animal appears asymptomatic, the neurological effect can continue for months by remaining facilitated.\(^7\)

Most of the research that is current on the spine is found in human chiropractic references, yet it has been done on rats, mice, cats and lampreys. Previous models and beliefs of spinal stability have considered that the spine is, by structure alone, anatomically stable and capable of supporting gravity loads. Research has proven the importance of the multifidus muscles as part of the local segmental control of the spine. The multifidus muscles are critical for spinal stability and an important role in decreasing the forces on the larger muscles of the body. The levelness of the pelvis is important in spinal stability. In maintaining spinal stability, the stabilizing muscles serve as a support system that is integrated through the central and peripheral nervous systems linking each segment together into a kinetic chain. This kinetic chain is part of the neurophysiological mechanisms of the joint protection system, which can be altered through injury, pain, or a problem with the proprioceptive input. Posture is maintained by constant activity against gravity.

Central pattern generator (CPG) refers to the network of neurons that produce patterned motor behavior in the absence of phasic input. Networks within the spinal cord, even when isolated from the brain and sensory inputs, generate the basic pattern that underlies walking as well as other motor behaviors that can be produced by the spinal cord networks, such as hopping, swimming, scratching and running. Many of the behaviors fundamental to life are rhythmic activities that are controlled by neuronal networks. In mice a signature of locomotor-like activity can be obtained by comparing the pattern produced in the ankle extensors and flexors with ventral nerve root recordings from the left and right second lumbar with the fifth or sixth lumbar ventral roots. Most of the CPG research has focused on cats, rats and mice. The sensory afferents are now known to be involved in muscle and cutaneous reflexes, and they have important regulatory functions in preserving balance and ensuring stable phase transitions during the locomotor cycle. The general neural organization of CPG function in locomotion appears to be similar in all species studied. Coordination patterns of fore and hind limbs have features in common with those of the upper and lower extremities in human bipedal motion. In a recent porcine experimental model, it was revealed that a neuromuscular interaction exists between the intervertebral disc, the zygapophyseal joints and the paraspinal longissimus muscles. This study also suggested the existence of a complex reflex system which is responsible for the motion and stabilization of the lumbar spine.

To stabilize locomotor rhythm, feedback via spinoreticular neurons and inputs from other regions of the brain appear to be necessary. Additional support is provided by findings that the
brainstem acts as a site of convergence for several input, and it appears to provide a locomotion-related gaiting function. This gaiting function involves spinoreticular input from the CPGs and from the visual and vestibular systems, which enables the motor control mechanisms to be more responsive to factors in the locomotion environment.

Five functions in the control of locomotion from supraspinal areas have been identified: 1) Activating spinal locomotor CPGs. 2) Controlling the intensity of CPG operation. 3) Maintaining equilibrium during locomotion. 4) Adapting limb movement to external conditions. 5) Coordinating locomotion with other motor acts. The main supraspinal centers include the sensorimotor cortex, the cerebellum and the basal ganglia. The cerebellum’s principal function may be the timing of muscle activation, “fine tuning” the output by adapting each step cycle. Nervous system errors can occur anywhere along the kinetic chain of activity that has been accessed. Because the main feedback for locomotion, balance, and standing starts at the receptors of the feet and around the ankle joint, it doesn’t mean that lameness must begin there. Studies prove that sensory feedback is critical in modifying CPG-generated motor programs to facilitate constant adaptations to the environment. Without question afferent input plays an important role in stabilizing the resulting motor behaviors. Experiments have shown that sensory feedback can drive or terminate a rhythmic behavior without being necessary for the normal expression of the behavior.

Neuroarticular function may be assessed through the systematic evaluation of leg lengths and their reactivity. In humans this can be very specific, and I am sure that with further evaluation a similar method will be devised for quadrupeds. Currently the method is used to differentiate between pelvic and upper cervical subluxations. It will also help the examiner determine if there is a combination of subluxations. It is an excellent tool to help determine if all the subluxations at either end of the animal have been addressed after the adjustment is finished.

In the canine patient simply raise the pelvis so that the hind limbs are non-weight-bearing. This is fairly easy to accomplish in the small patient but may need to include placing the dog’s abdomen on your lap for the larger patient. Have the handler gently flex the neck both ways. In a patient with an upper cervical subluxation the leg length will change as the handler flexes the neck. When the neck is turned one direction the legs will even out, and the inequality will increase when the neck is turned the other direction. In some patient’s flexion toward the side that makes the inequality worse will be difficult. In an animal with only a pelvic subluxation leg length will not change with neck flexion. An animal with a combination of subluxations will have some improvement with flexion in one direction but there will still be a leg length inequality. The short leg will be on the side of the as ilium if the patient is checked in quadrupedal stance and on the side of the pi ilium if checked in bipedal stance.

In the equine patient it is difficult to get the hind limbs into a non-weight-bearing position but neuroarticular function may still be assessed. The tuber sacrales will be uneven when viewed from behind in a horse with a short leg due to muscle contracture. In an animal with an upper cervical subluxation the heights of the tuber sacrales will change as the neck is flexed in different directions. This may be felt with hands placed on the tuber sacrales when the neck is in neutral and left there throughout the entire flexion process. It may be visualized by balancing a short stick over the tuber sacrales and watching the movement as the neck is flexed.
Checking leg length in the quadruped can be very helpful in diagnosing problems of the spine in animals with or without gait abnormalities or lameness. It has no contraindications, is inexpensive and noninvasive. This important tool should become usual and customary in the examination of the quadruped. The utilization of leg length checks as a measure of spinal health allows all parties involved in the care of the animal why it is always the atlas. When the atlas has been cleared everyone is able to see that the animal is clear of subluxations, free of interference to its nervous system. This will allow healing to occur as it should, Above, Down, Inside Out.

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Chiropractic Successes in Food Animals
William L. Ormston, DVM, DVetHom, Certified in Animal Chiropractic

Objective

- To learn that chiropractic has a monetary value in Food Animal practice.
- To learn that chiropractic care helps chicken be more vigorous.

Animal chiropractic and specifically food animal chiropractic has been around since 1921 when the practice of animals being adjusted by chiropractors reached the radar of the American Medical Association and they took offence calling for the immediate cessation. C.D. Kinney, DC of Austin, Texas, reported on August 12, 1921 on treating a case of a bloated cow. Dr. Agnes Palmer frequently related the story of her first time adjusting a chicken around 1944. Upon returning to her home in Pennsylvania from the Palmer School, her parents challenged her to see what she was learning. Her father pointed out a chicken in the barnyard that was walking funny and said, "Well, see if you can fix that!" She rose to the challenge, adjusted the chicken, and its recovery made supporters out of her previously skeptical parents. The health and well-being of a chicken may not be held in high regard among city folk who have no idea of the value of a good layer, but it was understood by her parents.1

Most current successes in food animal would be most likely be linked to the show ring. Certified animal chiropractors all over the country report success with the treatment of show animals such as cattle, sheep, and goats. Chiropractic has long been accepted as an adjunct to veterinary medicine in musculoskeletal problems.2 The success of this chiropractic treatment can be measured by the number of young animal owners who continually seek out chiropractic care for their animals.

Performance of bucking bulls would also be considered an individual animal adjustment. A small rodeo company in Tennessee implemented a principled chiropractic adjustment for all of their bucking stock. Prior to the start of the bulls getting their atlases and low necks adjusted the average score for bulls was 16 to 18 per judge. After starting complete chiropractic care the numbers jumped to 21 to 23 per side.

However, in today’s agricultural economy, production medicine or herd health may be more important than individual animal medicine. Areas for improvement may include milk production, reproduction, mastitis, lameness, milk quality, young stock growth or illness prevention. The veterinary consultation includes visiting the farm to analyze records, interviews of farm personnel and observation of the animals to determine the causes of poor performance. The veterinarian may then suggest appropriate interventions and continue to monitor performance to assess the herd’s progress toward reaching their goals. Herds may be visited weekly, bi-weekly or monthly as needed.

There are studies that show that chiropractic care will enhance the immune system and reproduction in humans. What about reproduction in animals? Dr. Peck, DVM, Certified in Animal Chiropractic and owner of the largest dairy in New York started a study utilizing adjustment of the sacrum in open dairy cattle. The study was based on evidence that adjusting the sacrum of women decreased the rate of endometriosis and alterations of ovarian function.3,4
How about growth rates which have a huge impact on the economic viability of producers. A study to find the effects of chiropractic adjustments on Black Broiler chickens during rearing. The cost of chicken feed is a significant portion of the expense of raising meat chickens. Raising pastured chickens becomes expensive due to the effects of predation. This study sought to explore the potential benefits of the chiropractic adjustment on the economics of raising pastured Black Broiler chickens for meat. This study documented the effects of chiropractic adjustment on growth and production of Black Broiler meat chickens using weight and time variables.

Study parameters: 50 Black Broiler chicks were purchased from a chicken hackery within 2 hours of the ranch. Chickens were raised to reach a weight to meet or exceed 6 lbs. live weight. Chickens were managed at Know Your Food, a chicken producer in Meridian, Texas. The Chicken management system at Know Your Food includes feeding of commercially available organic starter/grower until market weight is reached. Brooder is a 6’ x 20’ cement floored wire enclosure in a metal building with supplemental heat available as necessary. Fans aid in circulation when needed. The grower is a 30’ x 10’ wire enclosure that is opened during the day and closed at night. When open the birds have access to native Texas grasses and wildflowers. Predation is the biggest problem.

Study protocol: 50 Black Broiler chicks were purchased from a chicken hackery within 2 hours of the ranch. Chicks were delivered on the day following hatching. As they were removed from the box the study chickens were adjusted while the controls were removed from the box, petted and both were placed in the brooder. Birds were identified by bands that were numbered and then flipping a coin to determine the group in which that number was assigned. Chickens were randomized by pulling a chick from the box in which they arrived and a numbered band from a cup. Chicks were weighed every week. Taken out of the brooder at 1 lb. and placed in grower until harvested at 6 lbs.

Chicks were then fed and maintained in the brooder until they were completely feathered. While kept in the brooder chicks had continuous free choice food and water. Every Friday chicks were weighed. The person weighing the chicks was unaware of which chicks were adjusted and which chicks were not adjusted. Each chick’s weight was recorded. When the chickens were fully fledged, they were placed in an outdoor pen. Chickens were provided continuous feed as well as access to pasture. Protection from predators included safety in a covered pen at night. They were weighed every 2 weeks on Friday and their weights were recorded as before by a blinded weigher and blinded scale.

Care was continuous until each chicken achieved a minimum weight of 6 lbs. Chickens who achieved the minimum weight were taken to a USDA butcher and slaughtered at this time. Not all chickens achieved this weight at the same time, and when they each achieved this weight, they were separated into two groups, adjusted and not adjusted. Chickens were transported in enclosed carriers inside a pickup truck to the butcher where they were humanely butchered, cleaned and frozen.

Each group of chickens was processed separately, and the butchering facility was instructed to process each group of chickens as a group, separate from the other group. The butcher was unaware of which chickens were controls or which were study chickens. The chickens were labeled in such a way as to maintain separate processing and boxing to keep the groups intact.
Those chickens that had been adjusted were processed for the name Adrian. Those chickens that had not been adjusted were processed for the name Norvil. Some chickens were lost to predation and trauma during the study. This is normal for pasture raised chickens.

Losses: Hawks are the main predator for pastured chickens. Loss to hawk predation was ongoing from the time the chickens were placed in the pasture. The hawk seemed to prefer the non-adjusted chickens, perhaps because their weight was more suitable to carrying off. A bobcat began to visit for a week and took 8 chickens as well. The bobcat appeared to prefer adjusted chickens.

One control chicken was found flopping around on July 12, 2018. It was removed from the group and the study, adjusted daily for 3 days, then every other day and until it recovered 14 days later. It was later butchered at 6 lbs. This chicken was accounted for in the statistics as a loss to the study. The losses of adjusted chickens and non-adjusted chickens were taken into account during the statistical analysis.

**Conclusion**

Average Days to Reach Target Weight

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<td>Adjusted</td>
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<td>Non-Adjusted</td>
<td>12 birds average 103.49 days</td>
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“Data was analyzed by a reputable scientist at a major university.”

Weight of adjusted and control chickens was not significantly different at the time of entering the grower. Chickens that were adjusted were significantly heavier than not-adjusted chickens (P<0.05) during the second week in the grower. Adjusted chickens showed a significantly (P<0.05) higher average daily gain when compared to chickens that were not adjusted. Chickens that were adjusted are significantly (P<0.05) more vigorous than chickens that were not adjusted. Once all the chickens were butchered, the data of weights and dates of loss or butcher were sent to a statistician at a major university. The statistician asked to remain unnamed in this study, perhaps because the is this study is outside his normal work parameters. The statistician reported that the adjusted chickens were more vigorous than the non-adjusted chickens.

The adjusted chickens reached feathered maturity sooner than the non-adjusted chickens. The final adjusted chickens reached butcher weight at 92 days. The final non-adjusted chickens reached butcher weight at 114 days. This is a significant difference when considering the cost to raise chickens for meat.

Once the chickens were butchered, chicken halves were anonymously labeled to disguise their identity. At this time sent to a chef in Dallas. This 5-star chef prepared all chicken halves simultaneously and in the same manner. The chickens were prepared using the same seasoning and with the same equipment.

**References**

The Science of Animal Chiropractic
William L. Ormston, DVM, DVetHom, Certified in Animal Chiropractic

Objectives
- To understand that Chiropractic care is well researched and scientifically valid modality.
- To learn to find peer reviewed studies that aren't published in mainstream veterinary publications.

I am often asked to prove animal chiropractic works. When I point to the numerous animals that have been positively affected by my own adjustments, I am told that is purely anecdotal. I have been told that I am a charlatan out to steal people’s money. At one time I attempted to do a research project in dogs that came into my veterinary clinic. The project was to assess the movement of the first 2 cervical vertebra with my hands and then either adjust or not adjust according to the paper that was drawn from a hat prior to entering the room. Some owners watched me check their dog and then asked what I was doing. When I explained that I was incorporating animal chiropractic into my practice most were very happy and asked me if I was going to check the whole spine. Those animals were removed from the study. When I palpated some animals, their upper cervical vertebrae were very messed up and not moving correctly. Since I had new knowledge of what this meant and since I had taken an oath that said, “First, do no Harm,” I could not leave these animals in the control or non-adjusted group. It became evident after just a few dogs that a true double blinded study may be difficult and against my Hippocratic oath. We currently have completed some studies and are waiting for their publication in peer reviewed journals to make the results official. Some will believe the results, some will say we tricked the data and the study isn’t valid, some will never accept the paradigm change.

At the ACES (Animal Chiropractic Education Source) ranch in Meridian, Texas we did a study with our meat chickens. Our chickens are organic and free range. We have always adjusted them, but in 2019 we put 50 into a study where half of the chickens were adjusted every two weeks and the other half were just picked up and weighed. The chickens were weighed every two weeks and processed at 6.5 lbs. The adjusted chickens were more vigorous and gained weight faster than the non-adjusted chickens. The average days to market for the adjusted chickens was 2 weeks less than the non-adjusted chickens. Samples were sent to a 5-star chef in Dallas and his diners chose the adjusted chickens over the non-adjusted chickens, preferring them stating that they were juicier. One of our students initiated a breeding study in dairy cows where she adjusted just the sacrum on 10% of the cows that didn’t get pregnant the first time they were bred. The initial results showed that the cows that got adjusted were 5% more likely to get pregnant than those that didn’t. There was an increase in second service conception rates from 30% to 35%. The study was discontinued as the owner of the cattle determined that the control group was costing the farm too much money.

We currently have an ongoing study with dogs that are paralyzed or exhibiting neurological deficits in the hind legs. In order to get in the study there must be video evidence of neurological deficits that any untrained observer could see. There also must be a change in the leg length when the neck is flexed. We only adjust the first two vertebra for the first seven days. At the end of seven days, the dog is re videoed and a positive outcome is based on improvement in the
video that again must be visible to an untrained observer. With over 50 dogs so far in the study, the positive outcome rate is over 95%. If you have a dog that you think would be eligible for the study, have your certified animal chiropractor contact us.

Studies have suggested that chiropractic adjustments can trigger changes in the body that are as varied as: improved or altered visual acuity and visual field size, reduced joint position sense errors, decreased reaction times, altered brain processing, changes in the way that our brain integrates sensory and motor information, altered spinal cord reflex excitability, changes to specific messages that get sent to muscles from the central nervous system, increased muscle strength in the legs and reduced (or prevented) muscle fatigue developing.

The effects of vertebral subluxations have been well documented by leading scientists and researchers from all over world. Dr. Chang Ha Suh, PhD, University of Colorado stated, “Subluxation is very real. We have documented it to the extent that no one can dispute its existence. Vertebral subluxations change the entire health of the body by causing structural dysfunction of the spine and nerve interference. The weight of a dime or less on a spinal nerve will reduce nerve transmission by as much as sixty percent”1 As early as 1981 an article in Science reported, “Nerve dysfunction is stressful to the visceral nerve and other body tissues and the lowered tissue resistance modifies the immune response and lessens the overall capability of the immune system.”2

A Dr. Murray, a leading researcher in the field of manipulation medicine, reported about spinal nerve interference and immune disorders. He stated that blocked nerve impulses in the cervical region can cause many clinical features from central motor impairment to lower resistance to infections. Chiropractic examinations are of a “decisive importance” for diagnosis of this blocked neurological flow. Chiropractic can often bring about successful results because it aims at the cause of the problem.3 Dr. Heidi Haavak has a book out, “Reality Check” that describes the science of chiropractic that is going on in New Zealand. She cites 5 animal studies that were used to prove chiropractic works in humans.4

The science of Chiropractic is founded on the premise that a proper nerve supply is essential in controlling and regulating bodily function. By releasing stress on the nervous system, Chiropractic permits the immune system to function more effectively. Studies done in Australia Canada that measured the effect of Chiropractic treatment on the immune system have shown that Chiropractic may influence T and B lymphocytes, NK (Natural Killer) cell numbers, antibody levels, phagocytic activity, and plasma bet-endorphin levels.5 A recent study by Dr. Ron Pero, a leading cancer and genetic research specialist, found that chiropractic patients of all ages had a 200% greater “immune competence” than people who had never received Chiropractic care and a 400% greater immune competence than people with serious diseases.

Research by Patricia Brennan, Ph.D., suggests that spinal adjustments may have a direct effect on certain aspects of immune function. Her group showed that when the middle of back was adjusted, the ability of white blood cells to release reactive superoxide radicals and hydrogen peroxide as they come into contact with different bacteria or fungi was enhanced.6
Pain can mimic depression. The same nervous pathways that are stimulated during depression are also stimulated during pain, especially chronic pain. This chemical look-alike pattern can also be similar to the flighty behavior seen during the time when the opioid receptors are not being stimulated often enough. Chiropractors take a natural approach to health by focusing on the source of problem, rather than masking symptoms with medication. A 2012 study, published in the Annals of Internal Medicine, followed 272 neck pain patients for 12 weeks and found that those who saw a chiropractor were twice as likely to be pain free compared to those who took medication. Of those who sought chiropractic treatment, 32% became pain free versus 13% of those who treated with medication and became pain free.7 Animals that are under routine chiropractic care have more balanced nervous systems than animals that are not under chiropractic care. They are better able to feel less pain and are therefore free to enjoy the life of being your pet.

Pain medication is frequently prescribed for patients with sciatica, but an article in the British Medical Journal reveals that there may little efficacy in this practice. Within the article, researchers reviewed 23 studies that compared placebo pills to various medications for the treatment of sciatica.8 Study after study, the drugs were found to be no more effective than the placebo pills. Additionally, drugs did not significantly help relieve radiating leg pain, one of the primary symptoms of sciatica. Two drugs helped reduce overall pain, but it was unclear how effective they were in the long-term. These findings led researchers to conclude that there is no clear evidence for demonstrating the efficacy or tolerability of common pain medications prescribed for sciatica. Chiropractic is a better approach to sciatica than drugs. A 2010 study found that Chiropractic does not pose the risks of surgery, but it is just as effective.9

According to an article in the European Spine Journal “Proper spinal function can help balance a key component of the body, the autonomic nervous system, which regulates many aspects of the health from blood pressure, heart rate, and breathing to gut function, sexual arousal and controlling stress.”10

According to another study, chiropractic care was effective in helping people suffering from lower back pain when included in a comprehensive treatment plan. 750 active-duty military patients enrolled in a study to treat lower back pain. Lower back pain is common in the military and can often result in absences from duty. Participants in the study received regular medical care, including pain medications, physical therapy, and exercises, or that same treatment plus chiropractic care. The participants received the treatment for six weeks and then were tracked for another six weeks. Researchers found that at every step along the way, the patients receiving the chiropractic care were doing better. Their pain was less frequent and less intense.11

Another study, cited by the American Chiropractic Association on their webpage, found that when chiropractic care was compared with medical care, chiropractic care was more effective. That study, published in Spine, found that 94% of chiropractic patients experienced a 30% reduction in their pain, compared to only 54% of the patients who only received traditional medical care.12

Both the Quebec Task Force on Whiplash of 1995 and the Bone and Joint Decade Neck Pain Task Force of 2008 agreed that chiropractic care is often beneficial for people who have non-
specific neck pain. Besides back pain, neck pain is the second largest cause of musculoskeletal
disability, and many people seek relief from it around the world.\textsuperscript{13}

Although for a long time, many many headaches were thought to be tension headaches or
migraines, the International Headache Society now recognizes that most headaches are
cervicogenic. Cervicogenic pain is pain that radiates from the neck into the head. The
International Headache Society reports that chiropractic care is often helpful in treating these
types of headaches.\textsuperscript{14} Animals with this type of headache will exhibit behavioral changes.
According to an article published by Gallup in 2016, 65% of American adults have sought care
for neck or back pain in their lifetimes, and 25% did so in the past year. 35.5 million adults
visited a chiropractor for their pain in the past year, too. 67% of the people that Gallup surveyed
about the chiropractic care found it to be effective.\textsuperscript{15}

In a Consumer Reports survey, published in Consumer Reports magazine in March of 2013,
chiropractic care was the number one best way to take care of back pain, according to
consumers. It beat out prescription medication, deep-tissue massage, and more.\textsuperscript{26} Chiropractors
are trained and licensed, just like other medical professionals. To become licensed, they must
earn a Doctor of Chiropractic Degree, which takes four years after at least three years of
undergraduate work. They also must pass the challenging National Board of Chiropractic
Examiners exam and must receive a state license. Once licensed, they must complete continuing
education requirements each year throughout their career. In 2015, The Joint Commission, the
organization that provides and reviews the accreditation of over 20,000 health care systems in
our country, added chiropractic and other non-drug care to its pain management standard. This
was a huge move that helped to legitimize this discipline nationwide. Furthermore, Congress
went a step further with their overall faith in chiropractic care. After adding chiropractic services
to Medicare and Medicaid, they also added it to their congressional health plan. All members of
Congress are covered for chiropractic, and many of them see chiropractors for their health.
The more people who understand the value of chiropractic care, the more people we will be able
to help. So, get out there and start telling everyone these great chiropractic facts. They’ll thank
you for them! Fortunately, in recent years, more and more chiropractors and their patients are
participating in studies and research. As these things grow and develop, several irrefutable
chiropractic facts have emerged. Some benefits have been scientifically proven, far beyond the
simple anecdotal evidence of the past.

More and more people are beginning to feel more confident about chiropractic methods and
treatments, and as a result, people are starting to flock to chiropractors nationwide in search of
relief from pain for themselves and their animals. In many cases, they are getting the relief that
they seek. There are still doubters out there, though. When you encounter one, it is now easier
than ever to prove that chiropractic is real, is effective, and is here to stay.

For current research on chiropractic care you can down Heidi Haavik’s book “Reality Check” by
texting Reality Check to 773-770-4377. You can also look at the links and information at
https://www.vertebralsubluxationresearch.com or at https://www.drmoknows.com
References
Cannabis in Veterinary Medicine
Part 1: The Ethnobotany of Cannabis, Current Legal Landscapes
Gary Richter, MS, DVM, CVA, CVC, GDVWHM

Objectives
- Review the history surrounding cannabis and its use as medicine
- Discuss the legal history of cannabis and provide a current legal framework for veterinarians

*Cannabis sativa*, is the species of cannabis from which all human cultivated varieties of cannabis are derived. The shared history of human civilization and cannabis dates to the very beginnings of civilization. Carl Sagan hypothesized that cannabis may have been the first agricultural crop cultivated by early man and the ethnobotanist Terrance McKenna theorized may have played a part in the formation of language and communication. The ability to communicate between tribes and the creation of a sustainable agrarian society were some of the first steps taken towards civilized society. It was no accident that a plant with uses ranging from fiber to fuel to food and medicine was at the center of this sea change.

The earliest known uses of cannabis date back 12,000 years in Central Asia. Cannabis was used for food, fiber, fuel, and spiritual uses although one of the first known medical applications of cannabis was as an anesthetic by the Chinese. Around 2700 BCE, the Emperor Shen Nong of China is thought to have begun a much more widespread use of cannabis for conditions including malaria, constipation, vitamin deficiencies, and gout. While the use of cannabis for a variety of medical diagnoses continued throughout the years, the beginning of its use in veterinary medicine is documented thousands of years ago in India and Pakistan. Ethnobotanical studies reveal its use to treat dysentery and trypanosomiasis in cattle.

Cannabis’ arrival in Europe came somewhat later, in the first millennium AD and during this time, the plant was predominantly used for fiber. There is some speculation that medicinal uses were not explored due to the plant’s physiologic effects being confused with opium and, as such, were considered not acceptable in society. It was not until the 19th century that the medical benefits of cannabis began to be realized in Europe.

An Irish physician named William O’Shaughnessy “discovered” cannabis while studying in India with the East India Company. He brought it back to Britain with him in 1842. Dr. O’Shaughnessy experimented extensively with cannabis, frequently by making an infusion of cannabis leaves and butter. His writings include the use of cannabis for the treatment of epilepsy, cholera, rabies, tetanus, and rheumatism. Dr. O’Shaughnessy wrote that cannabis “led me to the belief that in Hemp the profession has gained an anti-convulsive remedy of the greatest value.”
In the footsteps of William O'Shaughnessy, Walter, E Dixon, a British pharmacologist began testing cannabis’ effect in dogs and cats and thus became the first European to evaluate veterinary uses of medical cannabis. One of the most important discoveries he made was the unique effect cannabis has on dogs. Walter E. Dixon became the first to describe what would come to be known as “Static Ataxia.” Although he didn’t understand the cause, static ataxia is the result of THC toxicity and is only seen in dogs.

By the early 1800’s, cannabis as medicine was being explored in the United States as well. Cannabis was also used in veterinary medicine from the 1800’s to the early 1900’s and its use was detailed in the Veterinary Materia Medica and Therapeutics from 1905. Veterinary uses for cannabis included pain, spasm, nervous irritability, and colic. One recommended use of note was for “long continued pain or spasm” in that it was preferable to opium as it did not cause “constipation, anorexia, or indigestion.”

By 1914, anti-opium sentiment in the US was in full swing and cannabis was caught up in the fervor. There was no public understanding of the differences between cannabis and opium and, as such, they were frequently conflated with one another. The Harrison Act of 1914 was passed predominantly to deal with the country’s opium issue, but it set a precedent on how the US government would address cannabis. While the Harrison Act did not explicitly outlaw opium or cannabis, it levied a tax on their sale that was costlier than the substance themselves.

With alcohol prohibition enacted in 1920, many Americans considered all potentially intoxicating substances immoral and favored outlawing them. The propaganda to demonize cannabis reached new heights in the 1930’s with the release of such films as “Reefer Madness” which depicted innocent “All-American” young adults corrupted by marijuana and turned into violent criminals. The promotions of such misconceptions helped galvanize the negative public perception of cannabis.

Cannabis policy in the United States took yet another disturbing turn in the 1970’s with President Richard Nixon’s “War on Drugs.” In 1970, Nixon signed the Controlled Substances Act which classified drugs and pharmaceuticals according to their medical application and abuse potential. Schedule I drugs were/ are considered to have no medical use and a high potential for abuse. Cannabis was placed in Schedule I alongside drugs such as heroin.

Since the 1970’s the US has been through several iterations of the War on Drugs, all the while failing to differentiate substances like heroin and cocaine from cannabis. In the recent past however, cannabis has seen a resurgence of interest in both its medical use and its social acceptance as a recreational drug. In 1996, California became the first state to legalize the medical use of cannabis for human patients with a doctor’s recommendation. Since then, 31 states have passed laws allowing for the medical and/or recreational use of cannabis. The tide of
public opinion about cannabis use appears to be reaching a critical mass and there are even those within the Federal Government who now favor its legalization.

For the time being, however, non-hemp cannabis is still federally illegal in the US. Hemp based products are “mostly” legal although there have been challenges with these products as well. The 2018 Farm Bill officially de-scheduled hemp-based CBD from the FDA controlled substances list although the FDA still considers it a drug. Because of this, its inclusion in over the counter supplements is still an issue although many producers of hemp-based CBD supplements get around this by not claiming their product contains CBD. Instead, they use terms like “phytocannabinoid rich oil.”

Part of the confusion surrounding hemp, in particular, is affected by how the federal government classifies supplements. The Dietary Supplement Health Education Act (DSHEA), passed in 1994 created a legal category for dietary supplements as a subset of food. In 1996 however, the FDA Center for Veterinary Medicine (CVM) stated the DSHEA does not apply to animals. Thus, all animal products must fall within the category of either food or medicine. All supplements are classified as food or drugs depending on their intended use, ingredients, and method of deliver.

These regulations, of course, exist in conflict with the enormous animal supplement marketplace. Animal supplements of all kinds are routinely marketed and are generally left alone by the FDA unless a company is found to be making illegal label claims or there are complaints about a product being unsafe, etc. In other words, the entire animal supplement market exists in a “grey-zone,” legally speaking. The National Animal Supplement Council (NASC) is a private organization that evaluates animal supplements on a voluntary basis to validate them for quality and appropriate label claims. The FDA generally does not scrutinize supplements with the NASC seal as the product has already been vetted by NASC. When it comes hemp-based extracts, NASC is providing its seal for qualifying products providing consumers and veterinarians with an assurance that such products are of high quality.

Despite federal law and the ongoing confusion about the legalities of specific products, the Federal government took a historic step in 2018 and allowed FDA approval of Epidiolex®, a CBD product, for the treatment of certain forms of pediatric epilepsy. This is the first time the government has publicly acknowledged a medical use for cannabis of any kind.

While states have been busy legalizing medical and recreational cannabis use for humans, until very recently there has been no attention paid to veterinary uses for cannabis. For example, when California passed Proposition 215 in 1996 and opened the door for medical use of cannabis for patients with a medical recommendation, the state specifically designated an MD or DO as the only medical provider allowed to issue a recommendation. There was no consideration at the time for veterinarians to be allowed to issue recommendations for veterinary patients. As such,
the use of medical cannabis (excepting hemp-based products) for animals has remained technically illegal.

Fortunately, times are changing. In 2018, California passed Assembly Bill AB-2215, a first of its kind bill that allows veterinarians to “discuss” the use of medical cannabis for our patients. Just like the passage of the first medical cannabis law in 1996, this ground-breaking legislation is likely to be the seed that propagates to other states and ultimately shapes a national policy towards veterinary uses of cannabis medicine.

Paradoxically, when it comes to hemp, the legal situation for veterinarians is often murkier than with medical cannabis despite the passage the 2018 Farm Bill which de-scheduled hemp and hemp extracts. Individual states are taking different positions as it pertains to veterinarians and hemp products despite these products being available to pet owners nationwide as over the counter products. Currently in California, the Veterinary Medical Board is warning veterinarians away from the use of hemp products in their practices:

“Industrial hemp is not tested or regulated in the same manner as cannabis, so the veterinarian should use caution when administering, dispensing, furnishing, recommending, or discussing industrial hemp and ensure the product to be used is industrial hemp and not cannabis. and should only do so after the industrial hemp product has been approved by the FDA for use in animals. Further, any industrial hemp product intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease or intended to affect the structure or any function of the body of an animal is a drug. There are no FDA-approved drugs containing industrial hemp for use in animals. A veterinarian who manufactures, markets, or sells drugs not approved by the FDA is in violation of federal law.”

As veterinarians, we all must decide what is the best way to address the topic of cannabis within our practices. What you choose to do should depend on your state laws regarding cannabis in general and the position your Veterinary Medical Board has chosen to take. Most boards seem to be taking a hands-off approach and allowing veterinarians to practice medicine. That said, as veterinarians, it is our responsibility to understand our local laws and act in a way that each of us feel is ethically and legally appropriate. If nothing else however, in order to use medical cannabis safely and effectively in our patients, we need to be educated about what cannabis is, how it works, and how to use it appropriately.

References
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References


Cannabis in Veterinary Medicine
Part 2: The Endocannabinoid System
Gary Richter, MS, DVM, CVA, CVC, GDVWHM

Objectives
- Describe the structure and function of the endocannabinoid system
- Understand endocannabinoids, ECS receptors, and degradation enzymes

The Endocannabinoid System
The endocannabinoid system (ECS) was originally described by Israeli researcher Raphael Mechoulam in the 1970’s. What Dr. Mechoulam discovered was a previously unknown system of neurotransmitters and receptors that had profound implications on our understanding of how the body functions. The major function of the ECS is in neuromodulation. More specifically, the ECS can alter the physiologic function and behavior of body tissues. The ECS is widely found throughout the animal kingdom. All complex animals have an ECS as well as many of the most primitive animals including nematodes.¹

The ECS affects physiologic and cognitive processes throughout the body and promotes homeostasis and decreased endocannabinoid levels can lead to homeostatic disruption.² Research is ongoing into the physiologic effects of imbalances of the ECS and it appears that disruption of this previously unknown body system may have wide ranging and profound effects on health. Endocannabinoid deficiency is speculated to be a contributing cause of chronic, difficult to treat diseases such as migraines, fibromyalgia, and irritable bowel syndrome.³

Broadly speaking, the ECS consists of three major components: Receptors, Endocannabinoids, and Regulatory Enzymes.

Endocannabinoid Receptors
Endocannabinoid receptors are present on neurons throughout the CNS, PNS, and periphery. A variety of ECS receptors are found including G-Protein coupled receptors, ligand gated ion channels, and nuclear receptors.⁴ While there are many specific receptors, the most commonly found are the CB1 and CB2 receptors.

CB1 is the most abundant protein bound receptor found throughout the CNS. In addition to the CNS however, CB1 is found in a variety of tissues including fat cells, liver cells, musculoskeletal tissues, the GI tract, cardiovascular tissues, peripheral nerves, immune cells, and the reproductive tract. The ubiquitous nature of CB1 throughout the body gives us an idea of how vital the ECS is to body functions. CB1 mediates inhibitory action on a wide variety of neurotransmission systems including:⁵
- Dopaminergic
- Gamma-aminobutyric acid (GABA)
- Glutaminergic
- Serotoninergic
- Noradrenalin
- Acetylcholine neurotransmitter systems

Since the neurotransmitter systems listed above have profound effects on body systems and processes, CB1 therefore effects:
- Mood
- Cognition
- Reduction of pain and inflammation
- Appetite
- Nausea
- CB1 is also responsible for the psychoactive effects of THC

In contrast to CB1, CB2 receptors are predominantly found in the periphery and the immune system. CB2 is frequently expressed on T and B lymphocytes and macrophages as well as cells of the spleen, liver, kidneys, and skin. CB2 receptors function, not surprisingly, in immune modulation and in mediating inflammation. Research also indicates they play a role in maintaining bone density.6,7

Present discussions about the mechanisms of action of cannabis frequently focus on CB1 and CB2 receptors. While these are the most talked about and have been the subject of more study, there are numerous other receptors that interact with endogenous cannabinoids, and by association, exogenous cannabinoids. Some of these receptors and their functions are as follows:8

- G-Protein Coupled Receptors
  - GPR 18: Immune, Anti-inflammatory, Blood Pressure
  - GPR 55: Pancreas- Insulin Release
  - GPR 119: GI Tract- Regulates Energy Intake
- Ligand-Gated Ion Channels
  - TRPV1: Brain- Analgesia
  - 5-HT3: Brain- Analgesia
  - GlyR: Spine- Analgesia
- Nuclear Receptors
  - PPARa: Brain- Neuroprotection
  - PPARy: Brain- Neuroprotection

**Endocannabinoids**
The neurotransmitters, or endocannabinoids, for the ECS are generated on-demand rather than being stored within cells. Two endocannabinoids, anandamide (AEA) and 2-Arachidonoylglycerol (2-AG) interact with CB1, CB2 and the other endocannabinoid receptors discussed above. AEA is the primary endogenous ligand for CB1 and is a highly selective partial
agonist for CB1. 2-AG is the primary endogenous ligand for CB2 and is a moderate affinity full agonist for CB2.\textsuperscript{9,10} In addition, 2-AG also functions as a moderate affinity full agonist for CB1.\textsuperscript{11} Endocannabinoids function on both the cell surface and within the interior depending on the receptor they are interacting with.

**Degradation Enzymes**

The third piece of the triangle of the ECS is degradation enzymes. Just as the endocannabinoids are synthesized on-demand, they are degraded when they are no longer needed. The two major degradation enzymes are Fatty Acid Amide Hydrolase (FAAH) and Monoacylglycerol Lipase (MAGL). While FAAH provides enzymatic degradation of AEA, MAGL hydrolyzes 2-AG specifically.\textsuperscript{12} Fatty Acid Binding Proteins (FABP) mediate the transport of AEA to FAAH. It should be also noted that COX-2 also metabolizes AEA and 2-AG.

**Gut-Brain Axis**

While frequently thought of in the context of CNS neurotransmission, the ECS plays a significant role in the gut-brain axis as well. Because of the connection to the CNS, the ECS affects gut function both centrally and peripherally. CB1 receptors in the gut are expressed on enteric neurons and enteroendocrine cells while CB2 is found on neurons and immune cells. Activation of cannabinoid receptors within the gut results in reduction of motility, inflammation, pain, and immune activation. More specifically, CB1 receptors in the sensory ganglia control visceral sensation and may provide a link between stress and GI pain and some forms of IBS are associated with abnormal CB1 receptors and/or abnormal FAAH. Additionally, chronic stress and antibiotic related dysbiosis leads to upregulation of CB2 receptors within the gut.\textsuperscript{13}

**Clinical Endocannabinoid Deficiency\textsuperscript{14}**

Many brain disorders are associated with deficiencies of neurotransmitters. For example, Alzheimer’s correlates with acetylcholine deficiencies, Parkinson’s disease is associated with a dopamine deficiency, and clinical depression may be related to low levels of serotonin and/or norepinephrine.

If the ECS is so important to nearly all aspects of biological function, what happens in the event of dysregulation? Clinical Endocannabinoid Deficiency (CED) has only recently been described and may be a cause, at least in part, for several severe, chronic disease conditions affecting humans (and possibly animals).

All animals possess a normal underlying level of endocannabinoid tone which consists of a combination of AEA and 2-AG levels. Given what we know about the function of the ECS, deficiencies in one, or both, ECS neurotransmitters may be expected to result in clinical symptoms such as lowered pain threshold, disruption of digestion, alterations in mood/ sleep, etc.
There are multiple diseases that are being evaluated as potentially having roots in CED but three conditions with the most compelling data in this regard are fibromyalgia, irritable bowel syndrome, and migraines.

When we look at fibromyalgia, irritable bowel syndrome, and migraines, it becomes clear there are commonalities between them. All three manifest with hyperalgesic states. All are also classically a “diagnosis of exclusion” generating negative workups with patients. Additionally, all are associated with a degree of anxiety and depression. It is unclear if this last point is a symptom of or a sequela of the disease process, but it is a fact than many patients with one of these conditions have been labeled as having psychosomatic disease. Lastly, co-morbidity is common with patients. 97% of fibromyalgia patients report headaches and 31.6% of patients with chronic daily headaches fit the diagnostic criteria for fibromyalgia. The lifetime risk of these patients to develop another (or all three) conditions is common.

Inflammatory Bowel Syndrome (IBS), or as we commonly refer to it in veterinary medicine, Inflammatory Bowel Disease (IBD), is a disorder of unknown origin and mechanism of action. It has been suggested that IBS/IBD represents a combination of visceral hypersensitivity, gastrointestinal allodynia, and hyperalgesia. As discussed above, the ECS plays a large role in gut function including modulating GI motility, secretion, and inflammation. Inflammation in the gut is known to increase gut endocannabinoid concentrations as well. In addition, TRPV1 nerve fibers are upregulated 3.5X in the gut of IBS patients. This suggests that increasing AEA levels (or using FAAH inhibitors or THC) and/or desensitizing TRPV1(via CBD or other mechanisms) may be useful in the treatment of IBD/IBS.

Migraines in humans are characterized, in part, by photophobia and phonophobia which is the kind of homeostatic imbalance the ECS tends to correct. Chronic migraine patients have been shown to have significantly lower levels of anandamide (in CSF) than normal patients. Anecdotally, chronic migraine sufferers have also reported improvements in headaches with the use of THC, the phytocannabinoid analogue for anandamide.

Fibromyalgia is severe, but often vague, condition characterized as soft tissue pain that can “wander” throughout the body. The pain is often exacerbated by exertion and overuse. The condition is suspected to be a central sensitization consistent with neuropathic pain. Secondary hyperalgesia, which is often noted in patients, is also associated with CED. In fibromyalgia patients, cannabis has been shown to be more effective than many of the commonly used pharmaceuticals, including duloxetine, milnacipran, and pregabalin.

Summary
The endocannabinoid system is a recently described system of neurotransmitters, receptors, and degradation enzymes that have widespread effects in the body. The overarching purpose of the
ECS is to maintain homeostasis although it accomplishes this in a wide variety of ways. There is mounting evidence in support of implicating endocannabinoid deficiency as a possible cause/contributing factor to a wide variety of clinical diseases.

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Cannabis in Veterinary Medicine
Part 3: Phytocannabinoids
Gary Richter, MS, DVM, CVA, CVC, GDVWHM

Objectives
- Discuss the spectrum and activity of the phytocannabinoids
- Explore the pharmacokinetics of phytocannabinoids
- Discuss safety and efficacy of phytocannabinoids in veterinary patients

The Phytocannabinoids
As is always the case with botanical medicine, cannabis and other plants produce compounds that have activity in animal systems. This is especially true in the case of phytocannabinoids. Phytocannabinoids are exogenous, plant-based compounds that act on endocannabinoid receptors in the body. There have been over 700 compounds identified in cannabis including over 100 phytocannabinoids, over 200 terpenes, 30 flavonoids, as well as B vitamins and essential fatty acids. The phytocannabinoids have varying affinity for endocannabinoid receptors as well as other receptors in the body. Some of these plant-based compounds have profound physiologic effects and are the subject of intense medical research.¹,²

Δ⁹-Tetrahydrocannabinol, better known as THC, is one of the most well-known and well-studied of the phytocannabinoids. THC is a partial agonist of both CB1 and CB2 receptors and is phytomimetic for AEA. THC’s binding affinity for CB1 receptors is responsible for its psychoactive properties.

A medically critical attribute of THC is its ability to relieve pain. Much of this ability is not related to its binding to cannabinoid receptors, however. THC’s pain analgesic properties are in large part due to it being a positive allosteric modulator of mu and delta opioid receptors.³

Known physiologic effects of THC include:
- Analgesia
- Anti-neoplastic
- Anti-inflammatory
  - Via TNF-alpha
  - Affects cytokine production
- Anti-nausea
- Sedative/ anxiolytic
- Reduction of IOP
- Neuroprotective
The pharmacokinetics of orally ingested THC are as follows:

- Ingested THC is absorbed and distributes to the adipose, liver, lung and spleen
- THC is hydroxylated in the liver by CYP450 to 11-hydroxy-Tetrahydrocannabinol (potentially more psychoactive)
- 11-hydroxy Tetrahydrocannabinol is then further oxidized to 11-nor-9-carboxy-\(\Delta^9\)-tetrahydrocannabinol (non-psychoactive)
- Most excretion is through feces although some renal excretion occurs as well

One of the most interesting facets of THC is its level of safety. For a compound with the degree of highly profound physiologic effects, not to mention psychoactivity, THC is remarkably safe. It does not cause respiratory depression at any dose and thus, unlike opioids, will not lead to apnea. From a veterinary perspective, there is no known LD\(_{50}\) for cannabis in dogs. Doses of greater than 3000 mg/kg of pure THC have been given in research models without resulting in a fatality.\(^4\) Compare this to nearly all of today’s veterinary pharmacy (particularly analgesics and anti-neoplasitics) and it brings in to question why there is so much legal controversy over using phytocannabinoids as medicine in either human or veterinary patients.

**Note:** While there is no LD\(_{50}\) for THC, this does not mean THC is harmless. Serious toxicity including static ataxia (discussed later in this lecture series) as well as potential death can occur. THC related deaths, although rare, generally occur due to secondary issues such as aspiration pneumonia and sepsis.

Extensive studies on the pharmacokinetics of THC in dogs and cats have yet to be published. One small study evaluating adverse events in dogs with either CBD, THC, or a combination found (not surprisingly) that high doses of THC led to ataxia. Paradoxically, this study also found the CBD/THC combination group had a greater level of adverse events than the THC group. This result does not follow common logic and is not reflective of the real-world experience of many veterinarians whose patients are on cannabis.\(^5\)

Cannabidiol, also known as CBD, is the other “big player” in today’s discussions about cannabis as medicine. Unlike THC, CBD is both a CB1 and CB2 antagonist although it has relatively low to moderate binding affinity for both receptors. In addition to its effects on CB1 and CB2, CBD has other modulatory effects on the ECS. CBD has been shown to be a FAAH inhibitor in mice, although the same effects have not been seen in humans. It is unclear if the inhibitory effect of FAAH is present in species commonly treated in veterinary medicine. CBD also binds FABP which slows/limits AEA’s degradation by FAAH and thus may promote greater AEA activity. And like THC, CBD is also a positive allosteric modulator at mu and delta opioid receptors.\(^6\)

CBD also has a dampening effect on the psychoactivity of THC. The multi-factorial reasons for this include CBD’s inhibition of CYP450, which slows the transition of \(\Delta^9\)-THC in the liver to
the potentially more psychoactive 11-hydroxy Δ⁹-Tetrahydrocannabinol. Additionally, CBD is a negative allosteric modulator of CB1 and CB2, which reduces the effects of THC. This dampening effect is in contrast to the previously mentioned study suggesting increased levels of THC toxicity when THC and CBD are combined.

Known physiologic effect of CBD include:
- Pain control
- Anti-neoplastic
- Anti-inflammatory
  - COX-2 inhibition
  - Via TNA-alpha
  - Affects cytokine production
  - Affects NF-K Beta
- Calming/ anxiolytic
- Anti-convulsant
- Reduces blood pressure
- May decrease insulin resistance

The pharmacokinetics of orally ingested CBD are as follows:

1. Orally ingested cannabidiol is absorbed through the gastrointestinal tract
2. CBD is converted to 7-OH-CBD and 6-OH-CBD in the liver by CYP450
3. CBD appears to be a competitive inhibitor of CYP450
   1. Slows conversion of Δ⁹-THC to 11-hydroxy-Δ⁹-THC
   2. Concern for possible drug interactions

In a recent study looking at CBD use in dogs, CBD was found to be well tolerated, even at high doses of 10-20 mg/kg/day. The only hematological effect noted as an elevation in serum ALP, which was likely due to CYP450 interactions. Physiologic side effects were limited to mild gastrointestinal signs, pinnal erythema, and oculo-nasal discharge noted. Additionally, different preparations of CBD (infused oil, microencapsulated oil beads, transdermal cream) were evaluated. All were absorbed although the orally administered formulations achieved greater absorption sooner. Yet another study indicates CBD infused soft chews are absorbed better than infused oil and infused oil given with food is absorbed better than oil given without food. Lastly, a recently published small study looking at Pk of CBD in dogs and cats suggests that show lower serum concentrations than dogs at similar doses suggesting there may be differences in absorption and/or metabolism.

In addition to Δ⁹-THC and CBD, there are many other phytocannabinoids that show great promise as medicine. Research is ongoing for many of these compounds and the following is a synopsis of what we know about many of the so-called “minor cannabinoids.”
THCA
Tetrahydrocannabinolic Acid (THCA) is the non-psychoactive precursor of the more well-known Δ⁹-THC. THCA occurs largely in fresh, or newly harvested cannabis. The process of drying or heating the plant material leads to decarboxylation of THCA and conversion to Δ⁹-THC. Since a majority of cannabis plants (other than hemp) are grown for Δ⁹-THC, THCA is one of the most abundant phytocannabinoids.¹⁵

For all of the benefits of Δ⁹-THC, it must be used within tolerable limits. While a certain degree of psychoactivity is frequently an acceptable side effect in human patients, it is never an acceptable outcome in animals. THCA is a very attractive compound to use in veterinary patients because it is non-psychoactive.

Research into THC-A is ongoing and what we know at this point indicates this compound has wide ranging medical benefits. Some of these include:¹⁶

- Anti-emetic
- Anticonvulsant
- Anti-inflammatory (COX-2 Inhibition)
- Anti-neoplastic
- Antispasmodic
- Neuroprotective

As mentioned above, when THCA is heated or dried, it converts to Δ⁹-THC. Thus, in order to use THCA, it must be extracted from fresh, or relatively fresh plant material. The delivery mechanism for THCA in human is through ingestion as heating (such as smoking or vaporizing) will lead to the formation of Δ⁹-THC. As most cannabis medicines used for veterinary patients are ingested anyway, there is no difference here with regards to delivery method.

Whereas THCA is the molecular precursor to Δ⁹-THC, cannabinol (CBN) forms when Δ⁹-THC is exposed to heat and oxygen over time. In other words, CBN is found in high concentrations in cannabis that is old. Medical benefits of CBN are being studied although some of the properties we know of are:

- Mildly psychoactive
- It is a potent sedative (much more so than THC or CBD). As such, it is a powerful tool for fighting insomnia
- Anti-anxiety
- Anti-convulsive
- Antibacterial
- Anti-emetic
THCV
Tetrahydrocannabivarin, or THCV, is another cannabinoid with interesting medical properties. Like Δ⁹-THC, THCV has psychoactivity, although it is “different” than its more well-known relative. Some of the known properties of THCV include:\textsuperscript{17}
- Calming - possibly useful for panic attacks or PTSD
- Bone growth stimulant
- Appetite suppressant
- Anti-convulsant
- Blood sugar regulation

CBGA and CBG
Cannabigeric acid, or CBGA, is the precursor cannabinoid. All other cannabinoids ultimately stem from CBGA. Cannabigerol, or CBG, is the decarboxylated form of CBGA. CBG and CBGA are non-psychoactive and, as precursor molecules to both THC and CBD, they are found in cannabis strains grown for their THC content and those grown for CBD only (hemp).\textsuperscript{18}

Properties of CBG include:
- Analgesia
- Sedation
- Muscle Relaxation
- Anti-neoplastic
- Bone Stimulant

CBDA
Cannabidiolic acid, of CBDA is the precursor to CBD. Research into the medical properties of CBDA are ongoing. Properties associated with CBDA include:\textsuperscript{19,20}
- Anti-nausea
- Anti-inflammatory
- Anti-neoplastic

CBC
Cannabichromene, or CBC, is only found in small quantities in cannabis. This is another phytocannabinoids that may have great potential although research is in its early stages.
Properties of CBC include:\textsuperscript{21}
- Analgesia
- Muscle relaxant
- Anti-neoplastic
- Bone stimulant
- Anti-inflammatory
Sleep aid

Conclusion
The phytocannabinoids have direct effects on the ECS as well as activity at non-ECS receptors. Based on these interactions, we can expect cannabinoids such as THC, CBD, and others to have potential applications in the promotion of homeostasis and in the treatment of a variety of medical conditions. Therapeutic use of phytocannabinoids will be discussed in detail in the final presentation of this series.

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Cannabis in Veterinary Medicine
Part 4: Terpenes, Flavonoids, Cannabinomimetics, and
The Creation of Cannabis Medicines
Gary Richter, MS, DVM, CVA, CVC, GDVWHM

Objectives
- Discuss the spectrum and activity of the phytocannabinoids and terpenes
- Discuss cannabinoid-like effects of natural non-cannabis compounds
- Consider the multiple factors that lead to the ultimate content of a medical cannabis product

Terpenes
While cannabinoids like Δ9-THC and CBD get much of the credit, the terpenes may be the
unsung heroes of medical cannabis’ efficacy. Terpenes are volatile hydrocarbons found in the
essential oils of cannabis, and many other plants. Terpenes are made up of the base unit, isoprene
(C5H8), are the largest and most diverse class of natural compounds found on Earth. Many
commonly encountered compounds in life and in medicine are terpenes. Some examples include:1
- Limonene- responsible for the smell of citrus
- Squalene
- Vitamin A
- Natural Rubber

In the plant world, terpenes are produced for protection (anti-bacterial and anti-fungal), chemical
signaling, and as attractants. There have been over 200 distinct terpenes isolated from cannabis.
Terpenes are produced outside the main body of the plant in glandular structures called
trichomes. It is interesting to note it is the terpenes that are responsible for cannabis’ smell and
taste as the cannabinoids are odorless and tasteless.

Ten of the most commonly found terpenes in cannabis are:
1. Myrcene
2. Pinene
3. Limonene
4. Caryophyllene
5. Humulene
6. Linalool
7. Eucalyptol
8. Borneol
9. Phytol
10. Geraniol

Terpenes in cannabis, like many essential oils, have physiologic effects in their own right. When
combined with the cannabinoids, the terpenes can have a profound effect on how cannabis
effects the body. Two specific examples of the power of terpenes in cannabinoid medicine are
Beta-Caryophyllene, which is a CB2 agonist and myrcene, which is thought to potentiate the
effects of the cannabinoids.2

As is the always the case with whole plant medicine, a synergistic, entourage effect exists
between the cannabinoids and terpenes and combinations of these powerful compounds can lead
to powerful medical benefits. This is also why isolates of compounds such as the synthetic
cannabinoid Marinol® (synthetic THC) are frequently considered less effective than “real” cannabis. Following are examples of cannabinoid-terpene synergy.\(^3,4\)

### β Caryophyllene:
- + THC = Enhanced gastric mucosal cell protection
- + THC = Antipruritic and cholestatic jaundice
- + CBD = Enhanced anti-inflammatory effects
- + CBG = Antihyperalgesic and antifungal

### Limonene:
- + CBD = Increased anti-anxiety/ anti-depressant effects
- + CBC + CBG = Enhance antidepressant effect
- + CBD + CBG = Enhanced anti-cancer effects
- + THC = Enhanced anti GERD effects
- + THC = Enhanced anti-inflammatory and antioxidant effect

### Linalool:
- + THC = Enhanced sedation, muscle relaxation and analgesia
- + CBD = Enhanced anti-anxiety and analgesic effect
- + CBD + THC + CBDV + THCV = Enhanced anti-convulsant effect
- + CBG = Enhanced anti-inflammatory effects
- + CBN = Enhances TRPV2 agonist for burns
- + CBD + CBN + Limonene = Aids insomnia and anxiety

### β Myrcene:
- + THC = May enhance effects of THC
- + CBD = Enhanced anti-inflammatory effects
- + CBG = Enhanced anti-inflammatory effects
- + CBN = Enhance sedative effects
- + β Caryophyllene + THC + CBD = Enhanced analgesia
- + β Caryophyllene + THC + Pinene = Attention Deficit Disorder Relief

One final note on terpenes is with regards to their volatility. Methods of preparation and storage have a profound effect on the terpene content of cannabis products. In order to retain these precious compounds in medical cannabis formulas, great care must be taken to prevent their loss through evaporation or degradation.

**Flavonoids**

Another class of compounds produced by cannabis are the flavonoids. Flavonoids are plant-based antioxidants found in many fruits, vegetables, etc. There have been at least 29 flavonoids found in cannabis including apigenin, which has anti-anxiety and anti-inflammatory properties. Another flavonoid is the antioxidant compounds known as catechins. In addition, cannaflavinin A, a flavonoid unique to cannabis appears to have a potent anti-inflammatory effect. Lastly, quercetin, a well-known flavonoid commonly found in leafy vegetables, broccoli, red onions,
peppers, apples, grapes, tea, and red wine is also found in cannabis. Quercetin has a number of activities including being anti-proliferative, pro-apoptotic, anti-inflammatory, antihistamine, anti-fungal, and it is a CB1 agonist.\textsuperscript{5}

**Cannabinomimetics**

Cannabis is not the only plant to produce compounds that affect the ECS. A number of other species produce such metabolites. \textit{Radula spp.} (Liverwort) from New Zealand produce perrottetinene, which is similar to $\Delta^9$-THC.\textsuperscript{6} \textit{Lepidium meyenii} (maca or Peruvian ginseng) produces Alkylamides that mimic cannabinoids and \textit{Helichrysum umbraculigerum} produces compounds that mimic CBG and CBG-A.\textsuperscript{7,8} Polyacetylene falcarinol found in carrots, parsley, celery, and in \textit{Panax ginseng}, inhibits CB1 receptor activation by AEA in vitro and Kava Kava (\textit{Piper methysticum}) produces yangonin, a kavalactone which is a CB1 receptor ligand and is postulated to be responsible for Kava’s anxiolytic effect.\textsuperscript{9,10}

One of the more surprising herbs that produces a cannabinomimetic is Echinacea. Alkylamides from echinacea modulate TNF-alpha via CB2 receptors. Alkylamide-CB2 binding is stronger than with endogenous cannabinoids and decreased inflammation and modulation of cytokine production through Echinacea is in part due to CB2 binding.\textsuperscript{11} This may, in part, explain echinacea’s positive effects on GI tract health.

One of the most prevalent terpenes found in cannabis, b Caryophyllene, is also a CB2 agonist suggesting that this compound is both a terpene and a cannabinoid. In addition to cannabis, b Caryophyllene is found in Black Pepper (\textit{Piper nigrum}), Clove (\textit{Syzygium aromaticum}), Copaiba (\textit{Copaifera reticulata}), Holy Basil (\textit{Ocimum tenuiflorum}), Lavender (\textit{Lavendula spp.}), and Ylang Ylang (\textit{Cananga odorata}).\textsuperscript{12,13}

The endocannabinoid anandamide is also known as the “bliss molecule.” Interestingly, this compound is also found in black (\textit{Tuber melanosporum}) and white (\textit{Tuber magnatum}) truffles as well as in Cacao (\textit{Theobroma cacao}). Is it any wonder that truffles and chocolate are two of the most highly prized food items on the planet?\textsuperscript{14,15}

Lastly, and perhaps most unexpectedly, are the omega-e fatty acid epoxides. A previously unknown class of omega-3 PUFA lipid metabolites derived from EPA and DHA, the omega-3 endocannabinoid epoxides are found at concentrations comparable to those of other endocannabinoids. These epoxides are expected to play a critical role in regulating inflammation and may explain some of the anti-inflammatory activity of omega fatty acids.\textsuperscript{16}

**Creating Cannabis Medicines**

As mentioned previously, over 100 cannabinoids have been isolated from cannabis. In addition, over 200 terpenes and over 29 flavonoids have been isolated. The various cannabinoids, terpenes, and flavonoids effect the ECS and other body systems differently and thus, cannabis can potentially serve many medical functions. The spectrum and relative quantities of cannabinoids and terpenes have enormous effect on a formula’s medical utility.

There are many factors that affect the final content of a cannabis medicine formula beginning with plant genetics (genotype) and physical characteristics (phenotype). Methods of harvesting
and curing also play a critical role as the plant naturally produces cannabinoid acids (CBDA, THCA) and only with heating or drying do these compounds decarboxylate to CBD and D-9-THC. Lastly, the method of extraction will also affect medicine content in that differing methods (alcohol, CO2, lipid, thermal, etc.) will yield different spectrums of cannabinoids as well as having a dramatic effect on the terpene profile as terpenes are highly volatile and can boil off during processes involving high heat.

Once a cannabis medicine is created, for it to have value, we must know what it contains. A certificate of analysis (CoA) is a critical and necessary step for any cannabis product to have value as medicine. Laboratories can analyze cannabis for Cannabinoid and terpene content (mg/g, mg/ml, or %), pesticide and fungicide residue, bacterial and fungal contamination, residual solvents, and heavy metals. All these factors are necessary to determine the medical utility and safety of a given formulation.

In the field of medical cannabis, one of the most challenging things facing the industry is consistency. As a natural product, cannabis is always going to be subject to variation in plant yield which can be affected by genetics, growing conditions, etc. No two plants (even clones) will have the same cannabinoid and terpene profiles. For recreational use, this is not a major issue but when patients count on cannabis medicine to manage medical problems, it is vital that each new bottle purchased be the same as the last. While this issue has not been fully addressed yet, makers of cannabis medicines are exploring ways to provide consistency with their products. This also highlights the need for a CoA for every batch of product made so consumers know how one bottle may differ from the next.

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Objectives

- Discuss current research and the potential clinical applications for cannabis medicines
- Discuss THC to CBD ratios and dosing of cannabis for dogs and cats
- Explore product formats for animals

Cannabis in modern medicine and research is being utilized more and more in the treatment of a wide variety of medical conditions. The following is an incomplete list but represents the most common and scientifically justified applications:

- Anti-inflammatory
- Analgesia
- Seizure Control
- Anxiolytic
- Anti-neoplastic
- Lowers IOP
- Gastrointestinal support

Anti-Inflammatory

Chronic inflammation is as great of a challenge in veterinary medicine as it is in human medicine. One veterinary specific area that has been studies is eosinophilic dermatitis and hypersensitivity in cats. Research has shown that affected cats display an increased expression of cannabinoid receptors in their skin. A subsequent reduction in inflammation occurs due to PPAR activation. Although the cause and effect here is unclear, it is speculated the upregulation of cannabinoid receptors in a protective strategy to limit inflammation in affected cats. It is possible the use of cannabinoid receptor agonists may provide novel therapeutic options.1

Analgesia

Studies evaluating the efficacy of cannabis in treating osteoarthritis (OA) in dog have been completed as well. A recent study from Cornell University showed reduction in pain scores in dogs with OA when treated with CBD at 2 mg/kg BID vs. placebo with no negative side effects.2 Another study (currently unpublished) showed efficacy in the treatment 15 of 16 dogs with OA at a dose of 0.3 mg/kg/day for four weeks.3 It should be noted that while both of these studies evaluated CBD in the treatment of OA, other entourage compounds (cannabinoids, terpenes, etc.) were not evaluated. The Cornell study did use a full spectrum hemp oil, but the potential entourage effect of the product was not considered. It is unclear if the unpublished study used a full spectrum product or a CBD isolate. Regardless, further research may show greater efficacy at lower doses if they take advantage of other entourage compounds known to have analgesic effect.

Anti-Convulsant Therapy

Another well-known effect of cannabis is in the treatment of seizures. Research bears out what many people have known for a long time about cannabis’ ability to lessen seizures. One recent study evaluating children with intractable pediatric epilepsy showed marked improvements.
Despite the study population being children with intractable breakthrough seizures despite being on multiple pharmaceutical anti-convulsant therapy, over 50% had between a 50-100% reduction in seizures. An ongoing veterinary study from Colorado State University showed an 89% reduction in seizure frequency with the use of 2.5 mg/kg CBD. There was concurrently a 43% reduction in the control group although these patients were still on conventional anti-convulsant therapy.

**Anxiolytic**

Anxiety is a clinical problem of great significance in both human and veterinary medicine. The combination of genetic predisposition and the lasting effects of traumatic events often result in humans and animals with PTSD, phobias, and other anxiety disorders. CBD has been found have anxiolytic effects through both GABA and 5HT (serotonin) receptors. At the most basic level, the way humans and animals “get past” trauma is to forget the fear associated with the traumatic event. The brain is designed to allow events to be forgotten as it would not be advantageous for an individual to remember every event that has happened in life. Our ability to forget is an adaptation that allows us to function on a day to day basis and to leave in the past negative experiences that are of no benefit for us to remember vividly. It is speculated that one of the causes of lasting anxiety is the inability to forget these traumatic events. CBD may provide a pathway to allow to brain to forget what it needs to and allow the individual to live in less fear.

**Cancer**

Of all the disease conditions cannabis may be of benefit for, cancer may be the one with the most hope and the most doubt. Due to a lack of understanding of its mechanisms by the general public, cannabis is sometimes portrayed as the “cure all” for everything, including cancer. While clearly this is not the case, there is ample research into the anti-neoplastic effects of cannabis and the mechanisms by which it functions are numerous.

Cannabis inhibits the growth of cancer through multiple mechanisms. Some of the specific mechanisms include:

- Antiproliferation
- Apoptosis
- Autophagy (possibly leading to apoptosis)
- Cell cycle arrest
- Radiation Sensitizing
- Inhibition of FAAH (inhibited growth of thyroid carcinoma and reduced colonic carcinogenesis

**Glaucoma**

Cannabis has been shown to lower IOP in glaucoma patients. THC, at a dose of 5 mg sublingually reduced IOP for four hours. Smoked cannabis also led to a decrease in IOP although this is clearly not a therapeutic option in veterinary medicine. It should be noted that CBD was not shown to lower IOP.

**The Microbiome and Gastrointestinal Effects**

There is fascinating research into how cannabis effects the microbiome and thus, systemic health. As we know, 70% of the immune system lives in the gut and gut health is ultimately
critical to immunity and overall health. Following are some of the mechanisms by which cannabis affects the microbiome, gut integrity, and subsequently systemic health:12

- THC alters microbiome balance and prevents obesity in laboratory animals
- THC prevents weight gain despite a high fat diet
- CBD has both anti-inflammatory and bacteriostatic effects in the gut
- CB2 levels directly correlate to *Lactobacillus* concentrations and inversely with potentially pathogenic *Clostridium* species
- Orally administered lactobacillus induces mRNA expression of the gene that encodes for CB2 receptors (CNR2)
- Dysbiosis and translocation of bacterial fragments leads to metabolic endotoxemia and is associated with cognitive impairment, Parkinson's disease and Alzheimer's disease

Inflammatory bowel disease and colitis are common problems encountered in veterinary medicine. The human equivalents of these conditions are IBS and Chron’s disease. All these conditions are debilitating and have a large impact on quality of life of the affected human or animal. Frequently, the only therapies for these patients are steroids or other immune modulating/immune suppressive drugs. Cannabis, however, has been shown to be effective as well. A human study evaluating an 8-week course of THC rich cannabis led to significant clinical, steroid-free benefits in 10 of 11 Chron’s patients without side effects.13

**THC and Static Ataxia**

One final point before discussing cannabinoid ratios and dosing schedules is the very practical matter of patient safety. The single biggest safety concern regarding cannabis in veterinary medicine is that of THC toxicity. While fatalities from over ingestion or administration of THC are exceedingly rare, toxicity can and does occur albeit mostly when dogs ingest cannabis edibles that were intended for humans.

Excessive in any animal THC can lead to somnolence and depressed mentation in any animal but dogs manifest THC toxicity in very specific ways. Dogs have a higher concentration of cell membrane receptors in the cerebellum than any other species that has been studied.14 As a result, dogs manifest the signs of THC toxicity in a unique way known as static ataxia. Dogs intoxicated on THC will frequently adopt a sawhorse stance to maintain their balance. The frequently will sway to one side or the other and nearly fall over but catch themselves as the last minute. In severe cases, they may not be able to stand at all.

Unlike opioids, cannabinoids do not depress respiration and as such, overdoses are rarely fatal. You may recall in a previous discussion of there being no known LD50 for THC in dogs. That said, fatalities occasionally occur due to related complications. One such effect I have personally witnessed is a dog that consumed a large quantity of cannabis edibles intended for humans. The owner did not seek medical help for over 24 hours and the dog, unconscious for most of that time, vomited and aspirated. He later died of pneumonia and sepsis. This illustrates the need for medical attention any time an animal consumes a significant overdose of THC. As many of us have seen in practice, these dogs generally do fine with appropriate supportive care.
Choosing the Right Medicine and Appropriate Dosing
When considering cannabis as a medical option, it is important to keep in mind how the various components of a cannabis preparation may affect the patient. Some important factors to keep in mind are: 15

- The Entourage Effect- the quantity and distribution of major and minor cannabinoids, terpenes, and flavonoids affect the degree of biological activity and the spectrum of diseases treated
- The use of the appropriate ratio of THC and CBD as well as dose are critical to success
- Consider other medications being given concurrently with respect to their possible side effects (sedation) and their metabolism (CYP450)

While the full entourage effect is important, most cannabis medicines available currently are only controlling for CBD and possibly THC. While there may be other cannabinoids and terpenes present, products frequently do not list them on their label and precise dosing information for veterinary patients is not available. As the science of cannabis medicine progresses, components far beyond THC and CBD will come in to play. As a practical matter, dosing for THC and CBD content is the most important, and to a large extent the only consideration to make at this time with perhaps one exception (THC-A) noted below.

Ratios of THC and CBD frequently range as high as 20:1, to even ratios (1:1), to 1:20. The following are guidelines for medical applications for these various ratios. There is overlap in conditions treated from one group to the next since, as we have discussed, both THC and CBD frequently have similarities in their physiologic effect although sometimes the mechanism of action differs. Keep in mind these are guidelines and individual patient response varies.

**High THC Ratios:**
- 4:1 to 20:1 THC to CBD
- Severe pain- cancer, advanced DJD, etc.
- Appetite stimulation
- Anti-cancer activity

**Even Ratio**
- 1:1 THC to CBD
- Neurologic- spinal cord or brain injury
- Pain
- Inflammatory Bowel Disease, Pancreatitis, Colitis
- Anti-cancer activity

**High CBD/ Hemp**
- 1:4 to 1:20 THC to CBD
- Anxiety
- Seizures
- Cognitive dysfunction
- Pain
- Anti-cancer activity
• Insulin resistance/ diabetic control

Note that the list of conditions potentially treated with high CBD:THC medicines is the same as that for hemp. There is a lack of consensus within the medical cannabis community with regards to if these two preparations are equivalent. Legally speaking (in the US), hemp is defined as cannabis that naturally produces less than 0.3% THC. In the past, hemp-based cannabis products frequently were derived from industrial hemp grown for fiber. These products where frequently of low quality and often contained chemical residues as a result of industrial farming techniques.

Today’s medical grade hemp however is a completely different agricultural crop. Medical hemp is grown specifically for its cannabinoid and terpene content and visually is often indistinguishable from a plant containing THC. Well-made hemp medicines are safe and, depending on the product, may have a variety of entourage compounds such as minor cannabinoids, terpenes, etc. They merely lack the THC content. The debate over the necessity of THC (even in small amounts) for a more profound entourage effect is ongoing. For those living in areas where medical marijuana is still illegal, hemp products are the only option.

Cannabis dosing tends to follow a biphasic curve. With a biphasic curve, efficacy increases as dose increases up to a point of maximal effect or optimal dose. Unlike a linear curve however, increasing the dose beyond the optimal dose leads to a decline in clinical efficacy. This is important because sometimes the key to having better effect with cannabis may be to decrease the dose rather than increase it.

Much like the discussion about hemp, there is some disagreement among researchers about the biphasic dosing curve as it pertains to cannabis. Some hold it applies to all forms of cannabis while others feel biphasic effects are more pronounced with cannabis isolates, such as pure CBD or THC, and that the entourage effect of whole plant medicines leads to a more linear dosing curve.

The Biphasic Dosing Curve
With a decision made about what ratio is best for a patient, all that remains is a dosing calculation. The following dosing guidelines are based on the veterinary specific research discussed earlier, extrapolated data from laboratory and human studies, and personal experience regarding safe and effective dosing. As with the discussion of ratios, these doses are guidelines and adjustments can be made based on individual response and clinical judgement.

THC Dosing
• THC is always the limiting factor when dosing
• 0.05-0.15 mg/kg BID
• Start low and slowly increase due to the bi-phasic dosing curve
• Higher doses may be possible/ necessary on a case dependent basis
• Much higher doses can be tolerated over time due to the body’s ability to build up a tolerance to the psychoactive effect of THC

CBD Dosing
• 0.1-4.0 mg/kg BID
- Start low and slowly increase due to the bi-phasic dosing curve
- Higher doses of CBD may be beneficial in certain circumstances

**THC-A Dosing**
- 0.15-1.0 mg/kg BID
- More and more attention is being paid to THC-A, particularly for the control of seizures
- Start low and slowly increase due to the bi-phasic dosing curve
- Higher doses of THC-A may be beneficial in certain circumstances

Ultimately, safe and effective use of cannabis requires an understanding of the milligram amounts of THC and CBD (or other cannabinoids), the ratio of cannabinoids, and availability of a medicine in a concentration appropriate for dosing a veterinary patient. Additionally, if terpene content is available, this knowledge is helpful in determining the expected physiologic effects of the medicine in question.

There is a wide range of means by which cannabis can be dosed. Cannabis products are produced in many formats, not all of which are appropriate for animals. Following is a list of cannabis products and their potential use in veterinary patients:

**Medicine Formats with Potential Veterinary Applications**
- Oils or tinctures for oral consumption
  - Orally administered liquids have the benefit of being relatively easy to administer, although sometimes palatability can be an issue
  - Dosing of liquids is easy to adjust
  - Ideal administration of liquids is directly orally to provide for some transmucosal absorption as GI absorption is inefficient
- Treats
  - Treats have the advantage of ease of administration and palatability
  - They may not have the same effect per mg dosage due to GI absorption issues
- Topicals
  - Topical cannabis products can be beneficial for both superficial conditions (wounds, etc.) or deeper issues (joint pain)
  - Depending on the content of the product, licking the topical could lead to THC toxicity or other unwanted side effects such as excessive sedation or GI upset
- Aerosolized
  - Although still in the research phase, aerosolized products, similar to a metered dose inhaler for asthma will eventually become available. Efficient alveolar absorption may make these products beneficial for animals

One final note about choosing medical cannabis products. Even in areas where cannabis is legal, the framework for product safety may not be fully evolved. Legitimate medical cannabis is a nascent industry whose regulatory framework has yet to evolve to meet product demands.

Consider the following when evaluating medical cannabis products for veterinary use:
- Labeling- the product should contain enough information to be able to dose for CBD and THC (if present) on a mg basis
• Ask for a certificate of analysis and evaluate it
• Research the manufacturer to learn about their agricultural, production, and extraction methods
• Remember that well-meaning staff at dispensaries sometimes give disastrously bad advice about products and dosing- particularly when it comes to animals

References
5. Interview with Stephanie McGrath, “Preliminary data from CBD clinical trials ‘promising’”, July 19, 2018, Colorado State University News


Science of Spinal Manipulation
Pedro Luis Rivera, DVM, DACVSMR, FACFN, FCoAC

Objectives
- To provide a basic definition of spinal manipulation ("chiropractic adjustment").
- To describe the basic science behind spinal manipulation, from segmental to suprasegmental levels.
- To discuss basic indications, and contra-indications for spinal manipulation.
- To provide clinical examples of possible benefits of spinal manipulation

Introduction
Manipulation and mobilization of soft tissues and joints have been utilized for many centuries; it was not until the latter part of the 1800s that Daniel D. Palmer developed the term chiropractic. Chiropractic is a Greek word derived from cheir (meaning hand) and praktike/prakticos or praxis (meaning to practice).(1, 2)

As in any health care, its origins started at an elementary description of what the primary problem was. During the mid to late 1800s, Daniel D. Palmer developed a theory of a bone out of place (BOOP), causing nerve interference with secondary dysfunctions.(3) This latter basic explanation should not be surprising as, during the same period, the human medical treatments and services provided ranged from toxic purgatives, magnetic and herbal treatments to bloodletting, to name a few. Sadly, there are still some professionals that continue to promulgate archaic descriptions such as bone displacement, the back is out, or suffering of a pinched nerve.

Some of the respected definitions of what chiropractic medicine include:
- The National Institute of Health states that: "Chiropractic science is concerned with investigating the relationship between structure (primarily the spine) and function (primarily the nervous system) of the human body in order to restore and preserve health"(4)
- The current definition by the American Chiropractic Association is: "Chiropractic is a health care profession that focuses on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health. Chiropractic services are used most often to treat neuro-musculo-skeletal complaints, including but not limited to back pain, neck pain, pain in the joints of the arms or legs, and headaches."(5)

Terms and definitions
- **Motion unit, or segmental unit**: a motion unit comprises of two adjacent bones and all of the articular, intra-articular, and peri-articular components that surround them.(3, 6) We will be utilizing the term motion unit primarily.
- **Triad symptoms**: These are the changes that licensed health care professionals to look for when diagnosing hypomobile motion units or "segmental dysfunction. These changes include heat, tenderness, and lack of motion.(7)
- **Subluxation**: The term subluxation describes a motion unit that is used "to designate contiguous vertebrae that displayed an abnormal positional relationship" and "is a complex of functional and/or structural and/or pathological articular changes that
compromise neural integrity and may influence organ system function and general health. To avoid any confusion, we will be utilizing the term hypomobility primarily.

- **Vertebral subluxation complex:** The vertebral subluxation complex (VSC) describes a motion unit (i.e., motion units not moving correctly) with clinical consequences. Some of the components include, but are not limited to, kinesiopathology, neuropathology, myopathology, vascular pathology, connective tissue pathology, inflammatory Response, pathoanatomy, pathophysiology, and pathobiochemistry. Of the components described, kinesiopathology (movement changes) is considered the common denominator.

The early and archeological theory of the adjustment was it would "restore the biomechanics of the vertebral column and indirectly influence neurologic function." Please note that even though the term indirectly was used by the cited author, it must be noted that spinal adjustments do affect the nervous system and neurophysiologic functions, BOTH, directly and indirectly.

As trained and licensed professionals, we must understand the challenge of discussing joint kinesiology without considering primary innervation and function of muscles, ligaments, components of the intervertebral foramen, boundaries of the intervertebral foramen and muscle-tendon systems. The reader is advised to review the latter neuro-anatomical topics in appropriate veterinary and chiropractic texts.

**What Are Adjustments, And What Do They Accomplish?**

SMT differs from other manual therapies in that it provides an adjustment. A chiropractic adjustment is defined as a controlled manual procedure that provides a high velocity and low amplitude thrust into a specific joint and joint (motion) angle. The goal of any adjustment is to bring movement into joints that have not been moving correctly, to elicit neurophysiological changes.

Some local changes secondary to the adjustment may include:

- Gapping of the joint
- Breaking up intra and peri-articular adhesions
- Releasing synovial folds that have been entrapped or extrapped
- Stimulation of afferent fibers
- Stimulation of specific spinal cord segment
- Ultimately, stimulating the cortex with its modulatory effects

Afferent stimulation originating from any receptor helps not only at the local, spinal segmental levels, but suprasegmental levels as well. Hypomobility of a motion unit can disturb neurologic function through the sensitization and plasticity of peripheral mechanoreceptors and secondary central nervous system changes. A well-known effect of the chiropractic adjustment is the modulation of A-delta fibers. Other studies have shown that SMT modulates the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx).

SMT puts great emphasis on evaluating tenderness, muscle tone changes, and lack of motion of
each motion or segmental unit, be it along the vertebral column or extremities to properly identify and treat, as accurate as possible, the hypomobility of the motion unit. It is essential to understand that hypomobility of a joint may affect a multitude of receptors and somatic or visceral structures. Golgi tendon organs (GTO), muscle spindle cells (MSC), synovial folds, joint mechanoreceptors, and visceral organs as some of the structures previously discussed.(27-29)

Documented changes in decreased spinal mobility correlating to increase injuries on athletes(30) and changes affecting blood pressure and nociceptive modulation have also been published.(19, 20, 31-33) As subsequent changes can lead to other clinical presentations, it is highly recommended that practitioners keep in mind several cascades/responses to help them in developing valid and clinical differential diagnoses. The latter discussed changes include somato-somatic, somato-visceral, somato-autonomic, viscero-somatic, and viscero-visceral responses.

Relevant Neuroanatomy for Practitioners of Manual Therapies
To receive and provide a final response, the body must rely on simple peripheral receptors that respond to tension, vibration, pain, temperature, static, and dynamic stimuli. These named receptors can respond to stimuli by transducing and transmitting the said response to a peripheral nerve with the end-result of stimulating and influencing supra-segmental regions. Receptors can be found in the skin (and all of its layers), muscles, tendons, ligaments, joint capsules, among other areas. Receptors (depending on their function) can detect touch, pressure, vibration, temperature, and pain.

Some receptors that the licensed professional should know, and understand include, but are not limited to:
- Muscle Spindle Cells (MSC's) are specialized receptors that give you change in length of the muscle and rate at which is moving.
- Golgi Tendon Organs (GTO) are neuro-tendinous receptors found at the origin and insertion of the muscle.

Embryologically, the central nervous system (CNS) originates from the ectodermal layer of the embryo. The spinal cord extends from the foramen magnum to the last one to two vertebral bodies depending on the size of the dog. The spinal cord is organized into the cervical, thoracic, lumbar, and sacral segments. Each spinal cord segment has its own dermatomal and myotomal representation.

The spinal cord divides into the gray and white matter. The gray matter mainly contains cell bodies of neurons and subdivided into four sections. The dorsal horn contains sensory nuclei that receive afferent sensory information, which becomes divergent. The intermediate column and the lateral horn comprise autonomic neurons innervating visceral and pelvic organs. Finally, the ventral horn contains several kinds of motor neurons that innervate specific end-organs. The white matter of the spinal cord contains myelinated nerve fibers that either ascend or descend within the spinal cord.

Parameters of Range of Motion as It Applies To SMT
Every joint in the body has its own specific or primary movement. It is not our goal to review how joints move within a three-dimensional complex (with translation or motion within each
axis) but to briefly describe the range of motion (ROM) as it applies to SMT/AC.

Before an adjustment is provided, each joint is assessed for motion (termed motion palpation) to identify the hypomobile motion unit. Parameters to be evaluated include neutral (N), active range of motion (AROM or motion produced by muscle contraction), and passive range of motion (PROM or movement that is provided by applying external force). Once the affected segmental unit is evaluated, the joint is brought into tension, by driving said joint through its physiological AROM to the end of its PROM to what is considered the end of joint play. Once this latter region of motion is reached, the adjustment (HVLA) is administered, which would bring this joint slightly past the end of joint play into a region of the movement called paraphysiological range of motion or paraphysiologic space.\(^\text{[34,35]}\) If the adjustment extends beyond this latter range of motion, damage to the usual anatomical barriers and injury to the patient will occur.

SMT has been shown to improve specific mobility as it pertains to shoulder flexion and abduction after manipulation of the thoracic spine in human patients who have undergone surgery for rotator cuff problems.\(^\text{[36]}\)

**Efficacy and Safety**

There have been several research articles published showing the efficacy of VSMT or "Animal Chiropractic."\(^\text{[37-40]}\) Most of the published articles discussing efficacy and safety has been on the human side.\(^\text{[11,41-43]}\)

The majority of articles addressing safety (in the human field) have shown a very low incidence of injuries from adjustments as compared to other procedures.\(^\text{[11,44,45]}\) Some authors have misused, misinterpret the literature, or simply confuse terms when citing or writing articles.\(^\text{[46-49]}\) All of the latter points suggest that the entire article should be read and not just the abstract. Some articles have been published, describing erroneous and incomplete information such as describing what lay people or other professionals that are not trained chiropractors, as providing a "chiropractic adjustment."\(^\text{[46,50]}\) This latter display of unethical behavior, disrespect to other professions, and misinformation should be considered fraud.\(^\text{[51]}\) Other national agencies have published information showing the statistical significance of comparing spinal manipulation over

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Figure 1: Yellow highlighted region within the "brackets" represents "active range of motion" or AROM. The solid black line dividing the yellow area is considered "neutral" position. The orange highlighted region with thick solid "down arrows" represents the "passive range of motion" or PROM, to the right or left of diagram. The red highlighted region represents the paraphysiologic space. The most lateral aspect to the right or left of the paraphysiologic space in red, would be considered the limit of the normal anatomical barrier (not to be exceeded). Adapted from Bergmann TF, Chiropractic Technique, In: Gatterman, M., Ed. Foundations of Chiropractic – Subluxaiton 2nd Ed., St. Louis MO., 2005; p. 137.
other treatments.(52,53)

Indications
Clients seek spinal manipulative therapy care because of the positive results that the owners have had with their chiropractors. Unresolved or obscured lameness, behavioral problems, discomfort or pain that is unresponsive to conventional medical care, and patients unable to maintain their training level, or athletic conditioning, are some of the reasons that treatments are sought.

Contraindications
Some contraindications include, but are not limited to, neoplasia, fever, hemorrhage, fracture(s), and immune-mediated problems.

Properly applied manipulative therapy can be safe and effective.(11,42,44) Only licensed health care providers that have completed postgraduate training, and in good standing with their respective licensing boards (DC, DVM or VMD) should offer spinal manipulation. (see resources section).

Conclusion
Spinal manipulative therapy (VSMT) or "animal chiropractic" (AC) is a health care modality that is being provided more frequently in veterinary practices. As veterinarians are not trained in this health care modality, it is recommended that postgraduate training is sought.

Education is exceptionally crucial to gain a basic understanding of what this health care modality can provide, how it works, and how it could be used, and safely implemented to improve on patient outcomes.

Resources
- American Veterinary Chiropractic Association: www.animalchiropractic.org
- College of Animal Chiropractors: www.collegeofanimalchiropractors.org
- Healing Oasis Wellness Center: www.healingoasis.edu
- International Veterinary Chiropractic Association: www.ivca.de

Conflict of Interest
Author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
27. Pickar, J.e.a., Response of lumbar paraspinal muscles spindles is greater to spinal manipulative loading compared with slower loading under length control. The Spine Journal, 2007: p. 583-595.
Objectives

- To describe the basic neurological examination as it pertains to manual therapies.
- To provide a simple definition of functional neurology.
- To provide and describe functional changes to assess the patient.
- To describe and define the term "central integrative state" (CIS) as it applies to the neurological examination.
- To provide quantitative methods that the doctor can use to assess the CIS of the patient.
- Neurology will be presented simply and with clinical correlation so that the attendees can integrate said information.

Definition

Functional neurology should be defined or described as understanding how the nervous system (NS) works and the cascade effect that it produces at the local, regional, and suprasegmental levels. Simply put, understanding how the NS works, so that we can use it on a clinical way to assess the condition or to improve on patient outcome. It would be wise to remember that any treatment that may be beneficial if provided incorrectly, it could also be counterproductive to the patient. However, we should also emphasize that developing a 4-5 differential diagnosis during the initial evaluation and case intake is as important as understanding how the NS works. After all, referring to further diagnostics or specialized conventional medical care should be dictated based on the reliable and viable list of differential diagnoses.

Introduction

Nothing brings a seasoned practitioner to a complete stop than discussing or even thinking about the neurological examination of a patient. Our goal is to make this aspect of veterinary medicine, one that brings joy and options when evaluating and discussing treatment protocols and outcomes for our patients.

The nervous system (NS) can be stimulated through three simple ways; via extero-receptors, interceptors, or through the limbic/amygdala system. Even with the complexity of the NS, its expression is through two systems; the autonomic and the somatic. This latter functional neurological view can help practitioners identify the longitudinal level of the lesion (LLL).^{1,2}

The complete neurological examination can be divided into several sections:

- Mentation
- Cranial nerves
- Posture and postural reactions
- Spinal reflexes
- Palpation; mentation, posture, and gait

The neurological examination starts as soon as you see the patient! Some observations may include:

- Watching them interact with the owner
- Responding to the environment stimuli
• Moving against gravity
• Maintaining a steady gate
• Generating purposeful motion
• While preserving balance and muscle tone

**Step by Step**
Every examination starts with an excellent history and chief complaint. Mentation can be described as **BAR** (bright, alert and responsive), **inappropriate** (dull but responsive to external environment), **stuporous** (unresponsive to external environment except excessive nociception leading to pain), and **comatose** (unresponsive to external environment and pain).

Normal mentation requires a functioning cerebral cortex (CC); however, we cannot forget that the health of the CC is directly dependent on its presynaptic pool fibers originating from other cortical associated regions, brainstem and the peripheral nervous system.\(^{(1,3)}\)

Posture and body position can be evaluated by observing the head, trunk, and limb positioning. Changes like head tilt, head turn, kyphosis, lordosis, scoliosis, spasticity, and any type of involuntary movement should be documented. Gait should also be evaluated on a non-slippery surface, under normal and dimmed light. Gait neurological connections are considered hard-wired connections found within the spinal cord pattern generators and brainstem central pattern generators.\(^{(4-6)}\) Ample time should be devoted to differentiating between lameness and neurological ataxia.

Cranial nerve (CN) examination provides clinically relevant information on neuro-localization, prognosis, and the need for further diagnostics. Cranial nerves are considered peripheral nerves; however, cranial nerve nuclei are part of the central nervous system. It is suggested that the clinician must review basic neuroanatomy as it pertains to said CNs nuclei. For example, if we detect that a patient has paresis as they relate to CN's III and IV, we might need to require an MRI centered on the mesencephalon as that is the origin of the respective CN nuclei.\(^{(7,8)}\) The author evaluates the CNs on a numerical scale; sluggish (-1), absent (0), normal (1), excessive (+2).

<table>
<thead>
<tr>
<th>CN nuclei</th>
<th>Name</th>
<th>Location of its nucleus</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Olfactory n.</td>
<td>Rhinencephalon (frontal cortex)</td>
</tr>
<tr>
<td>II</td>
<td>Optic n.</td>
<td>Diencephalon</td>
</tr>
<tr>
<td>III</td>
<td>Oculomotor n.</td>
<td>Mesencephalon</td>
</tr>
<tr>
<td>IV</td>
<td>Trochlear n.</td>
<td>Mesencephalon</td>
</tr>
<tr>
<td>V</td>
<td>Trigeminal n.</td>
<td>Metencephalon (more information to be provided during the lecture)</td>
</tr>
<tr>
<td>VI</td>
<td>Abducens n.</td>
<td>Metencephalon</td>
</tr>
<tr>
<td>VII</td>
<td>Facial n.</td>
<td>Metencephalon</td>
</tr>
<tr>
<td>VIII</td>
<td>Vestibulocochlear n.</td>
<td>Border between Metencephalon and Myelencephalon</td>
</tr>
<tr>
<td>IX</td>
<td>Glossopharyngeal n.</td>
<td>Myelencephalon</td>
</tr>
<tr>
<td>X</td>
<td>Vagus n.</td>
<td>Myelencephalon</td>
</tr>
<tr>
<td>XI</td>
<td>Accessory n.</td>
<td>Myelencephalon</td>
</tr>
<tr>
<td>XII</td>
<td>Hypoglossal n.</td>
<td>Myelencephalon</td>
</tr>
</tbody>
</table>
Accurate evaluation of cranial nerves should be easy and enjoyable. The following tests can evaluate specific CNs: (2, 9-12)

- Pupillary light reflex = evaluates CNs II; Edinger Westphal n., and III
- Palpebral reflex (medial canthus) = CNs V1 and VII
- Palpebral reflex (lateral canthus) = CNs V2 and VII
- Corneal reflex = CNs V1, VI and VII
- Gagging or swallowing reflex = primarily CNs IX and X
- Tongue extrusion = Cn XII
- Flexion of the temporomandibular joint = CNs V3
- Muscle tone of the brachiocephalicus, omotransversarius, and trapezius muscles = CN XI
- Others

Spinal reflexes can be classified based on a numerical scale. All reflexes should be compared for symmetry to the contralateral side. The numerical scale used by the author is as follow:

- Absent response = 0
- Reduced response = +1
- Normal response = +2
- Increased response = +3
- Clonic response = +4

Reflexes to be evaluated include but are not limited to:

- Panniculus
- Biceps
- Triceps
- Extensor carpi radialis
- Patellar
- Cranial tibial
- Calcaneal or gastrocnemius
- Sciatic

**Plexuses to Keep in Mind**

Cervical: This region composed of cervical spinal nerves from C1 to C5(6). Dural innervation, sub-occipital muscle innervation, spinal accessory nerve, and phrenic nerves are among some of the major region(s) that this plexus affects.

Brachial plexus: This region composed of spinal nerves from C(5)6-T1(2). This plexus provides not only stability to the secondary curvature of the quadruped but also the entire sensory and motoric innervation to the thoracic limb and pectoral musculature.

Lumbo-sacral plexus: This region is composed of spinal nerves L4 – S2. This plexus provides not only stability to the Sacro-pelvic region but also the entire sensory and motoric innervation to the pelvic limb.
### Common Changes Found with Specific Spinal Cord Lesions

<table>
<thead>
<tr>
<th>Spinal cord region</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 – C4 (5)</td>
<td>Nerve root signs; tetraparesis and or UMN</td>
</tr>
<tr>
<td>C(5)6-T2</td>
<td>UMN signs/changes to pelvic extremities; LMN signs/changes to thoracic extremities</td>
</tr>
<tr>
<td>T3 – L3</td>
<td>Normal thoracic extremities; UMN signs to pelvic extremities</td>
</tr>
<tr>
<td>L4 – S3</td>
<td>LMN sign to pelvic extremities with the possibility of bladder changes</td>
</tr>
<tr>
<td>Coccygeal</td>
<td>Referred pain to LS region, others</td>
</tr>
</tbody>
</table>

The practitioner needs to remember that all reflexes originate secondary to the passive stimulation of a peripheral receptor. The practitioner should take time to learn and understand how these receptors work and how they relate to the nervous system, and most importantly, how they can be used to improve patient outcomes!

When discussing functional neurology, as it applies to the neurological examination, clinicians must also keep in mind (as alluded previously) the patient’s central integrative state (CIS) of the neuronal pathways and individual systems. Please remember that neurons need several things to stay healthy and viable. These basic requirements include:\(^{(1)}\)

- Oxygen
- Glucose (nutrition)
- Neuro-trophic factors
- Correct and healthy stimulation by its presynaptic pool

The result of adequate cellular stimulation is the production of adenosine triphosphate (ATP), and protein. These cellular products are crucial in maintaining the CIS of the cell and its connections.

Sadly, some practitioners forget to assess parameters used (quantitatively) to determine if the patient is exceeding the metabolic rate leading to a negative cellular balance or neuronal degeneration (ND, aka transneural degeneration [TND]).

Good cellular CIS, as can be surmised, will lead to the production of healthy connections with the ultimate goal of contributing to the plasticity of those connections. Of course, plasticity can be a double-edged sword depending on which receptors or pathways are stimulated.

**Cases:**
- #1
- #2

**Conflict of Interest**
The author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.
References

Cerebellum, Biomechanics, and Performance: Parts I & 2
Pedro Luis Rivera, DVM, FACFN, DACVSMR, FCoAC

Objectives
- To provide a basic description of the functional anatomy as it pertains to the cerebellum.
- To describe the basic functional neurology of the cerebellum, emphasizing the afferent and efferent information to and from the cerebellum.
- To illustrate several approaches to avoid exceeding the cerebellar metabolic rate, hence improving patient outcomes.
- To provide clinical examples during the PowerPoint presentation to help the attendee integrate the clinical information presented during the lecture.
- To make you think outside the box!

Introduction
Embryologically, the cerebellum develops from the metencephalic vesicle within the prosencephalon.(1-3) The cerebellum develops as an out pouch of the dorsal aspect of the brainstem, in specific the pontine region and its 4th ventricle. Anatomically, it is well position to receive ascending as well as descending presynaptic stimulation. Ascending information originates from peripheral receptors, from the connections within the brainstem and descending information from cortical fibers. When intended movement occurs as a response to external stimuli, the cerebellum continuously compares the desired motoric response, to the actual response, and provides error corrections as it pertains to direction, force, timing, and velocity to attain the desired effect.(4)

The cerebellum, also known as the little brain, accounts for ten percent of the mass of the central nervous system (CNS); however, interesting enough, contains more cells than the rest of the CNS combined.(5) Anatomically, it is also well protected by not only the meningeal layers but by being encased dorso-rostrally by the tentorium cerebelli and dorso-caudally by the occipital bone of the skull.

The primary function of the cerebellum can be divided into motoric or non-motoric tasks. Motoric features include but are not limited to coordination of extremities during movement, posture, and equilibrium. Nonmotoric functions include but are not limited to memory, emotions, planning, modulation of spatial and temporal parameters, among others.(6,7)

Basic Anatomy
The cerebellum divides into several regions, the cortex (with its cell bodies), internal white matter, and the deep cerebellar nuclei. The cerebellar cortical anatomy can be discussed either by describing specific lobes or by illustrating its functional regions.(8) The cerebellar cortex is divided into two ways:

- Transversely into the cranial, caudal, and the flocculonodular lobes.
- Longitudinally, into vermal, paravermal, lateral hemispheres, and lastly the flocculonodular section.
Deep within the cerebellar white matter, several cerebellar nuclei can be identified. These latter nuclei be discussed later.

From the functional point of view, the author prefers to discuss the cerebellar anatomy utilizing the longitudinal operational divisions. By understanding the functional division, you would understand the primary area that it affects. The three functional subdivisions are: \(^{6,9-11}\)

- **The vestibulo-cerebellum** = flocculonodular lobe. As it is the oldest part, it is described as the archicerebellum. This area receives input primarily from the vestibular nuclei located in the brainstem and influences balance, posture, and the vestibulo-ocular reflex.
- **The spinocerebellum** = vermal and paravermal regions. Also described as the paleocerebellum. This area of the cerebellum receives afferent information directly from the spinal cord. The vermal area, influences the proximal extremity muscles, and those of eye movements. The paravermal region influences distal extremity muscles.
- **The cerebrocerebellum** = lateral hemispheres. Also described as the neo- or pontocerebellum. This part receives information from several areas of the cortex, and as cushion, deals with planning, execution, and modulation of its tempo.

Disturbances of the cerebellum may lead to nystagmus, ataxia, hypotonia, dysmetria, dysdiadochokinesia, intention tremor, or asynergy, among others.

The cerebellum is connected to the brainstem by three pairs of columns or **peduncles** consisting of white matter: \(^{6,10}\)

- Rostral (cranial) peduncle – also known as the brachium conjunctivum and connects the cerebellum with the midbrain.
- Middle peduncle – also known as the brachium pontis and connects the cerebellum with the pons.
- Caudal peduncle – also known as the restiform body (or restiform/juxtarestiform) and links the cerebellum with the medulla.

The rostral cerebellar peduncle contains mainly efferent connections to the midbrain and cortex, but it also has afferent fibers from the ventral spinocerebellar tract. The middle cerebellar peduncle is composed primarily of afferent fibers originating from the pontine region of the brainstem. The caudal cerebellar peduncle is composed of **both** afferent and efferent fibers.
Afferent fibers include axons from the vestibular nuclei, spinal cord, and brainstem. Efferent fibers include axons to vestibular nuclei and the reticular formation.\(^{6,9-12}\)

The primary blood supply to the cerebellum originates from the caudal and cranial cerebellar arteries. The cranial artery arises from the circle of Willis, with the caudal artery originating from the basilar artery. Please note that BOTH are influenced directly by the cervical vertebral arteries.

**Deep Cerebellar Nuclei (DCN)**

These nuclei found embedded deep within the white matter core known as the *arbor vitae*. From medial to lateral, the nuclei are:\(^{4,10}\)

- Fastigial nucleus
- Interpose nucleus. Please note that in the highest mammals, this nucleus divides into two distinct nuclei, globose and emboliform, namely.
- Dentate nucleus

All efferent information arising from the DCN is facilitatory (excitatory) to motor connections. Some of the areas that these DCN influences include:

- Fastigial nucleus: projects to the reticular formation and vestibular complex.
- Interpose nucleus: sends information to the magnocellular division of the red nucleus.
- Dentate nucleus: sends information to the contralateral superior colliculus.

**Modulatory Effect of The Cerebellum**

The cerebellar cortex is very similar throughout and is composed of three layers from superficial to deep: molecular layer, Purkinje layer, and granular layer. The molecular layer contains two types of cells; basket and stellate, namely. The Purkinje layer contains the Purkinje cells. The granular layer, located just above the deep region of the white matter, is composed of the granule and Golgi cells. Functionally, all cells found within the three layers of the cerebellum are inhibitory, with the only exception of the granule cells.

The main function of the Purkinje cells is to modulate the DCN. All afferent fibers to the cerebellum are excitatory; however, the only cells that are inhibitory and hence modulates the DCN are the Purkinje cells.

**Afferent Stimulation Of The Cerebellar Cells\(^{11,12}\)**

The cerebellum receives two main types of afferent input through the mossy and climbing fibers. **Mossy fibers** originate from the spinal cord, pontine region, and vestibular system. They enter the cerebellum primarily via the caudal and middle cerebellar peduncles and proceed to synapse and stimulate the granule cells and DCN. The granule cells’ axons extend to the molecular layer, where they bifurcate, travel parallel to the cerebellar cortical surface, ultimately synapsing and modulating the Purkinje cells. **Climbing fibers** originate from the contralateral olivary nucleus (brainstem), and the somatosensory areas of the cerebral cortex. These latter afferent fibers synapse to stimulate directly and in multiple regions of the Purkinje cell.
Physiological Cascades That Must Be Considered

When discussing functional neurology, as it applies to all receptor therapies, clinicians must keep in mind the patient's central integrative state (CIS) of the neuronal pathways and individual neuronal systems. Please remember that neurons need several things to stay healthy and viable. These basic requirements include:

- Oxygen
- Glucose (nutrition)
- Neuro-trophic factors
- Correct and healthy stimulation by its pre-synaptic pool

The end-result of cellular stimulation should be the production of adenosine triphosphate (ATP) and protein. The intracellular production of ATP, and protein helps to keep the normal cellular electrical gradient. Proteins and ATP is used constantly to:

- Replenish, repair, and restore cytoskeletal structures such as microfilaments or microtubules.
- To maintain membrane channels, Sodium-Potassium pump, and axoplasmic tubules.
- Production of neurotransmitters.

Sadly, when practitioners treat the patients, they forget to assess parameters used (quantitatively) to determine if the patient is exceeding the metabolic rate of the receptors and the post-synaptic cells and or connections. When we start exceeding the metabolic rate of any neuronal connection(s), there will be decreased supplies of nutrients and oxygen that would lead to downregulation of protein production. This latter step, if not reversed, can lead to TND/ND. Those cells that start exceeding its metabolic rate will invariably become more sensitive to any external stimuli with the hope of trying to maintain adequate concentration of protein and or ATP, hence starting/creating a vicious degenerative cycle with less nutrition, oxygen and further cellular deterioration with apoptosis as the end result.

Good cellular CIS, as can be surmised, will lead to the production of healthy connections with the ultimate goal of contributing to plasticity of those connections. Of course, plasticity can be a double edge sword depending on which receptors we are stimulating. For example; Would you prefer to create plasticity on small diameter fibers that deals with nociception (A-delta and “C” fibers) or large diameter fibers that originate from different mechanoreceptors (A-alpha, A-beta, Ia, Ib, or II)?

We will try to discuss the cellular changes on a simplistic step by step basis:

- A cell is stimulated by its pre-synaptic pool (by either chemical or electrical means).
- Cell membrane releases some products (Ca+2 or cAMP as examples) secondary to the primary stimulation.
- Realize that Ca+2 and cAMP are the most well-known cellular “first messengers.”
- Primed or excited cells will cause a specific release and activation of immediate early genes (IGE, sometimes described as “cellular immediate early gene response” [CIEGR]). This response is further subdivided into two cascades, Type I or Type II CIEGR/IGE.
  - Type I response addresses (to my understanding) specifically the nucleus of the cell. This cascade has the primary function of activating a third order messenger that MODULATES the expression of nuclear DNA.
✓ Type II response addresses the expression of mitochondrial DNA with the primary goal of ATP production.

- Third order messengers activated inside the nucleus of the cell (by Type I-IEG mentioned above) also addresses the activation of reverse transcriptase and expression of messenger ribonucleic acid (mRNA). This latter messenger (which is considered a nuclear expression) carries plans for production of specific proteins necessary for maintaining CIS of the cell.
- Of the third messengers, “c-fos” is the most well-known as it stimulates the c-AMP response element binding protein (CREB).

Once again, proper stimulation of the receptor will help to maintain proper CIS and downstream pre-synaptic stimulus ending at the cortical area.

How can then practitioners make sure or at least assess/evaluate that the treatment protocol that is being provided does not exceed the metabolic rate or “the patient’s energy resources” to maintain and provide a positive and uneventful recovery? This latter evaluation/assessment can be provided by utilizing parameters that can be quantitated! Heart rate, respiratory rate and blood pressure to name a few. These latter parameters, depending on how comprised they are, should be evaluated several times throughout the treatment session.

Understanding the above simple cellular changes, will allow the practitioners to facilitate changes leading to productive plasticity. Plasticity can be described as the ability of a cell to develop either short or long-lasting up-regulation through CIEGR. These latter changes will help the cell to be able to respond faster to stimulation (aka time to activation or TTA. However, those cells that have excellent (or good) CIS should not develop or have changes that might be confused with TND.

Receptor classification can be based on their type (Type I – IV); individual classification (i.e., free nerve endings, Muscle Spindle Cell, Golgi Tendon Organ, etc.); or based on types of nerve fibers utilized.

Classification based on type of receptors:
- Type I: found within the joint capsule (outer layer), ligaments and tendons. This type provides both static and dynamic stimulation.
- Type II: found within the joint capsule (inner layer). This type provides dynamic stimulation.
- Type III: found within the ligaments and tendons
- Type IV: found within the joint capsule, periosteum, ligaments, tendons and blood vessels

Types of receptors based on nerve fiber type: large diameter fiber (Ia, I b and II) and small diameter fibers (AΔ and “c”). The previously described fibers can be considered myelinated (Ia, I b, II and AΔ) and non-myelinated (“c”).
Cliff Notes for Cerebellar Functions
Cerebellar function is primarily considered reflexogenic; and its function is to help produce smooth, accurate and purposeful motion. To achieve the latter goals, it requires information originating from the peripheral receptors, and motor cortex. The cerebellum indirectly helps to modulate the motor activity of the upper motor neurons (UMN), motor cortex and indirectly, modulating or influencing the ventral horn cells (aka lower motor neurons or LMN).\(^{(12)}\)

Summary Of Cerebellar Connections\(^{(11,14)}\)
- All afferent fibers going to the cerebellar cortex are excitatory.
- The primary cerebellar cortical efferent fibers (Purkinje cells) are inhibitory.
- Output of the Purkinje fibers is inhibitory; however, it depends on the balance between the excitatory and inhibitory connections.
- The output of the deep cerebellar nuclei are of an excitatory nature to the pyramidal and extra-pyramidal systems.

Case Presentations
1. 
2. 
3. 
4. 

Conflict of Interest
Author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
Objectives
- To present basic neuroanatomy as it pertains to the cranial cruciate ligament.
- To provide etiologies that could lead to cruciate ligament (CCL) disruption.
- To present and discuss functional neuroanatomical changes that may lead to CCL disruption.
- To provide the attendees with options to improve on patient outcomes that may help the patient avoiding surgery.
- To provide clinical and relevant examples to help the attendee integrate the presented information.
- To make you think outside the box!

Introduction
The cranial cruciate ligament (CCL) is one of many ligaments that connects the femur to the tibia and is considered one of the most important stabilizers of said joint. The described stabilization is provided through the prevention of cranial displacement and internal rotation of the tibia, and the prevention of hyperextension of the knee. The stability of the stifle is provided by the synovium, joint capsule, caudal cruciate ligament, articular cartilage, menisci, muscles that cross the joint, and collateral ligaments.\(^1\)\(^-\)\(^3\) Disruption to any of the stifle stabilizers can cause secondary problems that include inflammation, pain, joint instability, lameness, meniscal injury, altered kinematics, and degenerative joint disease.\(^3\)\(^-\)\(^5\) The latter cascade complex is described as cranial cruciate ligament disease (CCLD).

CCL rupture repair is one of the most common orthopedic procedures conducted on the canine patient. Although the veterinary surgical community has many techniques to address the repair, the ultimate choice rests with the surgeon. The estimated national cost to treat CCLD is well over one billion dollars per year.\(^6\)

Conditions That May Predispose To CCLD
As obesity is the most commonly encountered problem with our canine patients, it would make sense for it to be the number one factor to predispose to CCLD.\(^7\)\(^,\)\(^8\) Sadly, 40% of adult dogs are considered overweight or obese.\(^7\)\(^-\)\(^9\) Obesity has been documented to create a pro-inflammatory condition on the patient.\(^10\)\(^,\)\(^11\)

Some conditions that may predispose to CCLD include patellar luxation, synovitis, joint sepsis, immune-mediated diseases, metabolic conditions, conformation deficiencies, and age-related degeneration, among others.\(^5\)\(^,\)\(^8\) Conditions that will be addressed during the presentation include conditioning of the patient and training methods (frequency, duration, and intensity, namely). It is important to point out that canine athletes are sometimes being pushed to the extreme by their owners. In the author’s opinion, it is imperative to educate the owners in that muscle fatigue, and repetitive micro/macro trauma and re-injuries are the number one reason of injury to athletes.
Anatomy of The Stifle Joint

The canine stifle joint is a synovial joint composed of the femorotibial, femoropatellar, and proximal tibiofibular articulation. As it is a synovial condylar joint, it provides flexion and extension with cranial and caudal translation, the ability for compression, and collateral movements.\(^{12, 13}\) When compared, the canine knee joint is angled between 120-140°, vs. humans angled at about 180° (at almost its maximal extension). As described previously, the cruciate ligaments, with the collateral stabilizers (collateral ligaments, and menisci) contribute to knee stability while in motion as it is being stressed during fast loading conditions, like when dogs take a sharp turn chasing a ball or during lure coursing.

As the canine stifle joint is a constant, and tonic (static) flexed position, it brings to light the other part of the equation as it pertains to STABILITY of the joint, the muscle. This latter joint stress is present even during relatively sedentary activities. Some of the muscles that provide stability, and that will be discussed during the lecture includes: \(^{13}\)

- Tensor fasciae latae m.
- Biceps femoris m.
- Semitendinosus m.
- Semimembranosus m.
- Quadriceps femoris m.
- Musculus articularis genus m.
- Sartorius m.
- Gracilis m.
- Long digital extensor m. *
- Gastrocnemius m. *
- Superficial digital flexor m.
- Popliteus m.

The attendee is recommended to review the basic normal anatomy described and presented on other veterinary anatomy textbooks.\(^{14, 15}\)

As there are at least twelve (12) muscles that provide stability and mechanoreceptive input for proprioception, avoiding fatigue, and altered pelvic limb biomechanics is crucial to avoid CCLD.

When discussing CCL disruption or anatomy, we must also consider the menisci found within the joint. The biggest ones are the medial meniscus (MM) and lateral meniscus (LM). The MM is the one that is most commonly damaged with chronic CCLD or with severe traumatic incidents. Biomechanically, when there is a lack of CCL stability, the femoral surface applies abnormal pressure to the MM leading tears.

Why Does CCL Fail?

Although acute trauma is the most common reason that veterinarians give to clients as the main cause for CCL failure, it is the author’s opinion that muscle weakness causing pelvic limb altered function is the most common cause of this condition. Conformational, genetic, and nutritional components cannot be ruled out.
Conventional Options for Treating CCLD

- Medical management, including an external brace, pain control, rehabilitation protocols, and regenerative medicine.
- Surgical management including either extracapsular, intracapsular, or a type of tibial osteotomies.
- Do nothing
- Euthanasia

Things To Consider To Avoid Surgery\(^{(16, 17)}\)

From the functional neuroanatomical point of view, the most critical aspect would be to maintain muscle sensitivity by improving alpha/gamma gain\(^{(18-20)}\). However, other options are:

- Ruling out peripheral pelvic limb nerve entrapment syndrome
- Maintaining or improving afferent input to the spinal cord
- Providing clients with take-home exercises and routines that they can utilize to maintain the patient's conditioning (and strength) without exceeding its metabolic rate.

**We will be discussing several aspects of this conservative treatment during the clinical presentations.**

Clinical Case Scenarios

First scenario: What if the muscles that stabilize the knee are weak or have undergone paresis (weakness) altering the afferent input originating from the receptors within the muscle fibers (muscle spindle cell, Golgi tendon organ and or joint mechanoreceptors) or any of the agonistic/homologous muscles that allow them to have sensitivity and help to determine if the joints are being put through an aberrant range of motion (ROM)? The latter would definitely alter the afferent input, integration, and interpretation of said information (which occurs at the cerebral cortex) and, last but not least, the output through the motor unit hence altering the response to the skewed information!

Second scenario: For this scenario, we will identify the affected knee as the LEFT leg. What if the muscles that stabilize the contralateral knee (right knee) are increasing their rate of firing (maybe causing spasms) hence causing weakness of the muscles on the left knee via reciprocal or cross-cord inhibition? Again, the problem is on the RIGHT knee, but the orthopedic changes are being felt and developed on the LEFT knee.

Third scenario: What if there is femoral nerve (innervates Quad’s and Sartorius muscles), cranial gluteal nerve (innervates the Tensor fascia lata), or sciatic nerve (innervates several hamstring muscles) problems? If that is the case, then it would be important for the doctor to understand the location/origin of the spinal nerve segments that make up that specific nerve that is being affected (i.e., deep understanding of the Lumbo-Sacral Plexus).

Fourth scenario: What if you have scar tissue contracture affecting the blood supply to that transverse the epineurium, perineurium, and endoneurium? As you might imagine, it would affect the nutrients and oxygenation of the peripheral nerve fibers that make up the specific nerve. It is important to remember that peripheral nerves contain not only sensory and motoric fibers but autonomic as well. How would you explain the aetiopathogenesis of this scenario?
Conflict of Interest
The author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
**Objectives**

- To discuss and describe the importance and correlation of the somato-autonomic and somato-visceral response to manual therapies.
- To provide and briefly describe the anatomy of the spinal nerve, gastrointestinal innervation, and vagus nerve.
- To provide some clinical examples to help the attendee integrate the presented information.

**Introduction**

Manual therapies can influence other somatic areas, but often it is forgotten that the visceral and autonomic aspects can be affected as well.\(^{(1-4)}\) Noxious and innocuous stimulation of somatic afferents has been demonstrated to evoke reflex changes in autonomic efferent activity and effector organ function.\(^{(5)}\) These phenomena have been documented and shown in the intestinal tract, reproductive, urinary bladder, cardiac, and adrenal medulla, among others.\(^{(6,7)}\)

**Anatomical Considerations**

First, we must understand that all afferent stimulation to the spinal cord is excitatory to the autonomic nervous system (ANS).\(^{(4,8)}\) The ANS helps the body cope with the external stimuli to maintain or to achieve homeostasis.\(^{(9)}\) This homeostasis should be viewed as a modulatory effect that can be influenced through the stimulation of peripheral receptors. The ANS also regulates vital functions of the GI tract, such as motility, secretions, and blood supply.\(^{(10)}\)

Spinal nerves have dermatomal and myotomal representation and can influence visceral organs. However, the area that has the broadest description is the visceral aspect of this equation is the vagus nerve.\(^{(11,12)}\) As the topic of somato-visceral influence is extensive, we will be centering on the issue of how the somatic system may influence the function of the vagus nerve. Anatomical areas to be discussed during the lecture includes:

- Nucleus of the tractus solitarius
- Raphe magnus
- Nucleus ambiguous

**Anatomy of The Spinal Nerve**

The dorsal root and ventral root come together as it leaves the intervertebral foramen (IVF). The IVF is bordered by the ligamentum flavum, dorsal longitudinal ligament or intercapital ligament, transforaminal ligaments, cranial and caudal pedicles. Each spinal nerve root is composed of several (up to six) rootlets.

The articular facet joint, a synovial joint, is composed of:\(^{(13-17)}\)

- Facet processes of two adjacent vertebrae
- Lined with hyaline cartilage
- Highly innervated with nociceptors
- It contains a large synovial fold.
The joint itself is surrounded by a thick joint capsule with the ligamentum flavum making its most ventro-medical aspect.(18) Anatomically, each articular facet is located dorsal to the intervertebral foramen and, if affected, can influence several or all of the components of the intervertebral foramen. There are several structures that the clinician must keep in mind that traverse the intervertebral foramen, these include:(17)

- Dorsal root ganglia
- Spinal nerve (union of the dorsal and ventral roots)
- The dural root sleeve with cerebrospinal fluid
- Lymphatics
- Artery, vein
- Connective tissue

The bottom line, nociception, can originate from any of the above listed anatomical structures, and surrounding connective tissue, muscles, and ligaments can affect the expression of the ANS.

**Anatomy of The Gastrointestinal Tract – Cliff Notes**

The gastrointestinal tract of vertebrates is innervated by a local enteric plexus (aka = enteric nervous system or ENS) and influenced by the ANS (parasympathetic and sympathetic) neural circuits located along the brainstem and spinal cord.(20, 21) The ANS is considered to be extrinsic to the enteric nervous system with the vital function of modulating gut inflammation.(10, 21) This organ system regulates the secretory and intestinal reflexes necessary for digestion and absorption of the ingested nutrients.

The ENS resides primarily within the intestinal walls, and it is considered a distinct part of the CNS that may act independently or in response to the modulation of the ANS.(10) The ENS further divides into the myenteric (outer) and the submucosal (inner) plexuses. The myenteric plexus (aka = Auerbach's plexus) controls GI movements, while the submucosal plexus (aka = Meissner's plexus) controls secretions, blood flow and provides information about stretch receptors of the intestinal wall.(22, 23)

**Anatomy of The Vagus Nerve – Cliff Notes**

As described previously, most of the parasympathetic innervation of the intestine is through the vagus nerve.(10,22,23) The vagus nerve (VN) is the cranial nerve with the widest influence. Most of the VN preganglionic fibers that travel to any viscera originates at the dorsal motor nucleus of the vagus. The VN also contains a large collection of visceral sensory fibers innervating the thoracic and abdominal visceral. This latter connection of visceral sensory efferent fibers enter the solitary tract and terminate in the nucleus of the solitary tract. Some of the vagal afferents going to the larynx, esophagus, and lower pharynx terminate in the spinal trigeminal nucleus.(24) Vagal (upper cervical) fiber arises from the nucleus ambiguous to innervate muscles of the larynx and pharynx.

**Case presentations and integration:**

#1

#2
Conflict of Interest
The author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
What is Rehab and What Can We Do with It?
Pedro Luis Rivera, DVM, DACVSMR, FACFN, FCoAC

Objectives
- To emphasize that the only other credentialed veterinary medical professional IS the Veterinary Technician.
- To describe several therapeutic modalities used to improve patient outcomes.
- To list and explain what is required for the veterinary technician to provide knowledgeable and competent therapy to the patient.
- To provide clinical cases to help attendees integrate the provided information.
- To give ideas on how veterinary technicians can gain skills that will make them much more marketable and provide them with a rewarding re-vamping of their careers.

Introduction

As we know, credentialed veterinary technicians have a high percentage of burning out to the point of literally changing professions. Although it is the 21st Century, still veterinary technicians are not being viewed as the only other licensed veterinary health care professional that there is. Sadly, there are still some employers that see veterinary technicians as glorified kennel help and allow anyone that helps with animals/patients to call themselves a veterinary technician.

Massage and rehabilitation therapy has been practiced on animals for as long as people have been working with animals. It was in the mid-to-late 1980s that the American Physical Therapy Association started a subcommittee to study further the inclination of practitioners that have been trained for humans to also work on animals. It was not until 1993 / 1996 and 2000 that the American Veterinary Medical Association activated the "Alternative and Complementary Therapy Committee." The committee developed the following preamble and description; sadly, the veterinary technician was not included:

Preamble:
Veterinary medicine, like all professions, is undergoing changes with increasing rapidity. Additional modalities of diagnosis and therapy are emerging in veterinary and human medicine. These guidelines reflect the current status of the role of these emerging modalities within the parameters of veterinary medicine for use in providing a comprehensive approach to the health care of non-human animals. Use of these modalities is considered to constitute the practice of veterinary medicine. Any exceptions will be indicated in the following guidelines. Such modalities should be offered in the context of valid veterinarian / client / patient relationship. It is recommended that appropriate client consent be obtained. Educational programs are available for many of the modalities. It is incumbent upon veterinarians to pursue education in their proper use. It should be borne in mind that because the emergence and development of these modalities is a dynamic process, as time passes, the following information may need to be modified.

Veterinary rehabilitation therapy is defined as "using use of non-invasive techniques, excluding veterinary chiropractic, for the rehabilitation of injuries in non-human
animals. Veterinary physical therapy performed by non-veterinarians should be limited to the use of stretching; massage therapy; stimulation by use of a) low level lasers, b) electrical sources, c) magnetic fields, and d) ultrasound; rehabilitative exercises; hydrotherapy; and applications of heat and cold. Veterinary physical therapy should be performed by a licensed veterinarian or, where in accordance with the state practice acts, by 1) a licensed, certified or registered veterinary or animal health technician educated in veterinary physical therapy or 2) a licensed physical therapist educated in non-human animal anatomy and physiology. Veterinary physical therapy performed by a non-veterinarian should be performed under the supervision of or referral by, a licensed veterinarian who is providing concurrent care”.

Description of massage therapy as discussed at that time:
Massage therapy is a technique in which the person uses only their hands and body to massage soft tissues. Massage therapy on non-human animals should be performed by a licensed veterinarian with education in massage therapy or, where in accordance with state veterinary practice acts, by a graduate of an accredited massage school who has been educated in non-human animal massage therapy. When performed by a non-veterinarian, massage therapy should be performed under the supervision of or referral by, a licensed veterinarian who is providing concurrent care.

Sadly, most people (including professionals) think that massage and rehabilitation therapy are two different therapies, but one cannot exist without the other. Overall, rehabilitation therapy, massage included, should be a pleasant and productive experience.

The primary goal of rehabilitation therapy is to decrease pain and maintain/restore function. Restoration includes supporting and promoting optimal function and conditioning of a patient to avoid re-injury. By understanding and visualizing that the stability of a joint is dependent on the muscles, tendons, and ligaments crossing a joint, then it would make sense that ALL rehab patients must be evaluated from the neuro-anatomical point of view.

What Do You Need to Provide Rehabilitation?\(^{(3-5)}\)
First and foremost, you need a solid knowledge base in anatomy, neurology, biomechanics, and specific condition(s) that you are to treat. However, the most crucial part of this equation is your BRAIN and willingness to find different ways to treat a patient, not a condition. It is imperative to understand that not all patients with a specific condition will respond to the same treatment.

To evaluate a patient, you must work closely with the primary health care provider (licensed veterinarian). All patients must undergo a complete and thorough physical and neurological examination, evaluation of previous diagnosis, gait evaluation; pain assessment; musculoskeletal and range of motion evaluation, to name a few parameters.

What Equipment Is Necessary to Provide Rehabilitation?\(^{(1, 3, 6, 7)}\)
The shortlist for equipment includes:
1. Hands
2. Goniometer
3. Gullick (aka Girthometer)
4. Pain questionnaire
5. Penlight, deep tendon reflex hammer, and stethoscope
6. Pinwheel

Hands are utilized to assess the range of motion (ROM) but also to evaluate the thickness of scar tissue and muscle mass. Hands can also be used to break up adhesions, provide the patient with a slow stretch, stretch and hold, or release trigger and tender points while being treated. Mobilization and improving ROM allow the body (through the central nervous system) to decrease pain, improve the lubrication of joints, and improve muscle tone are some of the positive outcomes.

The goniometer is used by the technician to assess the passive range of motion (PROM), and it provides excellent and repeatable measurements that can be used to document the improvement of the patient. As you might imaging, the measurements should be recorded on non-sedated patients and preferably while standing (if possible). All measurements should ALWAYS be compared to the contralateral side. The Gullick is used to assess muscle mass or circumference. To provide consistent measurements, the technician should use consistent landmarks as a reference point.

Pain assessment and evaluation is crucial to provide a response to treatment protocol and to provide a prognosis. Pain can be assessed based on attitude, facial expression, body posture, activity level, appetite, or elimination habits. However, the best assessments are those that have been proven and that provide statistically significant information. The Colorado State pain score and the Glasgow Composite are some of the validated, to name a few.

Penlight can be used to evaluate the patient for trans-neuronal degeneration, assess the autonomic nervous system (ANS), mesencephalic central integrative state, and to make sure that we are not exceeding the patient's metabolic rate.

**Manual Therapy Techniques**

Afferent stimulation originating from any receptor helps not only at the local, spinal segmental levels, but suprasegmental levels as well.(9-12) Hypomobility can disturb neurologic function through the sensitization and plasticity of peripheral mechanoreceptors and secondary central nervous system changes.(11, 12) A well-known effect of the manual therapies is the modulation of A-delta fibers.(11-14) Other studies have shown that SMT modulates the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx).(15)

Manual therapies assess and evaluate tenderness, muscle tone changes, kinesthetic changes along the vertebral column, or extremities to accurately identify the primary reason for said changes.

Documented changes in decreased mobility could lead to increase injuries on athletes(16), and changes affecting blood pressure and nociceptive modulation have also been published.(12,17-20) As subsequent changes can lead to other clinical presentations, it is highly recommended that therapists keep in mind several cascades/responses to help them in developing valid and clinical differential diagnoses. The latter discussed changes include somato-somatic, somato-visceral, somato-autonomic, viscero-somatic, and viscero-visceral responses.
Some techniques to be discussed and demonstrated:

- Effleurage
- Petriissage
- Stretch
- Stretch and hold
- Transverse frictional massage

**Relevant Neuroanatomy for Practitioners of Manual Therapies**

To provide a purposeful response, the body must rely on simple peripheral receptors that respond to tension, vibration, pain, temperature, static, and dynamic stimuli. These named receptors can respond to stimuli by transducing and transmitting the said response to and from the peripheral nerve with the end-result of stimulating and influencing supra-segmental regions. Some receptors that can be affected are found in the skin, muscles, tendons, ligaments, and joint capsules.

Some receptors that the licensed professional should know, and understand include, but are not limited to:

- Muscle Spindle Cells (MSC's) are specialized receptors that give you change in length of the muscle and rate at which is moving.
- Golgi Tendon Organs (GTO) are neuro-tendinous receptors found at the origin and insertion of the tissue.

It is important to remember that when muscles are not working correctly, the stability of the patient and the normal range of motion of joints will not occur. If joints do not move successfully, then afferent input from the peripheral receptors to the CNS will be affected, increasing the possibility of injury.

**Other therapies**\(^{(2, 3, 21-23)}\)

**Cryo and Heat therapy**

These are the simplest therapies that will have a significant impact on your patient. Both therapies may alter the physiological process that affects the overall tissue healing to relieve pain, reduce muscle spasms, decrease metabolic rate, and change nerve conduction velocity. Heat therapy can be used to help with collagen and connective tissue flexibility. However, if they are misused, both therapies can worsen the patient's condition!

**Laser Therapy**

Laser stands for an acronym: Light Amplification by Stimulated Emission of Radiation

It is part of a bigger umbrella of therapeutic tools that include Light or Photo-Therapy. As you might imagine, light produces an electrical field generated by photons. Another name that LASER therapy is known as is Low-Level Laser Therapy (LLLT).

Simply stated, LASER is an artificial source of light that emits radiation through the process of photon liberation, which creates a light emission. This latter light beam is considered monochromatic (one wavelength), and collimated (concentrated through a mirror).
An essential biologic response to a laser is its non-thermal effect that influences various cellular functions. A well-known feature is the production of adenosine triphosphate (ATP) through mitochondrial stimulation. When ATP is available as an energy source, healing time is accelerated among decreasing some of the clinical signs that go with tissue damage.

Other effects attributed to LASER therapy include but are not limited to:
- Oxygen production
- Adenosine triphosphate (ATP) production
- Activation of "Cytochrome C Oxidase" (latter enzyme is one of a superfamily of proteins that act as the terminal enzymes of respiratory chains).
- Cell proliferation / activation
- Maintaining proton gradients across the cell and mitochondrial membrane
- Reduction of cyclooxygenase and prostaglandin E2 production
- Pain control
- Decrease healing time

**Before You Start Any Rehabilitation Therapy, You Should:**
- Center yourself
- Be in a reasonable frame of mind with a positive mental attitude
- The therapy room should be quiet with no interruptions
- Ask for permission from the patient before you touch them!

**Case presentation:**

#1 Canine case
#2 Equine case
#3 Canine Case

**What Else Can Veterinary Technicians Use Rehabilitation For?**
Veterinary technicians can use the knowledge of rehabilitation therapy to improve their curriculum vitae and marketability further! Currently, rehabilitation therapy is a crucial part of both small and large animal treatment protocols. Veterinary technicians are not only good observers, but have training in anatomy, basic neurology, surgical procedures, and to evaluate patients.

As a veterinary technician, trained in rehabilitation and working with a licensed veterinarian, you would be able to:
- Help determine the best therapeutic protocol for the patient.
- Be ready to provide treatment using either Laser, Therapeutic Ultrasound, Electrical Stimulation, ROM, Therapeutic Exercises, among other modalities to help improve on treatment outcomes.
- Be able to assess improvement, and as such, providing other treatment ideas to address the individual patients.
- Bounce ideas back and forth with the primary veterinarian to improve patient outcomes!
What Other Equipment Should You Consider?
Now that you have been providing rehabilitation therapies to patients, I would start viewing other equipment:

- Air cushion (several sizes)
- Exercise balls/balloons (several size and shapes)
- Therabands
- Electrical stimulation (NEMS, TENS)
- Therapeutic laser
- Underwater treadmill

Contraindications to Rehabilitation Therapy
As with any health care modality, cancer, infections, immune-mediated problems, fractures, organ failures, and pregnancy are some contraindications to rehabilitation therapy.

National Organizations to Consider

- American Association of Rehabilitation Veterinarians (www.rehabvets.org)

Conflict of Interest
The author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
2. Rivera, P., History of Veterinary Massage and Rehabilitation, in Veterinary Massage and Rehabilitation Therapy - Postgraduate State-Approved Certification, H. Oasis, Editor. 2017-20: Sturtevant, WI.
3. LoGiudice, R., Veterinary Rehabilitation, in Veterinary Massage and Rehabilitation Therapy - Postgraduate and State-Approved Certification Program, H. Oasis, Editor. 2017-20: Sturtevant, WI.
Objectives
- To address and describe functional neuroanatomy not emphasized nor discussed during your veterinary technology or veterinary medical program.
- To provide clinical cases to help the attendee integrate the information.
- To help you think outside the box.

Introduction
Most veterinary technicians spend several years completing all of the pre-requirements needed to attend the chosen Veterinary Technology program, and at least a minimum of two years of college attending said program. After completing their veterinary technology degree, then they can sit for their national competency test and then embarking on taking their state licensing examination. Some veterinary technicians go further by completing several years of training before taking the next step and completing some specialty boards.\(^\text{(1)}\)

Specialty Boards
The National Association of Veterinary Technicians in America (NAVTA) has a committee that governs specialties, the Committee for Veterinary Technician Specialties (CVTS). Veterinary Technician Specialists are veterinary technicians that have met stringent requirements and criteria such as experience, advanced knowledge and skills, and advanced board certification examination.\(^\text{(1, 2)}\)

Relevant Neuroanatomy for Practitioners of Manual Therapies
For the body to receive and provide a final response, it must rely on simple peripheral receptors that respond to tension, vibration, pain, temperature, static, and dynamic stimuli. These named receptors can respond to stimuli by transducing and transmitting the said response to a peripheral nerve with the end-result of stimulating and influencing supra-segmental regions. Receptors can be found in the skin (and all of its layers), muscles, tendons, ligaments, joint capsules, among other areas. Receptors (depending on their function) can detect touch, pressure, vibration, temperature, and pain.\(^\text{(3, 4)}\)

Some receptors that the licensed professional should know, and understand include, but are not limited to:
- Muscle Spindle Cells (MSC's) are specialized receptors that give you change in length of the muscle and rate at which is moving.
- Golgi Tendon Organs (GTO) are neuro-tendinous receptors found at the musculotendinous junction of the origin and insertion.

Muscle Spindle Cell and Lower Motor Neurons
Before proceeding, first, we must understand the difference between the alpha/gamma gain or sensitivity. The latter physiological symbiosis occurs between the LMN’s and the peripheral receptor (muscle spindle cell) and the muscle fibers. The muscle spindle cell (MSC) is a specialized mechanoreceptor found throughout the muscle (between muscle fibers and in parallel to them) with its highest concentration found within the equatorial region or “muscle belly.” The primary job of the MSC is to measure muscle length or stretch. However, as you might imagine,
if the change in muscle length or stretch is provided within a period of time, it would also provide the speed at which the muscle is contracting. The MSC is a fusiform shaped receptor, containing several fibers attached to each end of the receptor. These later fibers are called **intrafusal fibers**, which further divide into **nuclear bag, nuclear chain,** and **static or dynamic fibers.** It is interesting to know that the “polar ends” contain actin and myosin fibers, with their **ONLY job of maintaining the tightness or tautness of the intrafusal fibers.** The nuclear bag sends afferent information to the spinal cord via Ia nerve fibers (originating from the annulospiral ring). The nuclear chain sends afferent information to the spinal cord via **TWO types of nerve fibers**, type Ia (from the annulospiral ring), and type II (origination from the flower end spray). (3, 5-7)

The αMN (efferent fiber) job is to stimulate the neuromuscular junction of the muscle fibers (also known as **extra-fusal fibers**). The βMN job is to influence both MSC and the extra-fusal fibers. The γMN job is to stimulate the small muscle fibers (actin and myosin) found within the polar ends of the MSC. The bottom line, αMN job is to provide TONE, and the γMN is to provide the SENSITIVITY to the muscle.

The afferent information originating from the Ia and II fibers (from the annulospiral ring and flower-spray receptors respectively) becomes divergent as it enters the dorsal horn, influencing many connections at the spinal cord level. Some of the connections include but are not limited to:

- Modulating/dampening pain at the dorsal horn through the stimulation of an interneuron.
- Stimulation interneurons at the Lissauer’s tract and substantia gelatinosa of the gray matter.
- Stimulation of the intermedio-lateral cell column.
- Co-activation of the α and γ motor neurons of the extra-fusal (muscle) fibers that the stimulation originated from.
- Inhibition or modulation of the α and γ motor neurons influencing the antagonistic muscle.
- Sending information to the cortex (to provide **proprioception**) and to help modulate the suprasegmental modulation of the lower motor neurons.
- Sending information to the ipsilateral cerebellum.
- To my understanding, the most important and constant modulation of the γMN is through supra-segmental control.
- Stimulation of the contralateral cortex
- Others

**Some Topics “LOST TO TRANSLATION” While at School**

**Cervical Plexus and Temporomandibular Joint**

The cervical plexus is composed of the first six (6) pairs of cervical spinal nerves. The stomatognathic system includes the region from the shoulder girdle cranial, including the secondary curvature, muscles, ligaments, tendons, cervical spine, and the temporomandibular joint. (8) The temporomandibular joint (TMJ) is a small synovial joint divided into two independent joints by a fibrocartilaginous disc. The TMJ located between the zygomatic arch and the condyloid process of the mandible. (8, 9) It is crucial to understand and visualize that the neck
has a considerable effect on posture, and adding motion onto the entire trunk and thoracic limb.\(^{(10)}\)

The “cliff notes” as it pertain to the cervical plexus:\(^{(11,12)}\)

- Branches from C1-2 cervical spinal nerves help innervate the dura matter and sensory to the dorso-caudal aspect of the skull
- Branches from C1-3 spinal nerves help to innervate the suboccipital muscles and hyoid apparatus
- Branches from C(1)2-4 spinal nerves help innervate the structures influenced by the spinal accessory nerve
- Branches form C(2)3-6(7) spinal nerves help innervate the phrenic nerve
- Remember that segmental innervation to local/regional muscles does occur

**Secondary Curvature & Musculature**

The secondary curvature of the spine develops as the quadruped starts picking up the head and neck against gravity and starts to improve more muscle tone. During locomotion, the neck stores elastic energy, which is converted to kinetic energy.\(^{(10)}\) Vertebrae of young animals develop based on the gravitational forces and mechanical pull that they are exposed. This secondary curvature has several anatomical differences such as vestigial ventral longitudinal ligament, large articular (zygapophyseal) joints, and large transverse processes.\(^{(8,13)}\)

Remember that the *secondary curvature* is important as it is the anatomical region for the origin of the *brachial plexus*. The secondary curvature is protected by several muscles, of which SERRATUS VENTRALIS, SPLENIUS, and PECTORAL muscle groups will be emphasized in this lecture. These muscles have a very important function not only to support the neck and head but also to provide stability to the secondary curvature. Please note that stability is crucial to decrease the probabilities of developing the degenerative joint disease of the cervical facets with its secondary developmental consequences. After all, locomotion of quadruped is influenced by the energy that is stored by the cervical region.\(^{(10)}\)

**Brachial and Lumbosacral plexi**

It is essential to understand that from C2-S1, there are two articular facets (zygapophyseal joints) between each vertebra (cranial and caudal) and more synovial joints depending on the region of the spine that is being described. For example:

<table>
<thead>
<tr>
<th>Vertebral segment</th>
<th>Types of joint surfaces</th>
<th>Total # of joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3-6 (independently)</td>
<td><em>Four</em> facet or zygapophyseal joints&lt;br&gt;<em>Two</em> discs</td>
<td>6</td>
</tr>
<tr>
<td>C7</td>
<td><em>Four</em> facet or zygapophyseal joints&lt;br&gt;<em>Two</em> discs&lt;br&gt;<em>Two</em> costofovea or demi-facets</td>
<td>8</td>
</tr>
<tr>
<td>T1-about T10</td>
<td><em>Four</em> facet or zygapophyseal joints</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Two discs</td>
<td>Four costofovea or demi-facets</td>
</tr>
</tbody>
</table>

All of the above listed joints are synovial with the potential, if affected, to be a source of nociception.\(^{(15-17)}\)

**Sacro-Iliac Joints**

Another aspect of the normal equine anatomy is the sacroiliac joints (SIJ). These joints can be described as having multiple innervations arising from the sciatic nerve branches (L6-S2 spinal cord level, covering the dorsal aspect of the SIJ) and the femoral nerve branches (L4-L6 spinal cord level covering the ventral aspect of the SIJ). In addition, in other mammalian species, sensory innervation to the SIJ has come as far cranial as L1 spinal cord segment.\(^{(18, 19)}\) Changes to the SIJ can have far-reaching performance effects than anyone can imagine.

The final diagnosis for back problems varied depending on the discipline or training that the patient was undertaking. The diagnosis that could be encountered include but are not limited to:\(^{(20, 21)}\)

- Kissing spinous processes (yes, including canine athletes!)
- Dorsal spinous ligament injuries
- Muscle pain
- Sacroiliac problem
- Concurrent conditions (polysaccharide storage myopathy)
- Primary joint conditions (fetlock, hock, stifle, and coxofemoral)

There is another aspect of the normal anatomy that is not presented in school as often, the anatomy and importance of the articular facet/zygapophysial joint. This synovial joint is composed of two facet processes of two adjacent vertebrae lined with hyaline cartilage, are highly innervated, and contains a large synovial fold.\(^{(22)}\) The joint itself is surrounded by a thick joint capsule and ligamentum flavum.\(^{(13)}\) Anatomically, each articular facet is located dorsal to
the intervertebral foramen and, if affected, can influence several or all of the components of the intervertebral foramen. There are several structures that the clinician must keep in mind that traverse the intervertebral foramen, these include:(23)

- Dorsal root ganglia
- Spinal nerve (union of the dorsal and ventral roots)
- The dural root sleeve with cerebrospinal fluid
- Lymphatics
- Artery, vein
- Connective tissue (including fat)
- Several meningeal nerves

Examples of Asymmetries
As we learned in school, the first sign of nerve damage (other than secondary to an ablative lesion) is more than likely to be paresis or weakness. Imagine if the serratus ventralis becomes weak, allowing the shoulder blade to change its angle? Some of the changes to keep in mind surely would include:

- How would it affect the glenohumeral stability and the joint per se?
- What would happen to the bicep’s tendon and its bursa as it goes over the cranial aspect of the inter-tubercular groove?
- What would happen to the flexor tendons with the change in angulature of distal joints? How would it affect the stay apparatus of the equine thoracic limb?

Nerve Entrapment Syndrome
The basic requirements for a neuron to stay alive includes oxygen, glucose, frequency of firing of its pre-synaptic pool, and neurotrophic factors. If we affect any of the soft tissue components of the rear limb leading to either increase muscle tone or development of adhesions or scar tissue, that could probably lead to decrease blood supply distal to that region. This latter change is defined as a nerve entrapment syndrome. Nerve entrapment does not describe a pinched nerve, but a consequence of decreased blood supply to that specific nerve. Other etiologies leading to nerve entrapment include but are not limited to:

- Increase muscle tone
- Scar tissue (secondary to inflammation from different mechanical etiologies)
- Periosteal changes
- Damage to fascia
- Cancerous growth.

Example
Visualize that the pectoral muscle being stretched causing a secondary increase in tone of the serratus ventralis and scalenus muscle groups on the caudal secondary curvature affecting the spinal nerves C8, T1 or T2 (not taking into consideration what happens with the multifidus, rotatores breves group, and inter-transversarii muscle groups). If by chance, only the nerve fibers that innervate the superficial and deep digital flexor muscles are affected, this would lead to a decreased sensitivity (balance between the alpha and gamma motor system) of that muscle group, causing an increase in stress to their respective tendons (and insertion sites). Now imagine the cascade that could affect their respective accessory ligaments, tendons, suspensory ligament, and lastly, the plausibility of damage to the fetlock due to over-extension injuries.
Conflict of Interest
The author is co-owner of the Healing Oasis Wellness Center, an accredited institution providing postgraduate state-approved certification programs and CE seminars.

References
2. NAVTA. Veterinary Technician Specialties. [cited 2020 26th April]; Available from: https://www.navta.net/page/SpecialtyInformation.
Stress- Fight or Flight or Is There Another Way?
Barrie Sands, DVM, CVA, HMCT

Objectives
- To provide an overview of stress and gain an understanding of the psycho-neuro-immuno-physiological basis of the stress response.
- To introduce to tools and techniques to manage stress and build resilience.

Introduction
The stress mechanism has evolved from a necessary protective tool into a normalized state of everyday being. It has become so common that the word has become incorporated into everyday language and its ubiquitous nature has driven us into a state of complacency. The effect of this has impacted individuals in profound psychological, emotional, and physical ways.

Stress is the underlying process that drives disease. The once necessary system called upon to protect our physical being is being habitually utilized in the form of constant mental chatter, worries, and negative, depleting thought processes. It is in these states that we learn to live in survival mode and become so familiar and accustomed to it that we don’t even recognize the smoldering undertone of the effects upon our physiology and emotional state of being. We have created a new baseline of stress, thereby increased the threshold.

With our understanding of the stress mechanism and how our thoughts are intimately involved in depleting or renewing our personal energy resources we can learn to manage and transform our stress into a new state of being that encompasses synchronicity within our bio-physiology and integrates an optimum state of whole body wellness.

Definition of Stress
As described by Merriam-Webster dictionary; it is a noun AND a verb.
As a noun it describes a function: a force or an influence:
- A force exerted when one body or body part presses on, pulls on, pushes against, or tends to compress or twist another body or body part
- A physical, chemical, or emotional factor that causes bodily or mental tension and maybe a factor in disease causation
- A state resulting from a stress especially: one of bodily or mental tension resulting from factors that tend to alter an existent equilibrium
- A state of mental or emotional strain or tension resulting from adverse or very demanding circumstances

As a verb it describes a phenomenon of our psyche:
- To subject to physical or psychological stress
  ex. This traffic is stressing me out;
- To feel stress
  o  ex. I’m stressing out about this big exam

History of Stress
What is stress? The word “stress” has been used for hundreds of years in physics to describe an external force that produces distortion or strain. In today’s world, the word and its use has
evolved to characterize a state of being. Across all global cultures it is one of the most widely used words in the world, and it is statistically the most pervasive cause of medical problems. The American Institute of Stress notes that 75%-90% of visits to primary care physicians are stress related complaints.\textsuperscript{1} We have heard the term “stress kills,” but how many of us are taking that seriously. A dialogue about stress cannot be without reference over all well-being.

The study of stress and the stress response encompasses many different avenues of investigation. Throughout history stress responses have been strongly linked to emotions, and the physiology of our emotional landscape. The importance of gaining a deeper understanding of the emotional system has become increasingly recognized as an important scientific undertaking, as it has become clear that emotions underlie the majority of the stress we experience, influence our decisions, provide the motivation for our actions, and create the textures that determine our quality of life.\textsuperscript{2}

In ancient times, there was the tendency to view emotions as operating separately and apart from rational or intellectual capacities. Historically, thinking and feeling or intellect and emotion have often been portrayed as opposing forces engaged in an incessant battle for control over the human psyche. The ancient Athenian philosopher, Plato, maintained that strong emotions made it impossible for him to think and described emotions as “wild horses that had to be reined in by the intellect.” Christian theology has traditionally regarded many emotions as sins and temptations to be overcome by reason and willpower. Rene Descartes, the 17\textsuperscript{th} century mathematician, philosopher, and metaphysician who is most commonly known for his philosophical statement, “\textit{I think, therefore I am},” best known by its Latin translation: “\textit{Cogito, ergo sum},” has been attributed with developing Cartesian dualism; also referred to as mind – body dualism which is the metaphysical argument that the mind and body are two different substances which interact with one another.\textsuperscript{3-4}

Later, in his \textit{Treatise on the Passions of the Soul}, Descartes’ views on the function of human emotion were clearly more sophisticated than the simplistic notion that emotions are antagonists to rational thought. Descartes considered emotions a double-sided coin. They give substance and sustenance to what otherwise may have been ephemeral thoughts.\textsuperscript{3} As a result, they can work both for and against us. Descartes was really highlighting the contrast between the potential of effectively managed emotions and the harm caused by unmanaged emotions.

This concept is more in alignment of our modern-day perspective which provides a more comprehensive understanding of the emotional system and illuminating the critical roles that emotions play in human experience, performance, and rationality.

Most contemporary researchers agree that mental states of cognition and emotion are distinct functions mediated by separate but interconnecting neural systems. Research centers are attempting to understand the essential dynamic interactions between these interconnecting neural systems. From a neuroscience perspective, several intriguing forms of interaction have been discovered that support a dynamic, bidirectional link between the body, emotional processing and the cognitive centers.\textsuperscript{4}
Introduction of the Autonomic Nervous System

The autonomic nervous system (ANS) is an elegant, involuntary, automatic system that goes on below conscious awareness. It is responsible for regulating 90% of the body’s functions, such as breathing, heart rate, and digestion. The ANS includes two branches; the sympathetic and the parasympathetic. It is in the balance and synchronicity of these two systems that creates optimal physiologic functioning.

In terms of physiology, the word “stress” was first described by Dr. Walter Cannon, a respected physiologist and neurologist of his time. In 1915, he published Bodily Changes in Pain, Hunger, Fear and Rage: An Account of Recent Researches into the Function of Emotional Excitement and coined the term fight or flight to describe an animal’s response to threats. Cann's work showed that major emotions are involved in the excitation of the sympathetic division of the autonomic nervous system. This excitation leads to many changes in a body’s smooth muscles, glands and bodily functions such as increased secretion of adrenaline, increased heart rate, blood pressure, perspiration, and decreased stomach motility; and in more quiescent moments the (parasympathetic) branch of the nervous system calms us down and slows the heart rate. Cannon ultimately believed that the autonomic nervous system and all the related physiological responses moved in concert with the brain’s response to any given stimulus or challenge. With this work he also introduced the concept of homeostasis, and since then the study of physiology has been based upon the principle of biologic maintenance of a static or constant steady state condition.

Twenty years of research conducted in the 60s and 70s, pertaining to the role the heart played in physiologic responses, by prominent physiologists John and Beatrice Lacey, introduced the concept of psychophysiology. As their research evolved, they noticed that the model proposed by Cannon only partially matched the actual physiological behavior. They observed that the heart communicates with the brain in ways that significantly affect how we perceive and react with the world. Their observations and research lead to the understanding that the biological processes vary in complex and non-linear ways and these dynamic and interconnected physiological and psychological regulatory systems are never static.

Fight or Flight

The intricate metabolic and physiologic fight or flight response to stress is an exquisitely designed fine-tuned built in response for physiological survival. The spontaneous and instantaneous nature suggests a highly intelligent coordinated system of communication throughout the body. The system is designed be used in short bursts in times of eminent threats, such as running from a bear or escaping from a dangerous situation. However, the problem today, in our ever changing fast passed society, is that the threats are more perceivable than actual situations. They are disguised under the feelings of tension, irritation, overwhelm, fear, anxiety, worry, frustration, impatience, judgment, anger, and depression.
Fight or flight is a complex protective mechanism involving many working parts within our body. The main systems driving it are the sympathetic nervous system, the brain stem, limbic system, and hormonal system; this is comprised of the medulla, the amygdala, the thalamus, the hypothalamus, and adrenal glands. We know these as the hypothalamic pituitary adrenal axis or HPA. These systems, when called into play set the physical body up for the fight or the flight. This causes our body’s natural inner pharmacy to create a flood of stress hormones circulating throughout the body. There is a cascade of 1,400 different biochemical released by the body as soon as it senses stress. The major players are cortisol and the catecholamine’s; norepinephrine and epinephrine. In response to these hormones, our heart pumps faster and sometimes harder, our pupils dilate, (to help to see better), our blood flow is shunted and directed to our muscle groups, our lungs get prepared by expanding the alveoli and increasing our respiratory rate, creating availability of more oxygen. It is a good system. As this is happening the “primitive” brain is activated and the neocortex or higher thinking brain is shut down. Why? Because it is not the time to ponder about sunsets, all the different species of birds, how you feel about hot fudge sundaes, whether or not the roof you replaced will hold up to the coming rainy season. It is a time to focus on the situation at hand.

The primitive brain allows us to focus on survival, keeping our attention to the threat and what that entails. We are virtually concerned with our environment, our bodies and time. We pay attention to where we are, where we need to go, how our body feels, and how long it may take to get to where we need to go, or do what we need to do. Most of these thoughts happen very fast, so fast that we are not aware of them. It’s all about your survival. This is great stuff if you find yourself in front of a bear or a mortal enemy, and you need to find a way to protect yourself. The human form wasn’t made to sustain the claws and teeth of a bear, and we are not inherently bullet proof, but we are designed to run, climb, hide, or make weapons and fight… sometimes a good fight, sometimes not. It is a very elegant system; we need to appreciate it for what it was designed to do. And, it was designed for short term use only.

The antelope grazing on the grass, sensing the presence of a lion, runs as fast and stealthy as it can and when the chase is over and the lion gives up, the antelope shakes it all off and goes back to grazing… as if nothing ever happened.

However, this is not what most of us do. We tend to live in a constant state of stress, we over use this system. Time and events over the last twenty years have sped up dramatically due to the high-speed technologies, and communication systems. On top of that, a culture of speed pushes you to multitask, trying to do two, three or more things at a time. We find ourselves glued to the internet, e-mails, face book, twitter, and Instagram. We are constantly exposed to an influx of information.

We become addicted to the stimulating pace of incoming information and demands and get pulled along by their momentum; all the while our emotional reactions are keeping up with the pace. We have redefined our threats; threats that stem from the inside.

**Stress and Emotions**
New threats come in the form of our perceptions and emotions. We are filled with worries,
intangible fears, and consuming thoughts of self-doubt, anxiety, and the emotions of self-preservation dictated by our subconscious programing. The result of this is an amplification of fear, anxiety, irritation and anger; while underneath it all we are feeling emotional overload, overwhelm, and pressed for time.

We are preoccupied and consumed with the myriad of thoughts that consume our daily lives. In 2005, the National Science Foundation published an article showing that the average person has between 12,000 and 60,000 thoughts per day. Of those, 80% are negative and 95% are the same repetitive thoughts as the day before.9

These thoughts propel us into the next day. We think about having to get up to go and do what we don’t want to. We focus on what is happening in politics, how upset we are at the president, and the economic situations. We have thoughts about money, paying the rent, paying the bills, having a job, not having a job. We have thoughts about our personal attributes, how we feel, our aches, pains and diseases; and all the self-judgments we have.

We worry about being late to work or school, being reprimanded, getting stuck in traffic, seeing a co-worker we may not like and having dinner with the in-laws, the list goes on and on. Then … because of the great technological advances we can get on the internet and really see how horrible everything is, who’s killing who, how the stock market is doing, the recent global affairs of a pandemic virus, and fears around our own mortality. We can see how many likes we got on our Instagram photo and then become disappointed and self-conscious when the fabulous picture of you and your cat only got five likes. It continues. You can fill in your own blanks.

You see, although there is no bear or lion, the fight or flight mechanism is still active, not as a “burst of flames” but as a low smoldering fire that is burning almost constantly.

**Symptoms of Stress**
Most of us have familiar stress symptoms that we have become habituated to. When we identify our stress symptoms we can learn when to use techniques and tools to help mitigate them.

- **Irritability** - Do you find yourself getting angry at little things more often?
- **Loss of sense of humor** - Do you find yourself being too serious, feeling depressed?
- **Worry** - Do you find yourself caught in distressing thought loops, replaying anxious experiences or projecting anxious situations into the future?
- **Excessiveness** - Do you eat, drink or use mood-altering substances excessively? Do you rely on stress to keep you going?
- **Forgetfulness** - Do you feel a mental grid lock or find yourself forgetting things more often?
- **Aches and pains** - Do you have recurring headaches, gastrointestinal distress, and tension in your body?
- **Nervousness** - Do you talk fast or excessively; do you feel more uncoordinated or have nervous tension?
- **Fatigue** - Do you feel run-down? Do you feel tired but unable to get restful sleep, or have trouble falling and staying asleep?
• **Illness** - Have you been sick with allergies, colds, or flu more often? Do you have chronic problems your doctor told you were stress related because no pill or other remedy has helped?¹⁰

**Is there another way?**

Stress creates energy drains in the physical, emotional, mental, and spiritual domains. It is in the emotional domain where we tend to lose the most energy. Stressful emotions arise in response to external challenges or events and ongoing internal dialogue and attitudes. The opposite of energy draining is building resilience. *Resilience is defined as the capacity to prepare for, recover from and adapt in the face of stress, adversity, trauma, or challenge.*¹¹ Experiencing positive emotions, increases energy, and builds resilience. DHEA, (*dehydroepiandrosterone*), a hormone produced by the adrenal glands is secreted in response to renewing feelings like care, gratitude, and appreciation. It has been called the *longevity hormone* for its positive physiological and anti-aging effects.¹² One study showed, that after using self-regulation techniques, increasing parasympathetic activity; resulted in significant reduction of cortisol and increases in DHEA.¹³

Since 1991, the HeartMath Institute Research Center has explored the physiological mechanisms by which the heart and brain communicate and how the activity of the heart influences our perceptions, emotions, intuition and health. The tools and techniques formulated for tapping into the innate intelligence of our hearts are research based, simple, practical and effective for managing and transforming stress. The challenge and opportunity are to learn how to interact with your stress circuitry to regulate its response systems, so they work for you rather than against you.

**Heart Focused Breathing**

Heart focused breathing is the first step into dampening the stress response and altering the physiology. It takes the attention off of the stress stimulus and into a place of intuitive guidance. The breathing activates the parasympathetic pathways and offsets the sympathetic drive. It is not unlike other methods of breathwork that is used to calm the nervous system. The technique is simple but not easy, as it can be challenging, in stressful moments, to remember to pause and breathe.

*“To awaken, sit calmly, letting each breath clear your mind and open your heart” - Buddha*

**Heart Focused Breathing Technique**¹⁴

1. **Heart Focus**
   
   Focus your attention in the area of your heart. It is sometimes helpful to place your hand or a finger over your heart center. Most of us will shift our attention to where we touch our bodies.

2. **Heart Breathing**
   
   As you focus your attention on the area of the heart, imagine your breath is flowing in and out through that area. Breathing a little slower and deeper than usual, suggested five seconds in – five seconds out.
References
14. HeartMath.org *Heart Focused Breathing*
Heart or Brain - Which is Smarter and Why Do We Care?
Barrie Sands, DVM, CVA, HMCT

Objectives
- To understand the relationship and interaction between the heart and the brain.
- To understand coherence and how being in a state of coherence can create an optimal state of wellbeing and health.

Introduction
In the last few decades, groundbreaking research in the field of Neurocardiology has established that the heart is a sensory organ and an elaborate information encoding and processing center, with an extensive intrinsic nervous system sufficiently sophisticated to qualify as a “heart brain.” A dynamic system’s view of the interrelations between psychological, cognitive, and emotional systems and neural communication networks provides a foundation for the information presented.

The concept of coherence is drawn on to understand optimal physiologic functioning which is naturally reflected in the heart’s rhythmic patterns. These communication networks are examined from an information processing perspective and reveal a fundamental order in Heart-Brain interactions and a harmonious synchronization of physiological systems associated with positive emotions. This lecture will discuss how the study of psychoneurophysiology and neurocardiology pertains to a state of coherence, and how this has shown to have significant impacts on cognitive performance and overall wellbeing and increase in resilience.

Function of the Heart
The heart has always been thought of as a muscle that pumps blood throughout the body supplying oxygen and nutrients to the tissues. Over the recent decades it has proven to be much more than that. The average human heart is about the size of your fist and weighs about 10 oz., it beats about 100,000 times/day, and 2.5 billion times over an average lifetime. It is the greatest generator of electrical activity in the body. The heart contains autorhythmic cells and has the ability to generate its own electricity. These cells spontaneously generate the pacemaker potentials that initiate cardiac contractions, and as pacemakers, provide a conduction pathway for pacemaker potentials. The sinoatrial (SA) node and atrioventricular (AV) node are the two internal pacemakers that are primarily responsible for initiating the heartbeat.1 This electrical activity is measured by an ECG.

The SA node generates an electrical impulse that travels through the atria to the AV node causing the AV node to fire. The signal rapidly spreads through the AV bundle reaching the top of the septum. These fibers descend both sides of the septum as the right and left bundle branches which extend into the myocardium. This process creates the depolarization and repolarization activity through the heart causing the contraction and the relaxation of the atria and the ventricles. The timing of this process is dependent upon a variety of factors.

The heart works in concert with the body by integrating sensory information from a variety of sources such as limb position as proprioception, chemoreceptors (blood chemistry) and baroreceptors (pressure sensors) from the heart; information from the cerebral cortex, the limbic
system, the medulla of the brain stem (a major cardiovascular center) and the activity between
the sympathetic and the parasympathetic nervous systems. This complex, non-linear and intricate
dynamics are overall represented by the heart rate, blood pressure and nerve activity.

The current understanding of the relationship between the heart, body, and brain surpasses the
outdated thought process that the heart beats at a steady rate, as measured as beats/minute and
that it is solely under the command and influence of the brain. What has been learned over the
last 30 years is that healthy, optimal function is a result of continuous, dynamic, bi-directional
interactions among multiple neural, hormonal, and mechanical control systems at both local and
central levels. In concert with all these regulatory systems, it is known that the normal resting
rate of the heart is not static, like a metronome, but highly variable.1,2

Heart Rate Variability
With research started by physiologists John and Beatrice Lacey in the 60s and 70s it became
apparent that when the heart rate was examined on a beat to beat basis compared to the
calculated mean value over time as beats per minute, there was found to be a consistent
variability between the beats. This variability is correlated with optimal physiological
performance. An optimal level of Heart Rate Variability (HRV) within an organism reflects
healthy function and an inherent self-regulatory capacity, adaptability, or resilience.3 Decades of
research evaluating HRV and its significance, is based upon multitude of complex algorithms
extrapolated from neurophysiological, and bio- hormonal systems that are involved in these
regulatory functions. Due to the extensive research, and correlative data over the last 30 years,
HRV has been used as an accurate predictor of morbidity and mortality.4

Overall physiological health is based upon the balance between too much and too little is HRV.
Too much instability, such as, with arrhythmias or nervous system chaos, is detrimental to
efficient physiological functioning and energy utilization. However, too little variation indicates
age-related system depletion, chronic stress, pathology, or inadequate functioning in various
levels of self-regulatory control systems.4

Heart Rhythms
In a healthy individual, the HR estimated at any given time represents the net effect of the neural
output of the parasympathetic (vagal) nerves, which slow HR, and the sympathetic nerves, which
accelerate it. The constant dynamic and rapid changes in the activity of the ANS creates the heart
rhythm patterns, and it is with in the balance the heart’s extensive intrinsic network of sensory
neurons also enables it to detect and respond to variations in hormonal rhythms and patterns.

With the constant input from the ANS, the heart rhythms form a sine like wave (Figure 1). The
rhythm pattern changes in reflection of the individual’s emotional state (Figure 2).5

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The Frequencies of the Heart - The Making of HRV

We are essentially, energetic systems, and as such we resonate at certain frequencies. Each of our biological systems vibrates over a time frequency interval. This is called oscillation.

The European Society of Cardiology and the North American Society of Pacing and Electrophysiology Task Force Report on HRV divided heart rhythm oscillations into 4 primary frequency bands: high-frequency (HF), low-frequency (LF), very-low-frequency (VLF), and ultra-low-frequency (ULF).

The High Frequency range is from 0.15 Hz to 0.4 Hz, which equates to rhythms with periods that occur between 2.5 and 7 seconds. This band reflects parasympathetic or vagal activity and is frequently called the respiratory band because it corresponds to the HR variations related to the respiratory cycle known as respiratory sinus arrhythmia. The mechanisms linking the variability of HR to respiration are complex and involve both central and reflex interactions.

Although the magnitude of the oscillation is variable, in healthy people it can be increased by slow, deep breathing. In terms of psychological regulation, it is also seen that lower HF power is associated with stress, panic, anxiety, or worry, and reduced vagally mediated HRV has been linked to reduced self-regulatory capacity and cognitive functions that involve the executive centers of the prefrontal cortex.

The Low Frequency range is between 0.04 Hz and 0.15 Hz, which equates to rhythms or modulations with periods that occur between 7 and 25 seconds. This region was previously called the “baroreceptor range” or “mid-frequency band” by many researchers, since it primarily reflects baroreceptor activity while at rest. Lower spectrum LF, is related to aging and impaired regulatory capacity. This power spectrum is positively affected by increase in respiratory-related vagally mediated activity, in other words when we sigh, or take a deep breath. The optimum resonant frequency of the system is approximately 0.1 Hz, which is also characteristic of the coherent state described later.

The Very Low Frequency is the power in the range between 0.0033 and 0.04 Hz, which equates to rhythms or modulations with periods that occur between 25 and 300 seconds. Low VLF power
has been shown to be associated with arrhythmic death, posttraumatic stress disorder (PTSD), high inflammation, and has been correlated with low levels of testosterone\textsuperscript{6,7}

In 1991 Dr. J. Andrew Armour of the University of Montreal, during a research study in the auto-transplantation of hearts in dogs, determined that the intrinsic cardiac nervous system and inputs to the heart, are the source of VLF generated input. In healthy individuals, there is an increase in VLF. This region is the most predictive of adverse outcomes. These intrinsically generated oscillations are modulated by the efferent sympathetic activation and are influenced by physical activity and emotional stress responses.\textsuperscript{6,7}

The \textit{Ultra-Low-Frequency} band falls below 0.0033 Hz (333 seconds or 5.6 minutes). Oscillations or events in the heart rhythm with a period of 5 minutes or greater are reflected in this band and it can only be assessed with 24-hour and longer recordings. Long-term regulatory mechanisms and ANS activity related to thermoregulation, the renin-angiotensin system, and other hormonal factors appear to contribute to this band. Also, circadian rhythms, core body temperature, metabolism, hormones, and intrinsic rhythms generated by the heart all contribute to lower frequency rhythms (e.g., VLF and ULF) that extend below 0.04 Hz.

Through the use of power spectral analysis, time domain analysis and other physiologically based mathematic relationships, technology was designed by the Institute of HeartMath to measure and interpret the relationships between these complex biological systems. The interactions between autonomic neural activity, BP, respiratory, and higher-level control systems produce both short- and long-term rhythms in HRV measurements.\textsuperscript{6,7}

HRV and the cardiovascular center responds to a variety of sensory input from the body, the autonomic nervous system and higher brain centers and is influenced by emotional states. Both branches of the ANS work simultaneously in a delicate balance. Vagal (parasympathetic) activation gives the ability to calm oneself by inhibiting sympathetic outflow. Autonomic dysregulation and imbalance have been associated with a wide variety of pathologies, including depression, anxiety, fatigue, hypertension, diabetes mellitus, irritable bowel, sleep disturbances, PMS, ischemic and coronary heart disease, arrhythmia and migraines.\textsuperscript{7}

\textbf{Neurocardiology – The “Heart Brain”}

Over the last three decades in the emerging field of neurocardiology, neurophysiologists, and neuroanatomists have extensively studied both the anatomy and the functions of the communication between the intrinsic cardiac system and the brain. Traditionally in the past, scientists have primarily focused on the heart’s responses to the brain’s commands. Recent research has shown that the heart sends more information to the brain, through afferent (ascending) vagal pathways, than the brain sends to the heart; this is estimated to be about ninety percent.\textsuperscript{8}

Based upon the pioneering psychophysiology research by John and Beatrice Lacey in the 1960s, Dr. Armour, in the early 90s, introduced the concept of a functional intrinsic cardiac system also known as the \textit{heart brain}. It was discovered that the heart has 40,000 neurons and within this extensive neural ganglia network, are neurotransmitters, proteins, and support cells; the same as those of the brain in the head.\textsuperscript{9}
The heart–brain’s neural circuity enables it to act *independently* of the cranial brain to learn, remember, and make decisions and even feel and sense. This intrinsic cardiac system plays an important role in much of the routine control of cardiac function, independent of the central nervous system and it is vital for cardiac stability and efficiency. The messages from the intrinsic cardiac system goes to the SA node and other heart tissues, and travels to the brain via ascending pathways in the spinal cord and the vagus nerve to the medulla, hypothalamus, thalamus, amygdala and then to the cerebral cortex.

**Heart Hormones**

In 1983, the heart was reclassified as part of the hormonal system. Although not typically thought of as an endocrine gland, the heart manufactures and secretes a number of hormones and neurotransmitters that have global impact throughout the body.

- **Atrial Natriuretic Peptide (ANP)** is secreted by the atria. It is nicknamed the balance hormone and plays an important role in fluid and electrolyte balance, regulation of blood vessels, kidney, adrenal glands and many regulatory centers in the brain. Increased ANP inhibits the release of stress hormones, reduces sympathetic outflow and interacts with the immune system. It has also been shown to influence motivation and behavior.

- **Catecholamines** - Norepinephrine, Epinephrine, and Dopamine

- **Oxytocin** is nicknamed the bonding or love hormone. Concentrations produced in the heart are in the same range as those produced in the brain. Beyond its functions related to childbirth and lactation, it is involved in cognition, tolerance, trust, friendship and the maintenance of pair-bonding. It is also a precursor to a neurotransmitter called Anandamide, nicknamed the bliss hormone, as it binds to CBD1 endocannabinoid receptors.

**Heart-Brain Communication**

The heart communicates with the brain and the body in four major ways:

1. **Neurologically** - through transmission of nervous impulses
2. **Biochemically** - via hormones and neurotransmitters
3. **Biophysically or Mechanically** - through pressure and pulse waves
4. **Energetically** – through electrical signals when the heart contracts and broadcasts through electromagnetic fields

The brain relies on neurological information from the heart. The heart rhythm pattern tells the brain what the body feels, and then your brain interprets the information and then decides what to do. As noted earlier the ascending information from the heart travels to the brain via the medulla, the subcortical structures, (the thalamus, and amygdala), and the cognitive center (the cortex).

The thalamus is designed to distribute incoming information to the appropriate brain centers and to synchronize cortical activity. The amygdala compares incoming information from the heart and the five senses and searches for emotional memories in the “memory banks” via pattern recognition processes. If the past experience was stressful then the amygdala triggers the stress response and the emotions associated with that experience.
Emotional assessments are made in two ways; via the slow tract and the fast tract. In the slow tract the information from the heart is sent to the thalamus, then the cortex and then to the amygdala, then to the body. In the fast track, information is sent to the thalamus and it goes directly to the amygdala, bypassing the cortex. This is a form of what is considered “amygdala hijacking.” Fast tract responses create strong reactions or lead you to behave in ways that you may later regret. This type of response is very common in PTSD.14

**Emotions and HRV**
A study done at Duke University Medical Center in 2004 found that the cumulative effect of daily mental and emotional stressors, decreased HRV which lowered the hearts ability to respond appropriately to the outside world. They found that high levels of negative emotions like anger and frustration were strongly associated with a reduction in the ability of the heart to respond to stress. Researcher Simon Bacon said,

> “Sick hearts show very little heart rate variability, so they are not responsive, leaving them vulnerable. Healthy hearts have a better ability to respond to anything that occurs. The bottom line is that the stress we experience throughout the course of the day can be bad for our hearts.”14

It is also found that people who practice managing their emotions and sustaining heart rhythm coherence have an increase in HRV.

**Coherence - What’s love got to do with it?**
The concept of coherence has been central to the emerging fields of quantum physics, cosmology, physiology and brain and consciousness research. Coherence can be defined as a synchronicity in two or more waveforms; order within a single oscillatory waveform; or clarity of thought, speech and emotional composure.15

Physiological coherence is used to describe the degree of order, harmony, stability in the various rhythmic activities within living systems over any given time period. In other words, coherence is when the heart, brain, hormone, immune and autonomic nervous system are synchronized and in alignment with each other. It has been proven that bringing the whole psychophysiological system into a state of global coherence, generates the harmonious order of these systems and creates vital benefits on all levels and can even transform an individual’s life. When measured by HRV analysis, when a person’s heart rhythm pattern becomes more ordered and sine wave-like, in this state of cardiac coherence, the frequency is measured at 0.1 hz.

A common question, why doesn’t “positive thinking” and daily affirmations change the way I feel? The answer is that positive thoughts or affirmations are often only superimposed on an underlying internal environment of emotional turmoil. There is a dis-connect or miscommunication between what the heart feels and what the mind thinks. Many common emotion regulation strategies operate on the assumption that all emotions follow thought, and thus by changing one’s thoughts, one should be able to gain control over one’s emotions.

Although this is a good start, in reference to the saying “fake it to you make it,” it will only take you so far. However, in the last decade, research in neuroscience has made it quite clear that emotional processes operate at a much higher speed than thoughts, and frequently bypass the
mind’s linear reasoning process entirely. Increased coherence facilitates higher cortical functions, increased mental clarity, increased ability to discern, improve focus and creativity, and overall performance and well-being.\(^\text{16}\)

**Conclusion**

There is a growing body of compelling scientific evidence demonstrating a link between mental and emotional attitudes, physiological health and long-term well-being. An important aspect of understanding how to increase self-regulatory capacity and the balance between the cognitive and emotional systems is the inclusion of the hearts ascending parasympathetic neuronal inputs on subcortical (emotional) and cortical (cognitive) structures. This information is conveyed in patterns of heart’s rhythm (HRV) as reflective of emotional states. Research from the HMI has found that intentional activation of positive emotions play an important role in increasing a state of coherence.\(^\text{16}\) In other words, the intuitive intelligent heart “knows,” and it is “positive feelings” that creates the ultimate shift in our physiology.

**Quick Coherence Technique\(^\text{17}\)**

- **Heart Focus**  
  Focus your attention in the area of your heart

- **Heart Breathing**  
  As you focus your attention on the area of the heart, imagine your breath is flowing in and out through that area. Breathing a little slower and deeper than usual, suggested five seconds in - five seconds out.

- **Heart Feeling**  
  Continue to breathe through the area of the heart. And as you do, recall a positive feeling, experience or memory of care, compassion or appreciation for someone or something and try to re-experience it. Allow yourself to feel this good feeling.\(^\text{9}\)

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Curing Alzheimer’s Disease: Part 1
Nancy Scanlan, DVM, MS, CVA, CHC

Objectives
- To learn the true causes of Alzheimer’s disease.
- To learn the five major types of Alzheimer’s disease.

Introduction
In order to prevent and cure Alzheimer’s disease, one needs to know the causes. Plaques and tangles do not cause Alzheimer’s disease, although they do cause brain damage. There is something that causes plaques and tangles. Thirty-five separate metabolic effects have been identified which, either singly or in any permutation or combination, lead to increased production of amyloid beta and decreased elimination of it. Various external factors can cause these effects, and genetic factors have an effect also.

There are five main types of Alzheimer’s disease, and each type is characterized by specific factors or groups of factors more likely to occur in each one. Multiple tests can identify which specific type a sufferer has, which of the metabolic effects they are suffering from, and what type of intervention, including various herbal and dietary supplements and dietary changes can be helpful. Cost of the full battery of tests can run $1400 or more. By knowing how to identify each type of Alzheimer’s disease, it is possible to start treatment without having to run every single test.

Alzheimer’s Disease was first described in a single case study presented by Alois Alzheimer in 1906, at the 37th annual conference of German psychiatrists. The patient exhibited signs of dementia at an early age, and her autopsy showed marked shrinkage of the brain, with plaques in interstitial spaces around neurons, and tangles in brain neurons.1

From an initial discussion of a single, rare case of dementia in 1906, it has grown to more than 5 million Americans and 44 million worldwide currently living with Alzheimer’s disease. Every 66 seconds, someone in the United States is diagnosed with Alzheimer’s disease. One in five people over 60 will develop the disease. It begins to develop in the brain 20 to 30 years before diagnosis, so there are an unknown additional number of victims waiting to be diagnosed. By 2025 7.1 million people are expected to be affected. Two out of three sufferers are women, and a woman in her 60’s is twice as likely to develop Alzheimer’s disease as breast cancer. Yet Federal funding for Alzheimer’s disease research is about $1.8 billion per year, compared to $3 billion for HIV/AIDS, and $6 billion for cancer. Costs for Alzheimer’s care far exceed other terminal illnesses such as cancer. The average total cost for the last five years of a person with Alzheimer’s disease is about $290,000, and the cost is currently on track to bankrupt Medicaid.2

From single case study in 1906, it has grown until in 1976 it was recognized as the most common form of dementia. In 1980 the American Alzheimer’s Association was founded, and Alzheimer’s disease was still not among the top 10 causes of death.3 In 1994 there were 16.5 deaths from Alzheimer’s disease per 100,000 deaths. By 2016 it was the 5th most common cause of death.2 In 2017, there were 31 deaths from Alzheimer’s per 100,000 deaths.4 Alzheimer’s disease in the US is currently at a state of steady increase.
Currently there are three primary stages of Alzheimer’s which have been identified:

**Preclinical**—There are brain changes, with accumulation of amyloid beta, synaptic dysfunction, and tau-mediated injury of neurons. Amyloid beta accumulation and tau mediated injury can be detected in the cerebrospinal fluid. PET scans can detect amyloid and synaptic problems, and functional MRIs can also detect synaptic dysfunction. (In the author’s opinion, there is a good possibility that at least some in this stage will not progress to the next stage.)

**Mild cognitive impairment (MCI)**—Memory and other problems in thinking are greater than “normal” for a person’s age and education. This is detected by standard tests, some of which are available online. The problems are not great enough to interfere with a person’s independence, including driving, and many in this stage can continue to work. People may stay in this phase, or they may progress to the next stage: Alzheimer’s dementia.

**Alzheimer’s dementia**—Those with Alzheimer’s dementia can’t function independently. Memory loss is more severe, and difficulty in finding correct words are great enough to cause some communication problems. Visual/spatial problems become apparent. As the disease progresses, increasing incapacity of the brain becomes evident, with loss of normal function including memory, communication, ambulation, and even ability to swallow, with death as the result.

The common form (Late Onset Alzheimer’s Disease) is sporadic. The chance of developing it increases if one has the ε4 allele of the APOE gene (also called the APOE4 SNP). But having this particular SNP does not mean one will definitely get the disease.

In contrast, the rare, Early-Onset Alzheimer’s disease is inherited, and is caused by mutations affecting amyloid precursor protein, presenilin 1, or presenilin 2. This type of Alzheimer’s dementia develops before age 65. If there is no familial history of this type of Alzheimer’s disease, one is not in danger of this type.

Heart disease in the US had a similar pattern of increase, until the recognition of the role of smoking and diet in heart disease as major contributors of its cause. Since then, although it is still a leading cause of death, the numbers of deaths from heart disease per 100,000 causes of all deaths have decreased. This strongly suggests that there are also environmental factors contributing to the rise of Alzheimer’s disease. The rise of junk food and fast food companies in the landscape, and as part of school lunches could conceivably be part of the problem.

School children originally went home for lunch. Later, school lunch programs were started and, during the Great Depression, were fortified by farm produce as one way for the government to support farmers. In 1955, vending machines were first allowed into schools. By 1968, 750 schools used vending machines instead of school lunches. In the 1970’s, there was an amendment to the School Nutrition Act, allowing outside companies to compete with the government for school lunch programs. A 1977 GAO report stated that school lunches were leading to obesity. Despite that the USDA, in 1979, stated that school lunches just needed to meet minimum nutritional standards, no longer requiring specific amounts of meat, dairy, fruit, and vegetables. In the 1980’s Handi-Snacks, Fruit Roll-Ups, pouches of Capri Sun and...
Lunchables became available as quick additions for lunch boxes and as a way to increase sales of processed meats. By the 1990’s, fast food companies were supplying the food for many school lunches nationwide.

Fast food companies themselves also followed this pattern of increased junk food available to children, as well as to adults. From 1940 to 1950, four fast food companies were founded, which still exist today. From 1951 to 1960, five more were added to the list, and an additional five from 1961 to 1969.

Junk food is not the only cause of Alzheimer’s disease, but research has shown several diets effective in decreasing the chance of developing Alzheimer’s disease. Despite that, the American Alzheimer’s Association has stated that “non-pharmacologic therapies do not slow or stop the damage and destruction of neurons that cause Alzheimer’s symptoms and make the disease fatal.” They believe that the key to treatment lies with earlier diagnosis in the Preclinical stage, before Mild Cognitive Impairment is identified. At that time, they believe that drug therapy will be more helpful. So, their approach is to support drug therapy and biomarker tests, even though they recognize some help from exercise and cognitive training.

Three of the four drugs currently approved for Alzheimer’s disease (rivastigmine, galantamine, donepezil) concentrate on increasing the amount of neurotransmitters. The fourth (memantine) blocks receptors where excitotoxins can exert their deleterious effects. They help symptoms temporarily but only address the effects of the disease, not the cause, and do not lengthen survival time.

To determine how to prevent and/or treat Alzheimer’s disease it is necessary to understand where the amyloid plaques come from and why they are produced. In 1984 the main protein which the plaques are comprised from was identified to be amyloid beta. That discovery was followed by identification and DNA analysis of, the precursor protein for amyloid beta (subsequently named Amyloid Precursor Protein (APP)). It was determined to be a trans-membrane protein of neurons. Why would a neuronal structure produce something toxic to neurons? Individual amyloid beta fibers have beneficial properties, especially as an antioxidant and an antimicrobial acting in the brain. There is a pathway that facilitates regular removal of A beta from the brain, especially during sleep, so normally it is removed before it can accumulate and form plaques. APP was also found to be essential for normal growth, survival, and post-injury repair of neurons.

APP can be split two different ways, depending on which of two caspases interact with it. The two peptides which are produced from the non-amyloid-producing split of APP—sAPPα and αCTF—promote nerve cell growth, and inhibit Aβ production, caspase activation, and programmed cell death. The peptides produced from the amyloid-producing split include Aβ production.

Based on this and other research, Dale Bredesen, MD, professor and researcher in the medical schools at UCLA and UCSF, and head of the Buck Institute for Age Research, identified three main causes of Alzheimer’s disease, with some sub-types based on combinations of the causes
and whether one single factor is predominant. This identification is important, because for successful treatment of a case, the specific causes must be treated. The 3 main causes are

- Inflammatory – when the primary causative factors create chronic inflammation
- Lack of substrate – where the primary causative factors are based on deficiencies of various nutraceuticals
- Toxic – where the primary cause is a toxic factor such as heavy metal poisoning, black mold exposure, or the types of toxins found in a toxic waste dump

There are a number of subtypes but 2 are most common:

- the sugar type (the most common subtype), a combination of inflammatory and toxic types.
- chronic silent infections with disease organisms such as Borrelia burgdorffii (Lyme disease).

He developed recommendations for laboratory tests which would identify the primary type of Alzheimer’s disease as well as specific contributory factors. Based on the test results he began treating patients with a complex of multiple factors including optimization of diet and sleep, reduction of stress, increase of exercise, and supplying herbs and supplements as needed depending on results of testing.

In 2011, he also submitted a request for funds for a 4-arm double-blind placebo-controlled trial for early Alzheimer’s disease therapy which included both lifestyle changes and individualized recommendations for supplements, depending on the results of extensive lab testing. The proposal was turned down by both public and private institutional review boards as being too complicated, and because more than one variable was being tested.

In 2013, Dr. Bredesen published an article proposing that those observations about amyloid beta and APP suggested that, like osteocytes and other cells, neurons have a balance between pro-apoptotic and anti-apoptotic forces. Noting the failure of single-drug trials he suggested that, like other more successfully treated chronic disease such as HIV, the answer was likely to be multi-modal treatment, and gave an example of 13 factors that would have to be addressed in Alzheimer’s patients, with 13 (or more) different treatments.

In 2014, he published a case series of 10 patients. Nine of ten had reversed their symptoms, and all six who had been forced to retire, had returned to work. The one who failed treatment was in a late stage of Alzheimer’s disease. Since then he has published 100 case studies of successful treatments. By 2017 over 200 had been successfully treated. Currently there are over 450 physicians trained in the procedure, so it is likely that the number of successful treatments is over 400.

This is not a cure. Those who have gone off the program usually start noticing signs of decline within 6 weeks. But most people who have had success have not fully followed the program, and still get good results. The program is still being fine-tuned, they are learning more about identifying which parts are most important, but the basic recommendations remain the same.

Alzheimer’s disease can be reversed.
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Curing Alzheimer’s Disease: Part 2
Nancy Scanlan, DVM, MS, CVA

Objectives
- To learn the dietary changes, supplements, and herbs that help most types of Alzheimer’s disease.
- To learn how to deal with more difficult factors such as chronic infection with HSV-1, Lyme disease, heavy metal poisoning, etc.

Introduction
Signs of stage I Alzheimer’s disease have been reversed, allowing sufferers to return to their jobs, start driving again, and otherwise live an almost normal life again. Stage II sufferers can also be helped, although not as dramatically as stage I sufferers. The program to do so is basically holistic, since it addresses so many different factors, and since each case is a very individual one. The program is a comprehensive one, involving diet, exercise, reduction of stress, and various supplements and herbs. Some people drop out, while others start slacking off as soon as they see positive results. Even those who only partially follow the program see some benefit.

Cases that are the most difficult to deal with usually involve some type of chronic exposure to toxins, such as living for years near a toxic waste dump. Other difficulties often occur with unrecognized chronic disease such as Lyme disease or HSV-1. This presentation will explore the easiest parts of treatment to initiate, as well as ways to track down and treat problems that are less obvious.

In Alzheimer’s disease, Amyloid Beta (A beta) plaques between nerve cells and Tau tangles within nerve cells cause pruning of synapses and, ultimately, cell death. A beta, with 3 other peptides, is produced by enzymatic action on Amyloid Precursor Protein, as a natural part of nerve cell function in the brain. Individual fibrils are sticky and have an antimicrobial action. Normally, individual fibrils are swept out by cerebrospinal fluid flow, which is ongoing, but the flow is highest during sleep.1

Amyloid Precursor Protein can also be divided in a different way, forming sAPPalpha and alphaCTF, which promote increased connections and cell growth.2 Thus 2 sets of molecules from the same primary molecule are responsible for both nerve cell growth and nerve cell death in the brain. 36 factors have been identified which influence which way APP divides, and balance between and among those factors can tip the balance towards or away from Alzheimer’s disease. Their action is influenced by diet, herbs, supplements, exercise, sleep, stress, hormones, other illnesses, exposure to toxic substances and, to a certain extent, by genetics.1

Diet alone plays a big part in the influence on those factors. The three diets which have been shown to do this are: The Dietary Approaches to Stop Hypertension (DASH) diet, the Mediterranean diet, and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet. Adherence to any of those diets decreases the chance of developing Alzheimer’s disease, as well as slowing its progression.3,4
While they all help, the MIND diet has the greatest effect. Those who strictly follow the MIND diet have 53% less chance of developing Alzheimer’s disease, while those who partially adhere to it can still have a 35% less chance of developing ALZ. The diet also decreases the chances of suffering from Parkinson’s disease or from stroke.5

The MIND diet was designed by Martha Clare Morris, Sc.D., an epidemiologist at Rush University Medical Center who used retrospective studies to create it and prospective studies to verify it, following adherents for up to 10 years. Morris started with a comparison between the DASH Diet and the Mediterranean Diet, both of which were shown to decrease the incidence and speed of cognitive decline. She correlated recommendations for individual food types and quantity research showing benefits or harm to the brain. The result was a diet with similarities to both of its predecessors, but some specific recommendations that were a little different. For example, recommendations for quantity of leafy greens are higher, and berries are the only fruit recommended. She noted the amount of brain protection from the DASH and Mediterranean diets were only seen among those most strictly adhering to them, whereas both strict and partial adherence to the MIND diet showed beneficial effect. Final recommendations for the diet consist of 10 recommended food groups, with recommended minimum amounts of each, and 5 groups to avoid, with maximum amounts of each.6 (See Table 1)

While diet alone can prevent Alzheimer’s disease, and can slow decline in disease sufferers, only one program has been shown to have close to 100% success in reversing its signs and symptoms. The program has helped over 100 patients from Subjective Cognitive Impairment through Stage II of Alzheimer’s disease. It has enabled those unable to function at work to return to their jobs. The program has been named ReCODE (for Reversing Cognitive Decline) by its creator, Dale Bredesen, MD.7 (There are some other programs being promoted, but they are only successful for a subset of Alzheimer’s sufferers. Not all their promoters realize this.)8

The complete ReCODE protocol is complex and difficult for many to follow. It is not a cure in the traditional sense – you can’t just go back to a bad diet once all your tests look good. Those who only follow parts of it often see lasting improvement, and those parts vary with each patient, so it is impossible to recommend one single program for all. Those who are able to stay on most of it still find lasting improvement. Those who make gains and then decide after several months that the ReCODE process is too difficult to follow see a reversal of gains beginning within 6 weeks of discontinuing it. 6 months is required to give enough time to allow for adjustments as values come back to normal, with the endpoint being a final protocol to stay on for the rest of one’s life. Some need longer because of the complexity of their problems. Symptoms continue to remain improved for those who have stayed on it for years. Brain mass and brain function remain at their improved level.7

The ReCODE Process
In order to determine which of the 36 factors are most in need of correction, a “cognoscopy” is performed. The cognoscopy assessment includes a combination of blood tests, genetic tests, a simple online cognitive assessment, and an MRI with volumetrics. (The MRI is not necessarily required for Subjective Cognitive Impairment.)

Tests in the cognoscopy not included by the average physician include:
The Ketoflex 12/3 diet is recommended for all types. Its aim is for a low state of ketosis, although it does not fit recommendations for essentially all popular ketogenic diets. Instead, it is closer to the MIND diet, with a few changes. The most prominent change is eliminating grains in the diet. More vegetables are recommended: 6 to 10 servings of fresh, whole, non-starchy vegetables per day, no food should be eaten 3 hours before bedtime, and 12 hours should elapse between the last meal of the day and the first meal of the next day. (14 to 16 hours should be used by those with the APOe4 allele.) Unlike the MIND diet, they also recommend mostly skipping wine or any other alcohol. It also recommends initially avoiding gluten and casein, and lectins if you have a problem with those. After signs have improved, a small amount can be added back in if desired, but for dairy products, only those derived from A2 milk.
**Type 1. Inflammatory Alzheimer’s Disease**

The inflammatory type is characterized by high markers of inflammation. Diets often include trans fats, sugars, fast food and processed meats. Other causes of inflammation include periodontal disease, leaky gut, and sensitivity to gluten, dairy, and/or grains. Body fat, especially abdominal fat, creates inflammatory adipokines. A change to the Ketoflex 12/3 diet is imperative for this type.

Antioxidants (both nutraceutical and herbal) also help greatly in decreasing inflammation. Chronic inflammatory diseases must be dealt with, both periodontal diseases and low-level chronic disease such as Lyme and Epstein Barr disease. For these, it may be necessary to use conventional drugs as well as holistic therapy.

**Type 2. Atrophic Alzheimer’s Disease**

The atrophic type is caused by lack of BDNF and substances absorbed from diet, and nutraceuticals, and from presence of redundant, strong synapses. Synapses can be strengthened through a lifelong learning program. BDNF is increased through exercise. Nutrient-dense foods, especially green leafy vegetables, should be increased. Vitamin D and folate are the most critical vitamins. Estradiol and testosterone can also help, through supplements or prescription (by somebody who fully understands their risks and benefits.) Additional nutrients may be recommended depending on the cognoscopy results.

**Type 3. Toxic Alzheimer’s Disease**

Primary causes of the toxic type are smoking, heavy metals, and toxic mold exposure. If you smoke, stop smoking. Amyloid normally binds heavy metals and biotoxins such as the mycotoxins from mold. In a system which is unbalanced, it loses this function as it is assimilated into plaques. Cruciferous vegetables and glutathione are nutritional aids to detoxification. Heavy metals are excreted in the greasy part of sweat, so exercise plays a part there, as well as saunas. If necessary, chelation therapy is used to get rid of metals.

**Glycotoxic Alzheimer’s Disease**

Humans evolved to handle about 15 grams of sugar per day. This is half of the amount in one 12 ounce can of soda. A big part of detoxification in this cause is to decrease sugar in the diet as much as possible. Insulin Degrading Enzyme degrades both insulin and for amyloid. When sugar and simple carbohydrates are decreased enough, lower levels of insulin result, leading to increased amounts of IDE available for degrading amyloid. Though it can take months to see a change in lab values, it often takes less than a month to see cognitive improvement when sugar is addressed.

Coconut oil or MCT oil is often, but not always, beneficial when starting, to induce a state of ketosis more quickly. Those with the APOe4 allele of the APOe gene do not respond well to coconut oil, so this should be avoided in those people. (This is one reason to get tested for this SNP). Some types of heart disease also become worse with MCT oil.

**References**


3. van den Brink AC, et al. The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease-A Re


8. Tao et al, Dietary Intake of Riboflavin and Unsaturated Fatty Acid Can Improve the Multi-Domain Cognitive Function in Middle-Aged and Elderly Populations: A 2-Year Prospective Cohort Study.


Table 1.
Supplements recommended by Bredesen in End of Alzheimer’s, pages 187-188

Note: it is important to use activated forms of vitamins. This means:
methyl-B12, not cyanocobalamin
methyltetrafolate, not folic acid
pyridoxal-5-phosphate, not pyridoxine.
Vitamin D-3

For all:
Professional-grade multivitamin-multimineral (with B-complex)
  Vitamin B1 50 mg
  Pantothenic acid 100-200 mg (especially for focus and alertness)
  Nicotinamide riboside 100 mg
  Magnesium should be included
Citicoline 250 mg BID for synaptic growth and maintenance
Resveratrol 100 mg
Ubiquinol 100 mg to support mitochondrial function
High quality source of omega-3 (DHA and EPA) (fish oil or algae oil, not flaxseed oil)
Cook meat, fish, and poultry with moist heat, lower temperatures, using shorter cooking times, and add something acidic like lemon, lime, or vinegar to reduce AGES.

For specific circumstances:
A probiotic if not eating fermented foods
If vitamin D blood levels are low, D 2500 IU per day plus vitamin K 100 mcg, until serum levels are 50 to 80
B6, B1, and folate if homocysteine is above 6
Vitamin C 1 gm if vitamin C is suboptimal or Copper:zinc ratios are higher than 1:2
Vitamin E 400-800 mixed tocopherols and tocotrienols, if Vitamin E blood levels are less than 13
If problems getting into mild ketosis with the Ketoflex 12/3 diet: MCT oil or coconut oil. NOT for those with APOE4 SNP

Type 1 Inflammatory Alzheimer’s disease or MCI or SCI with GI symptoms: triphala on an empty stomach. One capsule or make a tea from the powder in a capsule.

Type 2 Alzheimer’s disease: Acetyl-L-Carnitine 500 mg to increase Nerve Growth Factor

Type 3 Toxic Alzheimer’s disease or MCI or SCI: Tinospora cordifolia (gucuchi) 300 mg w meals, BID to TID to increase immune support Guggul extract 350 or 750 mg capsules to remove toxins in the gut
Your DNA profile – What to Do About Those Bad SNPs
Nancy Scanlan, DVM, MS, CVA

Objectives
- To become acquainted with different gene profiling companies
- To learn how to use nutragenomics to improve the outcome of bad SNPs

Introduction
Companies like 23andme.com and myheritage.com appear to offer the same service. Though there is a big overlap, each of them offer some SNPs that others do not. They only highlight some interesting factors (like whether you are genetically programmed to be a dog person or a cat person), ancestry results, and the most famous SNPs (like the APO E4 variant for Alzheimer’s disease). Other companies give a much more in-depth look at your results.

This presentation will compare companies to help attendees decide whether they want DNA testing, how in-depth of an analysis they want and what they want to do with the results. It will explore ways to decrease risk factors and increase beneficial SNP effects through lifestyle changes.

Genetic Terminology

**Genome**: complete set of hereditary instructions (DNA) for building, running, maintain, and reproducing a body.

**Nucleotide**: subunit of DNA, consisting of a sugar molecule, a phosphate molecule, and one of 4 nitrogenous bases. They come in pairs in a DNA molecule


**DNA**: Long molecule made of very long strings of nucleotides

**Gene**: area in a chromosome which codes for a protein, surrounded by other “extra” areas of DNA including regulatory sequences that can turn a gene on or off. Also affected by internal and external factors (e.g., diet, exercise, altitude). Affects characteristics directly or indirectly.

**Polymorphism**: Gene variations where each possible nucleotide sequence is represented by at least 1% of people

**Mutation**: less than 1% of people have that sequence

**Alleles**: different version of same gene

**SNPs**: (Single nucleotide polymorphisms) variations in one single nucleotide in a gene
Human genomes have about 3 billion DNA base pairs. On average, larger animals have larger genomes, but there are many exceptions: newts have about 15 billion, and lilies have almost 100 billion. The base pairs in humans are distributed in 23 pairs of chromosomes. Genes are sections within those chromosomes that affect growth and performance of various parts of the body. Human genes are usually about 27,000 base pairs long. Some are up to 2 million base pairs.\(^1\)

About 1 of every 1200 to 1500 base pairs differ from person to person. While that is more than 3 million differences, all humans are the same in about 99.9% of their DNA. Ninety percent of variations are pretty simple: substitution, addition, or omission of a single base pair. When the variation involves only one base pair, it is referred to as a single nucleotide polymorphism, or SNP. For example, one SNP may be characterized by replacing cytosine with thymine in a certain stretch of DNA. SNPs are the most common type of genetic variation among people.\(^1\)

More than 100 million individual SNPs have been found worldwide. Most have no known effect and may have little effect on health or survival.\(^2\) Some can help predict an individual’s response to certain drugs, susceptibility to environmental factors such as toxins, and risk of developing particular diseases. SNPs can also be used to track the inheritance of disease genes within families. SNPs describe the risk of getting a disease or of reacting a certain way to medication or the likelihood of needing certain types of treatment. For the most part they do not diagnose disease states and should not be used as the sole method for determining treatment.\(^3\)

It is common for the medical profession to recommend that a patient not be told about unfavorable SNPs if there is no effective treatment that is generally recognized or in use by the medical profession or associated organizations.\(^4\) Most sites go out of their way to warn those who have problems with anxiety or depression that reports about alleles that are associated by such diseases can cause emotional difficulties. 23 and Me, for example states:

“Genetic testing for these conditions in the general population is not currently recommended by any healthcare professional organizations. The Alzheimer's Association, a patient advocacy group, also does not recommend genetic testing for Alzheimer's disease in the general population.”\(^3\)

Others in the profession argue for patients being told their status if there is some possibility of benefit from something with an overall bad prognosis.\(^5\) Similarly, other sites describe SNPs associated with various diseases and lifestyle factors, grade them as favorable, unfavorable, or anywhere in between, and let the user decide what they want to access (e.g., lifewello.com, promethease.com, selfdecode.com). One site is like a Wikipedia of SNPs, allowing searches on specific SNPs, and the ability of users to upload comments. (snpedia.com)

SNPs can form a major part of decisions made in a personal wellness plan. For example, the APOE gene is associated with transport of apolipoprotein lipids. The e4 SNP is associated with increased inflammation and increased incidence of Alzheimer’s disease. We now know of a complex, holistic therapy that is being ignored by medical authorities. We also know, as part of that therapy, coconut oil is not recommended for those with the APOE4 SNP (vs other patients), and for an overnight fast to be effective, theirs needs to be 2 to 4 hours longer than for all others.\(^6\) The APOE4 SNP also makes it twice as likely that one will die from a second myocardial
infarction, compared to others who have suffered an initial myocardial infarction and do not have this SNP. Both groups have a decreased risk when they are given statins. However, the risk for those with the APOE4 SNP is reduced twice as much as non-APOE4 bearers, bringing it down to the same risk as for those without it. For those choosing to use drugs, this is a strong reason for researching your own SNPs and acting on them accordingly. For those choosing to use a lifestyle change to reverse heart disease, this knowledge could be the final incentive for doing so. For those interested in the novel Alzheimer’s therapy for prevention and treatment, this is also a strong reason to explore your SNPs.

There are a number of areas where knowledge of SNPs can be helpful: medical conditions and diseases (prevention and treatment), immune-mediated markers (allergies, inflammation, and autoimmune disease), medications (actions and side effects), nutrition (SNPs requiring increased amounts of nutrients) and fitness (best ways to train according to your SNPs).

The first place to find out about your SNPs is to find a company which will analyze your DNA. Most who do so offer an ancestry report along with the analysis, and most offer some kind of health report, usually for an additional fee. You must submit a DNA sample which may saliva, cheek swab, or blood, depending on which company you are submitting to. The sample is analyzed using a genome chip and a report is generated characterizing the SNPs which that company tests for. It is important to use a company which allows download of your raw data, since there are an increasing number of other companies which will let you upload your raw data to them for additional information.

In 2019, the three most popular companies which perform DNA analysis for the public were 23 and me, My Heritage, and Ancestry (the Big 3). At the time of this writing (April 2020) there are at least 14 more, although the Big 3 currently rank in the top 5 best in all popular reviews accessed. The Big 3 analyze 650,000 to 700,000 variants, and all of them allow you to download the raw data results. Though there is a lot of overlap, they are not the same. Currently, a different company, SelfDecode, tests for the most variants, analyzing about 900,000. 128,503 of them overlap with 23 and Me. (See Appendix for a comparison of 7 DNA analyzing companies which offer a health option)

Once your analysis is done you can download the raw data which includes the SNPs that company is most concerned with, and all the other SNPs that were analyzed. This is a VERY large file, so allow enough time to fully download it. (The author’s zipped text file from 23 and Me is 5.7 megabytes.) You can then upload it to any other site in order to get additional insights into your genome.

For additional information, there are two options: One group of sites analyzes the date to give you a more in-depth look at SNPs that relate to subjects such as fitness or nutrition. They give specific information related to SNPs which can affect your ability to absorb or use nutrients, heal from athletic injuries, athletic training and performance, and other items. Some are connected with health professionals, up to and including physicians with a special interest in a specific problem. All of these usually have more in-depth reports and information than the primary sites but limited to whatever their special interest is. Those with a certification or license also offer consultations.
The other option is the “everything” sites. They provide information all SNPs known to have some kind of effect on your body. The amount of information is overwhelming, and their search functions are not very intuitive. These are usually some type of subscription service, rather than just paying for specific reports. (Appendix)

SelfDecode is a hybrid between the two. There are a number of reports available. You can go deeper and deeper into each report for more information, including published research (with links to Medline). If you go deep enough you can hit the overwhelming information point, and you can do the same by starting with a broad search. The search function is more intuitive, and if you stay relatively shallow and double check the research citations, you can get enough published information, from in vitro to in vivo to studies using human data, to decide whether or not to incorporate that data into your own wellness program.

You may be satisfied with a basic report from 23 and me. It allows you to access information about your APOE status, and for possibility of Parkinson’s disease, as well as other more benign SNPs. If you subscribe to their update service, they offer interesting insights from time to time, such as whether you are more likely to prefer cats over dogs, or whether you are more prone to a fear of heights.

If you wish to dive deeper, there are 7 genes with SNPs, dealing with SNP-related problems which affect one’s health in general, and which can be helped with lifestyle adjustments as well as specific herbs and supplements. Basic recommendations for diet, environment, exercise, sleep, and stress reduction are basically the same to improve epigenetic influence on the SNPs, with some specific recommendations for problems for each gene.

**Diet:** Mediterranean diet, MIND diet, and Ketoflex 12/3. For the Dirty Dozen foods most likely to be contaminated with pesticides, use organic versions. Eat whole foods, not processed foods.

**Environment:** eliminate artificial flavors, colors, ingredients, odors, etc. as much as possible.

**Exercise:** 20 minutes per day, cardio, weight training, and stretching

**Sleep:** 8 hours per night, no food 3 hours before sleeping, 12 to 16 hours between last meal of the day and first meal of the next day.

**Stress reduction:** deep breathing, yoga, therapy or whatever else might be needed.

**The Genes**

*APOE4* is the specific SNP of most importance for inflammation in general. Bredesen’s program can reverse Alzheimer’s disease. Dean Ornish’s program can reverse heart disease.

*MTHFR SNPs* affect methylation of other genes which allows proper function of those other genes. Folinic acid or methylfolate with vitamin B12, Riboflavin (vitamin B2), leafy greens, and decreasing both mental and physical stress.
**COMT SNPs** can speed up or slow down the action of this gene, which affects focus, buoyance, mellowness, and calm through influencing the metabolism of estrogen, dopamine, norepinephrine, and epinephrine. If it is acting too strongly there will be problems with focus and concentration. This is helped with folinic acid or methylfolate and by eating a little more protein. If its action is too slow, the subject will not handle stress well and have anxiety problems, as well as problems falling asleep. Eating less protein, with the most at breakfast, next most at lunch, and much less at dinner can be helpful. Magnesium SAMe, vitamin B6, and calcium glucarate are helpful as well as liver support such as milk thistle.

**DAO** regulates diamine oxidase which metabolizes histamine. Problem SNPs cause decreased histamine breakdown with sensitivity to certain foods. Limit histamine-containing foods such as wine and fermented and aged foods. Diamine oxidase can be taken orally also.

**MAOA** regulates metabolism of serotonin, norepinephrine, and epinephrine. Problem SNPs that speed its actions can cause carbohydrate craving. Exercise, decreasing inflammation with curcumin, elimination of chronic infections, calming methods, 5-HTP or Griffonia simplicifolia extract, B6, methylfolate, magnesium, zinc, Ashwagandha, and phosphatidyl serine can all help. One may need outside support also for the carbohydrate cravings.

SNPs that slow the action of MAOA cause mood swings with headaches, irritability, problems relaxing, prolonged anxiety and problems eating the same foods that affect those with bad DAO SNPs. Slow, deep breathing (Pranayama), eating less protein and less histamine-containing foods, riboflavin, and lithium (which blocks some serotonin receptors, zinc, pantothenic acid, and herbs that help with stress. For sleep problems: phosphatidyl serine, SAMe, magnesium

**GST/GPX** are involved with detoxification using glutathione, especially with substances such as heavy metals, peroxide, and formaldehyde. Selenium, riboflavin, molybdenum, superoxide dismutase, pyrroloquinoline quinone are all helpful. Glutathione orally unless it can’t be tolerated. Leafy greens and cruciferous vegetables in the diet.

**NOS3** affects generation of nitric acid, which affects heart health and hypertension. For it to work properly, the MTHFR, GST/GPX, COMT, and MAOA genes must be functioning properly. Arginine and citrulline, folinic acid or methylfolate, vitamin B12, glutathione, magnesium, vitamin C, and breathing through the nose (note the mouth) are all helpful.

**PEMT** affects cell membranes and decreases problems with fatty liver. Must have a functioning MTHFR gene to be able to work properly. (PEMT coordinates 70% of all methylation actions). Choline (most important supplement, niacin vitamin C, phosphatidylserine, glycine, betaine, liver support.

**References**
1. What’s a Genome Available at http://www.genomenewsnetwork.org/resources/whats_a_genome/ Accessed 3/12/20
3. Choose your health reports Available at https://you.23andme.com/user/edit/health-report-configuration/ Accessed 3/12/20

Appendix
DNA testing and reporting sites (prices as of March 2020)

Ancestry - DNA: https://www.ancestry.com/dna/ $149
  – Autosomal SNPs tested: 650,000

23 and Me: https://www.23andme.com $199
  (BRCA test controversy: They may be missing 90% of positives: https://www.genomeweb.com/cancer/23andme-dtc-breast-ovarian-cancer-risk-test-misses-almost-90-percent-brca-mutation-carriers#.XmWKkKhKjIV
  – Autosomal SNPs tested: 650,000

My Heritage: https://www.myheritage.com $199
  – Autosomal SNPs tested: 700,000

SelfDecode: Selfdecode.com
  Offers their own test. Also currently accepts DNA data from 15 other sites.
  – Autosomal SNPs tested: 900,000
Third party sites with narrowed reports

Athletigen.com Free and paid
  Health, Nutrition, athletic responses, injury prevention

DNAFit $79–$149
  Fitness and diet include antioxidant needs, detoxification ability, endurance performance, power, injury risk, recovery from exercise, and more.
FitnessGenes.com $49.00 with upload of DNA, $199 they include DNA test
How you respond to, or will benefit from, ways of eating, exercising, supplementing or behaving, such as sleep, skipping meals, muscle fiber profile and more. In partnership with Gold’s Gym.

GeneHeritage.com $12
Reports: Medical & Health, Smell & Taste Sensitivities, Physical Characteristics, Digestion & Metabolism, Sports & Fitness, Diet & Nutrition, Personality & Intelligence

Genomelink.io First 25 free, then $14 per month gives access to 125 traits plus weekly updates
Food and nutrition, personality, intelligence, physical, sports.

Genopalate.com: $69.00 if you have raw DNA report, $189 if not. Add $40 for 5 recipes.
Recommendations for your body’s ideal nutrient intakes for 23 nutrients, find out if you are sensitive to lactose, gluten, alcohol, or caffeine, and unlock the 85+ foods that are the best match for your genes.

Glownaturalwellness.com – $325 or more, for women only
How to easily reach your fat-loss, health, energy, nutrition, and personal development goals.

Home DNA: https://homedna.com – $139 to $159 for people and pets. Weight, skin care, food and pet sensitivity; people, pets genetics. Unknown if you can download raw data
– Autosomal SNPs tested: 80,000

LiveWello.com $19.95 report
Gene library access, hundreds of free health reports, over 52,000 of SNPs have research studies that directly associate them with health conditions. Generate unlimited gene reports based on your diagnoses

Strategene.org, $45
Diet, lifestyle, environment epigenetic effects on health-related genes. Designed by an ND

Xcode.life $99 can merge data from Ancestry and 23andMe)
9 reports covering over 700 traits. BRCA separate
Maximum number of SNPs:

Promethease.com $12 per report, not real intuitive. Based on SNPedia.com. Deleted after 45 days. A literature retrieval system that builds a personal DNA report based on connecting a file of DNA genotypes to the scientific findings cited in SNPedia. Tells EVERYTHING. Can be overwhelming.
Nutrition for Cats with Chronic Kidney Disease
Lea Stogdale, DVM, Diplomate ACVIM Small Animals

Objectives
- To understand the predisposing causes and practical diagnostic tests that enable us to appropriately manage cats with chronic kidney disease.
- To integrate feline nutritional carnivorous requirements into the management of our geriatric feline patients with chronic kidney disease in order to maximize our patients’ quality and quantity of life.
- To recommend approaches to managing chronic kidney disease in cats that enable owners to comply in a practical and cat-friendly manner.

Introduction
Chronic kidney disease in cats is one of our most common, complex, and confounding problems. Dr. Stogdale summarizes the predisposing causes and practical diagnostic tests that enable us to stage each patient for appropriate management. Understanding feline nutritional carnivorous requirements is essential in managing our geriatric feline patients with kidney disease for maximizing our patients’ quality and quantity of life. Using case examples, Dr. Lea Stogdale will describe the practical management of kidney cats who can be resistant to dietary changes and medications. This includes the control of hyperphosphatemia and hypokalemia. She will emphasize nutrition, and will also discuss veterinary approaches, owner observations and easy medication strategies to maximize the cat’s acceptance and the owner’s compliance and satisfaction. This approach is very gratifying for the veterinary team as these cats live long happy lives with pleased and thankful clients.

The causes of CKD in cats are unknown. Some possible contributing causes include excessive vaccination, chronic infections and/or concentrated urine.

Excessive vaccination. The panleukopenia vaccination has been shown to produce anti-kidney antibodies. The feline panleukopenia vaccine is very effective resulting in an excellent antibody response that persists for over 10 years. An excellent antibody response plus antigen, in the form of repeated vaccinations, can result in a Type 3 immune reaction, an Arhus reaction: antibody combining with antigen, stimulating complement release. This reaction most commonly occurs in small arteriolar networks as occur in the kidney glomeruli and joints.

Prevention is selective vaccination, such as giving the panleukopenia vaccine to kittens at 12 weeks of age, a booster at one year and at 10 years of age. Rabies vaccination must follow the legal requirements of your area. Feline leukemia vaccines need only be given to cats who go outside and fight. Boosters are only required every three years. Except in specific circumstances, vaccines against FIV, FIP, and Giardia are not indicated.

Chronic low-grade infection may damage the kidneys. The most common source of chronic low-grade infection is gingivitis. The most common causes of chronic gingivitis are dental tartar and food allergies or reactions, caused or exacerbated by carbohydrate in the food especially in the form of grain gluten. Prevention is by feeding grain-free cat food plus bones for the cat to chew upon. Cats are not small dogs: feed them real bones. The aim is to have clean teeth every
day of every week of every year, not just clean teeth for a couple of months after an anesthetic and dental scaling. Bones need to be fed about twice a week. Any bones (except fish): beef, steak, chops, pork, turkey, chicken; cooked or raw – whatever the owner can and will feed, and whatever the cat will chew. Cats chew on bones similarly to how people chew on bones – crunching without swallowing chunks. Cats crunch bones.

**Cats have highly concentrated urine,** especially if they are fed predominantly dry cat kibble. Concentrated urine may damage the renal tubules due to the high levels of metabolic products, acids and toxins present. Dry cat food causes chronic dehydration. We know this by comparing urine specific gravities:

<table>
<thead>
<tr>
<th>Urine Specific Gravity</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>in normal humans</td>
<td>1.015 – 1.030</td>
</tr>
<tr>
<td>in normal dogs</td>
<td>1.025 – 1.035</td>
</tr>
<tr>
<td>in normal cats eating wildlife</td>
<td>1.030 – 1.050</td>
</tr>
<tr>
<td>in cats eating kibble</td>
<td>1.050 – 1.100</td>
</tr>
<tr>
<td>in cats eating canned food with water added</td>
<td>1.020 – 1.030</td>
</tr>
</tbody>
</table>

Cat urine specific gravity varies over a wide range depending upon the amount of moisture in their food. Cats do not like drinking, and they are inefficient drinkers.

For **prevention,** of course I recommend that cats, obligatory carnivores, be fed four mice a day, their natural diet; or a grain-free, low carbohydrate home prepared raw or cooked diet; or commercial complete and balanced raw diet; or good quality, grain-free canned cat food with some meat added; or at worst, canned cat food with a maximum of 1/4 cup per day of grain-free dry cat food. The aims are for the owner never to see their cat drinking, heavy litter boxes (with urine), and urine specific gravity < 1.030. The best holistic medicine is preventive medicine. In cats, this is appropriate, good nutrition.

The **early signs of CKD in cats** are subtle and rarely noticed by owners: slow weight loss with mild increase in drinking and urine volumes as the serum creatinine climbs above 140 μmol/L = 1.6 mg/dL. The earliest sign available to the veterinarian is a mild decrease in the cat’s body weight when an accurate scale is used. Cats need to be weighed at every vet visit on a pediatric, baby or cat scale; not on adult bathroom scales or walk-on dog scales. Reliable human baby scales are available online for less than $70.

The **tests** required for an initial adequate assessment of renal function in the cat are: Complete Blood Count, serum chemistry, T4, urinalysis including Culture and Sensitivity (C&S) and UPCR and BP.

**CKD Diagnosis using the International Renal Interest Society (IRIS) staging and guidelines.** These provide normal, healthy test levels rather than ‘laboratory reference intervals’ which include pre-clinical levels (abnormal test levels occur before obvious physical signs are detectable.
Evaluation Normal Levels CKD IRIS Stage 2

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Normal Levels</th>
<th>CKD IRIS Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney excretion ability by measuring Glomerular Filtration Rate (GFR) –</td>
<td>&lt; 1.6 mg/dL</td>
<td>≥ 1.6 mg/dL</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>&lt; 140 µmol/L</td>
<td>≥ 140 µmol/L</td>
</tr>
<tr>
<td>Secondary Renal Hyperparathyroidis – Serum Phosphorus (P)</td>
<td>3 – 4.5 mg/dL</td>
<td>≥ 3 – 4.5 mg/dL</td>
</tr>
<tr>
<td>1.0 – 1.5 mmol/L</td>
<td>≥ 1.0 – 1.5 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Erythropoietin production – Packed Cell Volume (PCV) or hematocrit</td>
<td>≥ 25%</td>
<td>≤ 25%</td>
</tr>
<tr>
<td>Kidney potassium tubular loss – Serum Potassium (K)</td>
<td>4.5 – 5.0 mg/dL</td>
<td>&lt; 4.3 mg/dL</td>
</tr>
<tr>
<td>= mmol/L</td>
<td>≥ 1.0 – 1.5 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Renal protein loss – Urine Protein : Creatinine ratio (UPCR)</td>
<td>&lt; 0.4</td>
<td>≥ 0.5</td>
</tr>
<tr>
<td>Hypertension – Blood Pressure (BP)</td>
<td>&lt; 160</td>
<td>≥ 160</td>
</tr>
<tr>
<td>Thyroid function status of the patient affects all the other tests – T4</td>
<td>&lt; 3.1 µg/dL</td>
<td>≥ 3.1 µg/dL</td>
</tr>
<tr>
<td>level.</td>
<td>&lt; 40 nmol/L</td>
<td>≥ 40 nmol/L</td>
</tr>
</tbody>
</table>

Management of CKD

The cat's nutrition, especially protein intake, is the major factor influencing:1,4
- Glomerular filtration rate as measured by serum creatinine
- Renal secondary hyperparathyroidism as measured by serum Ca and P
- Erythropoietin production as measured by PCV

Much of the evidence published in scientific journals recommends reducing dietary protein and hence the phosphorus intake.1,4,6 In these trials, kidney diets with lower protein and P levels resulted in longer patient life spans with fewer crises requiring veterinary attention. The problem with these trials is that the feline patients were fed dry cat food, or a combination of dry and canned cat food, or the type of food was unknown. We cannot interpret trials in cats unless the dietary details are known, including quality and quantity of protein, carbohydrate and moisture content, and fiber amount and type. Also, P levels were not effectively controlled.

Recently, protein restriction has been questioned.5,6,7 Cats are obligatory carnivores requiring a low carbohydrate diet with a minimum of 5.0 gm/kg/day protein to avoid lean muscle mass loss, and a high dietary fluid with soluble fiber. Recent research confirming this minimum level of protein was done by Purina.8 This also replicates the natural prey diet of feral cats that has a protein range of 5.5 – 11.5 g/kg/day.7,8

Practical problems with kidney, renal or lower protein diets in cats include:5
- Cats refuse to eat lower protein diets, or they eat less resulting in weight loss;
- Reducing the dietary protein reduces the GFR;
- Reducing the dietary protein below 5.0 gm/kg/day results in loss of lean muscle mass;
- Reducing the dietary protein results in anemia.

My aims in feeding my CKD cats are to maintain the patient's quality and quantity of life by maintaining hydration despite the polyuria, and to maintain the cat's appetite. To achieve this, I recommend feeding either canned cat food with a protein level of about 10% as fed or a similar
home prepared diet, whichever the cat prefers. To either of these diets, water needs to be added, just a little at first and increased as the cat will tolerate while maintaining adequate food intake. The aim is to add approximately the same amount of water as the volume of canned food: the cat should be drinking its food. Along with this soupy cat food, no or little dry kibble is fed. The results of this program are:

- Our CKD cats are living for over 5 years, significantly longer than the reported average of 3 years\(^9\)
- Their creatinine level remains stable for long periods, increases slowly but unpredictably
- Their serum phosphorus level can be controlled with phosphorus binders, remaining normal even when creatinine is over 5.0 mg/dL or 440 µmol/L
- No anemia occurs so no Rx Erythropoietin is required
- No crises occur requiring veterinary intervention as hydration is maintained
- The cats do not lose muscle mass becoming walking skeletons

Which canned food do I suggest? Whatever the cat will eat. My preference is to feed good quality grain-free canned cat foods but any canned cat food that the cat likes is fine. I do suggest that owners try to select cans with approximately 10% protein as fed.

**How much canned food is required by each cat each day?** The energy requirement of the average inactive, senior, house cat is approximately 40 kilocalories/kg/day.\(^{10}\) Canned cat food has about 1 kcal/g food as fed. Thus, a small 150 g can provides 150 kcal. Half a large 360 g can provides 180 kcal. The protein requirement of cats varies from 5-12 g/kg/day. The average, inactive, senior, house cat requires at least 5 g/kg/day to prevent loss of lean muscle mass.\(^{7,9}\) This requirement is higher in geriatric cats or in those cats who have any intestinal disorder (inflammatory bowel disease, allergies, cancer, and so on) due to decreased protein digestion and absorption. Most canned cat foods are around 10% protein as fed (9 – 11%). This results in these canned cat foods providing 1 g protein for each 10 g food as fed. That is: a 150 g can contains 15 g protein.

The average canned cat food provides: Energy 10 kcal/10 g food + Protein 1 g/10 g food

The average senior house cat requires: Energy 40 kcal/kg/day + Protein 5 g/kg/day

The average 11 lb = 5 kg senior house cat requires:

| Daily energy | 200 kcal = ¼ x 150 g can = ½ x 360g can |
| Daily protein | 25 g = ½ x 150 g can = ¼ x 360 g can |

The average 15 lb = 7 kg senior house cat requires:

| Daily energy | 280 kcal = 2 x 150 g can = ¾ x 360g can |
| Daily protein | 35 g = 2 ½ x 150 g can = 1 x 360 g can |

Many of our cats do not eat this amount of canned cat food every day because they are also consuming treats, some dry cat food and various meat scraps of fish.

**Omega 3 essential fatty acids** are beneficial for CKD cats as they reduce inflammation in the kidneys.\(^{1,3}\) Cats require the active EPA and DHA as they are unable to activate the precursors such as ALA. The dose is 100 mg/kg/day. Salmon oil capsules contain 300 mg EPA + DHA in each 1000 mg capsule. Cans of wild salmon (210 gm cans) contain approximately 3600 mg omega 3s. The average 5 kg cat requires one can per week.
Supplements for cats with CKD. I recommend supplements but advise owners that I don’t want the supplements to decrease their cat’s appetite or, if the owner has to pill their cat, I don’t want their cat angry and upset with them. Additional vitamins, anti-oxidants or herbs are beneficial but can be a challenge to get the cat to eat them voluntarily. Vitamin B12 injections monthly are given subcutaneously and are painless. They can be given by the owners at home.

For cats who are not enthusiastic about canned cat food (dry food addicts) or those who are inappetent, we need to advise their owners on how to change the food and enhance their cat’s appetite:1,4

- Change the food slowly;
- Warm the food;
- Mix in more or less water;
- Instead of water, use chicken or beef broth (salt is not a problem);
- Feed or add meat-flavoured baby food;
- Add some salmon, tuna or chicken to the food;
- Sprinkle catnip onto the food;
- Even add a few pieces of dry cat food onto the canned cat food; and/or
- Sprinkle crushed cat treats onto the canned cat food.

For the cat who will not eat what the owner and I select is best for this cat an appetite stimulant may be indicated.1,4 The two common ones are:

- Rx Mirtazapine 15 mg tablets 1/8 – ¼ tab SID
- Rx Clonazepam 0.25 mg tablets ¼ tab SID

I use Clonazepam as I find it very reliable with no medical side-effects. Initially, some cats are a little sleepy but this wears off after a few days. The dose is the amount required to achieve adequate food intake.

The acupuncture pressure point, Shan Gen or Base of Mountain, stimulates appetite. It is located slightly back from the cat’s nose in the midline. The technique is to use the tip of your index finger. starting at the top edge of the nose, gently rub back toward the cat’s eyes for 20 seconds or so. This can be repeated. Owners can be taught to do this. Then they need to evaluate its effectiveness.

Controlling serum P level, and thus parathyroid hormone (PTH) level, is very important, and is the reason for the usual recommendations to decrease the dietary protein level.1,3,4,11 Reduced P excretion by compromised kidneys results in secondary renal hyperparathyroidism. The increased parathyroid hormone (PTH) may be a renal toxin that makes the cat feel unwell and may contribute to the progression of kidney disease.

The recommended dose of P binders is often inadequate to lower P into the ideal range. We have to use as much as necessary and to mix the P binder into the cat food, for most cats. There are a variety of choices:1

- Epakitin® is powder available from Vétoquinol. This is chitosan, a natural polysaccharide from crab & shrimp shells. It traps negative ions, binding P and so preventing its
absorption. It contains some calcium carbonate but has no significant effect on either total serum calcium or ionized calcium. The dose is 1 scoop = 1 gm BID but we should dose sufficiently to reach the ideal P level. Most cats do not mind the Epakitin powder being added to their soupy canned cat food even when 2 to 3 scoops need to be added.

- Rx Aluminiun hydroxide is not considered safe: it causes constipation; binds 211 other drugs; and at higher dose levels it causes progressive RBC microcytosis and neurological signs.
- When Epakitin is not controlling the serum P level to 4.5 mg/dL = 1.5 mmol/L or less, or the cat is declining to eat food mixed with the powder, then it is time to use sevelamer hydrochloride, sold as ‘Renagel’® 800 mg tablets or lanthanum carbonate chewable tablets or powder, sold as ‘Fosrenal’®. Renagel can be crushed and mixed into food as it is tasteless. These are highly effective at reducing P levels. The dose starts at 1/8 tablet per meal, increase as required to control the serum P level.

Rx Calcitriol is activated Vitamin D3. Activation of Vitamin D3 occurs in the proximal convoluted tubules and is normal in Stages 1, 2 and 3 of CKD. If the serum ionized calcium level is normal then the cat has adequate Vit D3 activation. In the blood, calcium is bound to albumin. If the cat’s serum albumin level is normal (28—32 g/L) and the total Ca is in the top half of the normal range (2.5 – 3.0 mmol/L) then the ionized Ca level will be normal. Activation of Vitamin D3 is decreased in CKD Stage 4 (creatinine > 440 µmol/L = 5.0 mg/dL). By this time, the cat will be requiring fluid therapy by the subcutaneous route daily. Calcitriol can only be given if the serum P level is normal 4.5 mg/dL = 1.5 mmol/L or less and the owner is prepared to monitor the blood parameters every three months. Calcitriol not only activates Vitamin D3, it also increases P absorption from the intestinal tract.

What about using Rx Erythropoietin for the anemia of CKD. I find it is rarely if ever required if adequate protein is fed. I have only seen mild anaemia in my CKD cats in advanced stage 4 when the owner is discussing euthanasia due to inappetence and weight loss. Erythropoietin injections are expensive, PCV monitoring is required, and it does become ineffective in many cats due to antibody production. However, Rx Darbopoietin can be used instead. It is injected once a week along with Iron dextran. This causes very few side effects and rarely results in antibody production (which negates its activity). Start when the PCV is below 30 – 35% Darbopoietin is expensive.

Nutrition Summary: With respect to maintaining glomerular filtration rate, controlling serum P and PTH, and avoiding anemia, I recommend feeding mostly canned cat food (10% protein as fed) with water mixed in. Add a P binder as indicated by the serum P level. These cats eat well, maintain or gain weight, do not lose their muscle mass or become anemic, and they feel good. The lives for years and the owners are very happy.

Kidney potassium (K) tubular loss causing hypokalemia is very common in cats with CKD with a reported incidence of 20-30%. The specific cause is unknown; potassium is lost through the renal tubules. Hypokalemia causes decreased appetite and reduces GFR. Severe hypokalemia results in muscle weakness with head ventriflexion. The reference range for serum potassium is 3.5 - 5.0 mg/dL = mmol/L but recommended serum potassium is 4.0 - 5.0 mmol/L. My owners
have observed that their cats feel better and eat more when their cat’s K is 4.5 mg/dL = mmol/L or above.

The most important aspects of therapy are to keep the cat eating and not to reduce salt (this enhances K excretion). Potassium supplementation is at a rate of 2-6 mEq per cat per meal. Supplementation using K gluconate can be given as tablets, liquid, granules, powder or flavoured chews, either orally by the owner, mixed into the cat's food or taken voluntarily. At this time, my favourite K gluconate supplement is the powder from Summit Pharmacy – it is tasteless, and cats are readily accepting it mixed into their canned food. It is much more affordable than the delicious K chews.

Other aspects of CKD, such as hypertension, renal protein loss and hyperthyroidism will not be discussed in these notes but here is the diagnostic and therapeutic summary:

<table>
<thead>
<tr>
<th>Dx</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney excretion = GFR = Creatinine</td>
<td>IRIS Stage 2  &gt; 1.5 mg/dL</td>
</tr>
<tr>
<td>2ry Renal △ PTH — Ca &amp; P</td>
<td>P &gt; 3 mg/dL</td>
</tr>
<tr>
<td>Anemia due to ▼ protein + ▼ absorption</td>
<td>PCV &lt; 25%</td>
</tr>
<tr>
<td>Kidney K tubular loss — K</td>
<td>K &lt; 4.5 mg/dL</td>
</tr>
<tr>
<td>Hypertension — BP</td>
<td>BP &gt; 160 mm Hg</td>
</tr>
<tr>
<td>Renal protein loss — UPCR or UTI</td>
<td>Negative</td>
</tr>
<tr>
<td>Thyroid function — T4</td>
<td>T4 &gt; 3.1 mg/dL</td>
</tr>
</tbody>
</table>

**Long term management**

I encourage owners to monitor their cat’s progress by weighing their cat on a baby scale at home weekly. The cat’s weight along with the owner’s assessment of how their pet is doing and its appetite is reliable as to the status of the cat.

I recommend veterinary monitoring each CKD cat every six months or if the owner notices a problem. I monitor the usual clinical parameters of history, physical findings and body weight. If the cat does not have hypertension, proteinuria or urinary tract infection on the initial work-up, I do not repeat BP, UA or UPCR. Blood tests that I monitor are serum creatinine, K, P, Ca and T4. I also run a PCV and blood glucose (BG). The results of these tests will change my recommendations for this patient. These is efficiently measured by sending serum off to a commercial laboratory for a Kidney panel + T4 (information is available on each laboratory’s website) with the BG and PCV being done in clinic.

**Stage 3 CKD cats** may require more aggressive P binders and subcutaneous (SC) fluids. When fluids are required, I teach the owner how to administer them at home. Owners soon become proficient. I recommend a balanced electrolyte fluid SC 100 — 200 ml once a week to daily. Most cats accept this and there are remarkably few side-effects.
Summary - Cats with CKD:
Dx — Hx PE Weight CBC Chem T4 UA BP
Rx Hyperphosphatemia Hyperthyroidism Hypertension Proteinuria Hypokalemia
Keep cat eating any canned food mixed with water +/- Appetite enhancers or stimulants
Control P level to < 3 - 4.55 mg/dL = 1.0 - 1.5 mmol/L with P binder
Control K level to > 4.5 mg/dL = mmol/L with K gluconate supplement
Omega 3s as salmon or fish oil 100 mg/kg/day
Monitoring — Vet exam + blood tests every 6 mths, at least PCV, Chem, T4
Cats with CKD are unpredictable but most live many years of good quality life.

References
Objectives

- To understand the advantages and disadvantages of clients feeding raw meat diets to their dogs or cats.
- To understand the problems and risks of clients feeding raw meat diets to their pets.

Introduction

Increasing numbers of clients are feeding their dogs and cats raw meat-based diets. While raw pet foods are not suitable for most owners or all pets, some dogs and cats are healthier on these diets. Raw diets are effective in the management of some medical problems, especially gastrointestinal dysfunction. They can also resolve inappetence, obesity, and poor hair coat. Veterinarians need to inform clients about the safety issues for the family members and their pet. Every diet should be complete and balanced. The additional cost and time that feeding a raw diet involves also need to be considered. All this information must be recorded in each patient’s medical record. These topics will be discussed by Dr. Stogdale who supports many clients who feed their pets on raw meat-based diets.

In this opinion article, I discuss the approaches a veterinarian may take, and the consequences, when owners have decided, for whatever reasons, to feed their dog or cat a raw food diet, or to add raw meat to their pet’s other food, or to use as treats. A growing number of pet owners are choosing to feed raw meat-based diets (RMBDs) to their dogs and cats. In recent years, raw pet food sales have increased by at least 15% annually and approximately 15% to 25% of dogs and 10% of cats are fed some raw meat. In addition, owners often add raw eggs or meat to an occasional meal, or give dehydrated RMBD treats to their pets, usually omitting to inform their veterinarian. I will discuss the various types of raw pet foods, advantages and disadvantages of feeding raw food to dogs and cats, safety issues, and the challenges and opportunities that patients on raw diets present to veterinarians.

My priorities are always:
1. Safety for the family
2. Safety for the pet
3. That the pet is fed a complete and balanced diet
4. That we find the food on which the pet thrives
5. That the feeding plan is practical for the client, now and in the future

As no one diet suits every pet, during my nutritional consultations my pet feeding recommendations include the following options:

- Good quality commercial dog/cat food, dry and/or canned (the components vary but may include animal protein as the first ingredient, complex carbohydrates, and soluble fiber, but not include corn, wheat or soy, chemicals or artificial additives, colors, flavors, or preservatives)
- Home-prepared cooked complete and balanced diet
- Commercial raw meat complete and balanced diet
- Home-prepared raw meat complete and balanced diet
• To any of these, add some human food, often fiber as vegetables
• Any combination of these options

My recommendations depend upon an unhurried discussion with the client. Considerations include:
• What the client wants to feed
• Family situation such as pregnancy, children under the age of 5 years, any immuno-compromised family members
• Pet facial hair length (beards are difficult to clean after every meal)
• The pet’s nutritional history including which diets and foods the pet wants to eat
• Pet health conditions such as significant disease, immune-mediated disease, and current medications
• Owner financial concerns
• Client time constraints

The final decision is always made by the pet owner. As the client and I discuss their choice of their pet’s diet, I note the client’s decision, and my recommendations and safety precautions in the pet’s medical record. Then I put together a complete and balanced diet appropriate for that pet. At the end of the appointment, a copy of my notes is sent home with the owner and e-mailed to their regular veterinarian.

Types of raw diets available for dogs and cats include:
• Home-prepared RMBDs. To ensure that these diets are complete and balanced, calcium, vitamins, minerals, and taurine must be included. This advice can be obtained from a veterinary nutritional consultation by telephone or website.
• Commercial raw frozen, freeze-dried, or dehydrated meat diets that are not complete and balanced. These require the addition of a combination of bones, a vitamin and mineral mix, vegetables, and fruit.
• Commercial raw frozen complete and balanced diets with a variety of protein sources. Some are limited to one protein source, especially those using exotic meats. Freezing kills a variable percentage of different species of microorganisms.3
• Commercial freeze-dried complete and balanced diets that have been frozen under vacuum to remove nearly all moisture. Freeze-drying leaves the food nearly unchanged compared with raw frozen diets and kills a percentage of bacteria.4
• Commercial dehydrated complete and balanced diets have been heated slowly to remove nearly all the moisture. Whether the low heat has a significant effect on the nutritional quality of the food is unknown. The drying results in a reduction of microbial numbers but Salmonella and other pathogenic bacteria survive.5
• Commercial high pressure pasteurized (HPP) complete and balanced diets have been subjected to high pressure (43,500 to 87,000 psi) without heating. This process kills most bacteria including Salmonella and Listeria6 without altering nutritional quality.

Generally, raw pet diets are made from high quality food sources and aimed at the informed, discerning pet owner. They are more expensive than regular dog or cat kibble. The freeze-dried, dehydrated, and HPP foods are more costly than the raw frozen diets due to the additional processing. The costs may be substantial when feeding many cats or medium to large dogs.
Nevertheless, solving a problem with diet is better for the pet and cheaper than repeated veterinary visits and expensive medications.

**Advantages of feeding a raw meat** complete and balanced diet to dogs and cats include:

- If the owner believes that a raw diet is best for their pets, and wants to feed it, this is their choice. Some owners think that a commercial pet food is not good for their dog or cat and prefer to feed a more natural diet (minimal processing, no grain, and ingredients that they can understand). Owners feeding RMBDs report that their pet has a healthier body condition, higher energy level, shinier coat, cleaner teeth, and normal bowel movements. They believe that their pet has fewer health problems.  

- A raw diet is often considered to be the ancestral diet of pets. This is true for carnivorous cats. Several small rodents (6 to 12) a day is the ideal diet for each of our feline friends, but is impractical. However, dogs are omnivorous, carnivorous scavengers. They are physiologically adapted to eat everything: raw or cooked, meat, grain, vegetables, and rotten food, sometimes after rolling in it.

- RMBDs, as opposed to high protein cooked or extruded diets, are more biochemically complex with bioactive compounds. Raw diets are higher in antioxidants such as vitamin C, vitamin E, and some flavonoids. These may have some matrix effects and synergy that are beneficial to health. Heating food results in cooking toxins such as acrylamides and nitrosamines. These cause oxidative stress and are carcinogens. The effects of these compounds, interactions, or changes on the health of pets have not been studied.

- RMBDs may result in improved immune function. As 70% to 80% of each animal’s immune system is located within the intestinal tract wall, it is not surprising that food has a major influence on immunity, and therefore on disease predilection. However, direct health benefits have not been shown.

- My observations suggest that most dogs and cats fed RMBDs have a good, healthy body condition; they are not overweight. This may be due to twice daily, portion feeding, or to the high protein, low carbohydrate content. The cost of the diet may be a factor as the food is too expensive for overfeeding. In addition, these owners usually give their dogs limited numbers of good quality treats, such as dehydrated meat pieces.

In my experience, commercial or home-prepared raw diets can be medical problem solving for dogs and cats that have developed **food allergies**, especially to common meats such as chicken and beef. These allergies usually manifest as vomiting and/or diarrhea (including soft stool), recurrent ear infections, and/or excessive scratching or licking. Most commercial raw pet food limited ingredient diets (LID) are made in the company’s own grinding and mixing machines, and are generally not cross contaminated with other proteins. They are usually grain-free. The presence of bioactive peptides and antioxidants in RMBDs may contribute to the response. Solving the food allergy problem by feeding a non-allergic food and treats is obviously the best approach, especially as these patients are corticoid resistant.

In some cats, diarrhea, intestinal discomfort, and/or flatulence can be caused by dietary carbohydrates. This is due to the feline carnivorous alimentary system being relatively short in length and transit time, along with limited capacity for starch digestion and monosaccharide absorption. Sugars that are not digested provide nutrients for microbial fermentation in the colon, increasing colonic acid. In cats which have developed diabetes, diets high in protein and very
low in carbohydrates can be disease reversing or, at least, stabilizing. Feline RMBDs are typically higher in protein and lower in carbohydrate than most other cat diets.

This author could find no peer-reviewed articles that showed significant medical benefits from feeding RMBDs. There are many non-peer reviewed articles that suggest benefits to pets with food allergies, atopy, gastrointestinal disorders, idiopathic epilepsy, and cancer. However objective controlled studies are required.

In my experience, some dogs just “do better” on RMBDs. They are more active, lose excessive weight, have nicer breath, shiny coats, and normal feces. There is no good objective evidence that these diets improve the quality of the lives of dogs, or reduce the incidence of problems, but many pet owners firmly believe this to be so. It is very convincing in an individual patient when a food change makes a significant difference to the pet’s health and well-being, in the absence of other changes or medications at the time. In these cases, the patient is its own control, and the owner and the veterinarian can be delighted and thankful.

Disadvantages of feeding a raw meat, complete and balanced diet to dogs and cats include:
• Concerns over whether the diet is complete and balanced according to the Association of American Feed Control Officials (AAFCO) Dog or Cat Food Nutrient Profiles, especially with small companies which use only whole food ingredients, avoiding synthetic nutrient supplements. It is difficult to get all the vitamins and minerals from natural ingredients into muscle-based food in an economical combination. Vitamins and minerals usually must be added to a diet of meat and vegetables, and the calcium to phosphorus ratio needs to be approximately 1:1. Only a few raw pet food manufacturers have done the feeding trials to achieve AAFCO certification.
  • Concerns over cost.
  • Concerns over time. Most RMDBs require more time than simply feeding dry pet food.
  • Not all pets tolerate raw diets, even with some vegetables added.
  • Concerns over safety.

Safety issues associated with feeding RMBDs to dogs and cats. Most dogs and cats handle the bacteria in raw ground meat most of the time due to the consistent acidity of their stomach fluid. Occasionally, a dog fed raw meat does develop diarrhea from its food, but more commonly enteritis occurs due to dietary indiscretion.

Raw food is not appropriate for any dog or cat whose immune system is suppressed because of significant disease or immune suppressant medications. Pets with severe disease such as moderately advanced heart, kidney, or liver dysfunction, diabetes, or cancer should not be fed a raw diet that may contain pathogenic bacteria. If the owner wants to feed a high protein diet for diabetes or cancer, for instance, some raw diets may be cooked and vitamins added just before feeding, or an HPP product could be fed.

Safety for the owners. Meat (especially ground meat) and eggs for animal or human consumption carry microorganisms. Raw pet food poses similar risks for pathogenic bacteria as do raw meat and eggs for humans. Freezing, freeze-drying, or dehydration results in a reduction in bacterial counts but viable pathogenic bacteria survive. This is of real concern if
the household includes, or is planning, pregnancy, children under 5 y of age, the elderly, or any person who is immuno-suppressed. Information about safe meat handling is readily available from several sources. When safety is a concern for the owner, the family, or the pet, but a RMBD is preferred, an HPP food can be recommended.

In my many years of experience, I have found that most owners who feed raw commercial or home-prepared diets are informed and safety conscious. They practice safe food handling, dispose of their pets’ feces with care, and wash their hands frequently. Everyone needs to practice personal, pet, food (for humans and animals) and fecal sanitary habits due to the numerous recalls of human and pet foods because of bacterial contamination; and the fact that some healthy humans, dogs, and cats excrete Salmonella and other pathogens in their feces. With respect to zoonotic transmission of intestinal pathogens, numbers matter. The keys to understanding are 2 perceptive phrases: “The solution to pollution is dilution” and “size (in numbers) matters.” Therefore, washing with water, and a little soap, is usually effective, and is so widely recommended by public health experts.

Veterinarians do need to discuss both the possible benefits for the pet and the risks to the family’s animals and humans inherent in feeding RMBDs and record their advice in the pet’s medical record.

**Veterinary concerns and opportunities with clients feeding raw diets to their pets.**

Dog and cat patients fed raw diets raise some concerns for veterinarians:

- Safety for ourselves and our staff is the same as for our clients. We must assume that all pets can be carriers of zoonotic microorganisms. Veterinarians and staff must engage in hygienic practices at all times.
- Our responsibility to advise our clients about safety, and potential problems for our patients. As we inform our clients about the risks of feeding RMBDs we need to record our recommendations and advice in the patient’s medical record.
- Various veterinary associations have issued position statements discouraging the use of RMBDs including the CVMA, AVMA, WSAVA, and AAHA. The CVMA and the BSAVA recommend that veterinarians advise owners who feed RMBDs to ensure that “hygiene measures are in place to minimize the risk of the transmission of communicable disease.”

As a veterinary specialist, I decide which therapies and pet management approaches I discuss with my clients, and:

- Recommend a specific diet (e.g., LID diet, C&B pet food)
- Recommend medication use that is off-label (e.g., albendazole, allopurinol, amlodipine, apomorphine, atenolol, and so on)
- Advise owners who choose a strategy that I am unenthusiastic about
- Refer the client to a colleague (e.g., for physiotherapy or acupuncture)
- Disagree with but still support the client and the patient (e.g., owner declines rabies vaccination).
And in every case, I record my advice and the owner’s decision in the pet’s medical record, a copy of which is provided to the owner. I work with my clients so they have the best information for their decisions about the care of their pets.

**Challenges and opportunities that patients on raw diets present to veterinarians.**
A surprising number of veterinary canine (15% to 25%) and feline (10%) patients are being fed RMBDs, and/or are being given raw meat, eggs, or treats in addition to their regular food.\(^2,15\) Clients have learned not to inform their veterinarian (and all too often veterinarians do not take a thorough dietary history).\(^27\) Pet owners who choose to feed RMBDs have lower levels of trust in veterinary advice in general, as well as with respect to nutritional recommendations.\(^27\) These clients present opportunities for veterinarians, supportive and knowledgeable about the advantages and disadvantages of RMBDs, to provide veterinary services and advice to these generally well-informed and conscientious pet owners.

Clients who find that their veterinarian is only negative about RMBDs:
- Often omit or obfuscate what they are feeding their pet
- Consider their veterinarian poorly informed about the best nutrition for their pet
- May believe their veterinarian only cares about selling veterinary pet food and making money
- May complain to their friends, in person and on social media, about their veterinarian
- Distrust their veterinarian’s advice about both medical and nutritional issues, ignoring or questioning veterinary medical recommendations
- Take their pet veterinary needs elsewhere\(^27\)

This is bad medicine and poor business for these veterinarians. This negative attitude generates business for those practitioners who are informed about RMBDs. And these veterinarians are already very busy. I find that being supportive of RMBDs gives me credibility when I advise clients against feeding raw food for any of the reasons discussed.

**In summary,** some of the best informed and conscientious clients are feeding their dogs and cats RMBDs. While raw pet foods are not suitable for most owners or all pets, some dogs and cats are healthier on these diets. Raw diets are effective in the management of some medical problems, especially gastrointestinal dysfunction. They can also resolve inappetence, obesity, and poor hair coat. Veterinarians should inform clients about the safety issues for the family members and the pet. Every pet diet should be complete and balanced. The additional cost and time that feeding a raw diet involves also need to be considered. All this information must be recorded in each patient’s medical record. In veterinary practices, thorough cleaning and disinfection with regard to pathogenic microorganisms is already carried out in our handling of all our patients and their elimination products. Nutrition and exercise are essential considerations as we strive to optimize the quantity and quality of each pet’s life for the enjoyment of their family.

**References**


Performing Clinical Studies in Holistic Practice
Lea Stogdale, DVM, Diplomate ACVIM Small Animals

Objectives
- To discuss the challenges, rewards and imperatives of doing evidence-based studies of holistic medicinal practices.
- To give some guidelines for performing retrospective or prospective studies in holistic veterinary practice.

Introduction
Holistic or integrative or complementary veterinary medicine uses modalities and natural compounds that conventional or scientific practice has not validated. The same lack of evidence affects many procedures and medications used in conventional medical and veterinary practice. However, holistic medicine is often criticized for the lack of scientifically valid studies. Doing either a retrospective or prospective clinical study while working and leading a balanced lifestyle has its challenges, but can be done with planning and an adequate time span. Performing and analyzing a clinical study is personally educational and gratifying. Such statistically valid studies are essential information for the benefit of our patients, and for increased approval by our colleagues and by our professional and licensing associations.

Why would you spend your time, effort and fragile ego on doing a clinical study while you are busy working as a holistic veterinarian? You also have frenetic personal life, and you are trying to balance all your activities. First, you passionately believe that a number of your approaches to your patients are different and better than conventional veterinary medicine. This may be in diagnosis or therapy, in nutrition or pet handling, or in communication or attitude. You really want to prove that your approach is more effective, and you want to inform all your colleagues. Second, you want to educate yourself in objective assessment, the relevant literature, recording, writing, statistics, and the review and publication process. Third, you are up for the challenge of being proven wrong. If you prove that your thesis is incorrect, are you willing to change your mind and approach? If not, you and your patients and clients, your priorities, will not benefit. And fourth, you may like to give some lectures at holistic or state or national veterinary conferences.

Performing and publishing a well-researched, conducted and written clinical trial is challenging, energizing and enormously satisfying. It can re-awaken the practitioner’s excitement in their daily clinical work and in their professional choice. It also enhances the practitioner’s ability to critically and objectively evaluate all diagnostic and therapeutic approaches, literature from food and drug companies, textbooks, and all articles and lectures. It improves your scientific literacy. This makes daily practice more interesting, and benefits the patients and clients – our priorities.

The credibility gap of holistic veterinary medicine. Conventional medicine and veterinary medicine have credibility within their professions and with the general public because of the university training, and society’s belief in the scientific method. This is despite large amounts of received knowledge lacking adequate evidence. In family practice, a recent study determined that only 18% of recommendations were based on high quality evidence.1 In veterinary small animal medicine even fewer articles are high quality evidence based.2,3 In holistic medicine – well, we
really don’t want to talk about it. In veterinary medicine, including veterinary holistic medicine, there are depressingly few articles published that are statistically significant, double blind, randomized, conflict of interest free (not industry funded) trials with clinically important outcomes (quality or quantity of life).³

If we want our national or state veterinary medical associations to respect holistic veterinary medicine, we need to publish evidence based studies in respected peer reviewed journals. We need to ask clinical questions which generate answers that affect the patient’s quality of life, the patient’s quantity of life, and the client’s quality of life. All objective. By writing about holistic veterinary medicine in the language of conventional scientific articles, and by publishing in their journals, holistic veterinary medicine can become an accepted aspect of veterinary medicine. It will be viewed as an area worthy of study, and it will become easier for holistic veterinary research to receive grant money.

**Evidence-based medicine** (EBM) “integrates clinical experience and patient values with the best available research information” including high quality clinical research, systematic reviews and meta-analyses.⁴ There are few meta-analyses in veterinary medicine because there are relatively few statistically significant studies to select.³ Medical evidence is classified into 4 categories based on the level of bias (randomization, conflict of interest, confounding factors, objective outcome and so on) with 1 being the least biased and 4 being least reliable (simplified):⁴,⁵

1. Evidences obtained by meta-analysis of several randomized, controlled trials (RCT).
2. Evidences from well-designed RCT; prospective double-blind, placebo-controlled trial in the same species or retrospective cohort study or case-control study, with sufficient patient numbers for statistical significance.
3. Evidences from non-experimental studies such as comparative research, case controlled study, or study using historical controls.
4. Evidences from experts, editorials, consensus reports, textbooks, clinical practice, patient testimonials, and research in non-target species or in vitro.

Consider which of these is the most commonly cited evidence for holistic modalities—Level 4. In allopathic veterinary medicine, most evidence is Level 3 or 4. Level 2 evidence from well-designed controlled RCTs are much needed in veterinary medicine, and are especially required for holistic and alternative approaches to be accepted by the general profession.⁶ At least we should be aiming at Level 3 evidence for our complementary therapies.

Two examples of well planned, conducted and written clinical trials of complementary therapies, published in peer-reviewed scientific veterinary journals, serve as useful examples. They are open access and available online: “Efficacy of a single-formula acupuncture treatment for horses with palmer heel pain” by KA Robinson, ST Manning in the Canadian Veterinary Journal, 2015;56:1257-1260. “Effect of a probiotic on prevention of diarrhea and *Clostridium difficile* and *Clostridium perfringens* shedding in foals” by A Schoster, RH Staempli, M Abrahams, et al in the Journal of Veterinary Internal Medicine 2015;29:925-931.

**Patient-based evidence** (as opposed to EBM) occurs when a particular therapeutic approach makes this patient improve. In practice, this is our priority, however, by its very nature, it is often
subjective and could be caused by chance or variability in the problem. To prove objectively that it is this therapy that is resulting in the improvement, you have to stop the treatment and see if the patient’s problem recurs. And who wants to do that in the real world of practice? Not the veterinarian or the owner. For example, who wants to alter what the dog or cat is eating when you have found the food that has stopped the vomiting and/or diarrhea? Who is willing to ask owners to stop the therapy that has solved the dog’s urinary incontinence or the cat’s constipation or the horse’s lameness? In order to produce more than a case report, you require many such patients, and the outcomes need to be compared with the historical results of the standard, conventional therapy.

You decide that you want to study, analyze and publish your diagnostic or therapeutic approach to a veterinary medical problem. You are passionate about the positive results from the complementary modality that you use. You balance your professional and personal commitments to allow some time each week to work on your research project. What do you require?

- Passion, commitment and time over the long term, 2 – 3 years;
- If this is a retrospective study, computerized, searchable medical records;
- If this is a prospective study, excellent record keeping;
- Attention to detail (maybe a degree of Obsessive Compulsive Disorder / Personality);
- Critical review of all factors affecting your approach; and
- Realization that your thesis may be incorrect demanding your re-assessment;
  - or that you may never complete your project because life happens;
  - or perhaps failure to get published, but you will learn a great deal.

**Types of studies:** Case reports – interesting but not on the professional credibility radar.

- Case report series or cohort study – a sufficient number of cases are required to reach statistical significance despite confounding factors, with an objective outcome, compared with well reported historical data.
- Diagnostic differences to published data with outcome consequences
- Therapeutic differences with outcome consequences
- Other

A useful, clear and concise reference for selecting and planning clinical studies is the Royal College of Veterinary Science website: RCVS Knowledge. Evidence-Based Veterinary Medicine. EBVM toolkit. [http://knowledge.rcvs.org.uk/evidence-based-veterinary-medicine/ebvm-toolkit/](http://knowledge.rcvs.org.uk/evidence-based-veterinary-medicine/ebvm-toolkit/) Under their heading: “3. Critically appraising the evidence for validity” are useful check lists for appraising studies (Toolkits 3, 4 and 5) and for conducting studies such as a “Controlled trial checklist” (Toolkit 6), “Cross sectional study checklist” (Toolkit 7), “Case control checklist” (Toolkit 8), “Cohort study checklist” (Toolkit 9), “Systematic review checklist” (Toolkit 10) and “Qualitative study checklist (Toolkit 11).

If you are able to do a randomized trial, then the guidelines for reporting are published by the Consolidated Standards of Reporting Trials, CONSORT, “which is an evidence-based, minimum set of recommendations for reporting randomized trials. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 25-item checklist and a flow diagram.” It is available at: [http://www.consort-statement.org/](http://www.consort-statement.org/) One study of
Choose one topic and then narrow it to one aspect. The first step to performing and publishing an objective holistic study is to choose one of the areas about which you are passionate, experienced and successful. You may want to list three to six topics. Then you can gradually determine which one you will document in a practice survey or trial, and describe in a journal article. Choose one topic then re-assess: Is it too complex with too much data that interacts? Will it involve complex statistics? Or does it lack an objective, measurable outcome? Then select one only aspect that is quite specific and objectively measurable. For example, my thesis is that my approach to chronic kidney disease and hyperthyroidism in cats results in better quality of life and longer life spans for my patients. I defined the different aspects of this topic:

- Monitoring creatinine levels for IRIS staging
- Not reducing protein levels in the cats’ food
- Controlling phosphorus levels to IRIS values
- Maintaining food and fluid intake including with appetite stimulants
- Maintaining potassium levels in my normal range, ie. above minimal reference intervals
- Controlling total thyroxine (tT4) levels in my normal range, ie. below minimal reference intervals.

I could compare my patient’s longevity with historically reported data, and I may do so in the future. However, at this time I decided upon: Total Thyroxine Reference Intervals for Diagnosing Hyperthyroidism in Cats: Retrospective Study. This is currently “a work in progress,” and may, or not, be published.

Your choice of trial subject needs to have a specific, measurable diagnosis that has one therapeutic approach and a minimum of confounding factors. This means that if you are postulating that a single modality such as a Chinese herbal formula works for a specific disease problem, you are not also using diet change, acupuncture, homeopathy and other variables whenever you treat this problem. A published example studied whether Chinese rhubarb affected the progression of chronic kidney disease in cats; it did not. If you have a specific treatment protocol which includes a number of different modalities, the whole treatment protocol is what you report, not just one part of it. And that treatment protocol should be the same for all patients with that specific disease which are included in your study. And there needs to be historically reported data for you to compare your results.

Apply the S.M.A.R.T. evaluation to your topic: Specific, Measurable; Achievable, Relevant, Timely. And don’t forget that you need adequate patient numbers for statistical significance.

Write your hypothesis. This should be one to two sentences; an elevator pitch. For example: Background: Most veterinarians use total thyroxine (tT4) to diagnose hyperthyroidism in cats as other tests are unavailable due to cost, convenience, unfamiliarity or geography.

Hypothesis: That each patient’s own laboratory test values, when the pet is clinically normal, are the best indicator of that animal’s normal levels. For cats, their senior tT4 levels, while the cat is clinically normal, are more accurate than the commonly cited reference intervals.
Having written your hypothesis, ask yourself these preliminary questions into the feasibility of you doing this clinical study:

- Do you really want to spend your time, long term, immersed in this topic?
- Do you have the time and the energy? Child or parental care; TV; thirst for new information;
- Are you able to search your medical records for a retrospective study? Do a trial run using your key words. Or are you able to keep consistent, reliable records for a prospective study?
- Do you have sufficient numbers of cases to statistically validate, or refute, your thesis?
- Is this study adding to or challenging the veterinary literature? Check a recent textbook, for example, Textbook of Veterinary Internal Medicine. 8th ed. 2017.
- Will you need to work with another person? Who? Colleague, specialist, resident, clinical pathologist, statistician, other. If so, you will need to agree on your approach, on who does what, timelines, etc.

Again, you need to decide that this is a priority for you with respect to your time and interests.

Initial research and plans

Where to publish? Obviously I would like to recommend JAHVMA. However, if holistic veterinary medicine is to be respected it needs to be published in a profession-wide respected, peer reviewed journal such as JAVIM, JAVMA, JAAHA, CVJ or the Veterinary Record. Decide on your first choice, and always have a “Plan B,” so then decide on your second and third choices. Obtain sample articles similar to your study for each journal. Go to that journal’s website and download their “Instructions to Authors.” This gives you the nuts and bolts for sections, subsections, format and references, usually in exquisite detail. Follow the details.

As you refine your topic and do your literature research, start writing the article. Yes, really. This will save you an enormous amount of time, frustration and writer’s block later on. Also, as you think of some comment or another sub-topic that you may want to include in your article, add it to the appropriate section. You can always, rewrite, alter or delete it later. Double space.

List the article sections: Title, author, address details, conflict of interest
Abstract; Abbreviations; Introduction (with subheadings)
Method; Results; Discussion (with subheadings)
Graphs; photo images; diagrams; footnotes; References

Label your subsections as you think of them or come across them in your literature search. This helps you easily find your information when you want to add to it. Later, you can remove those subheadings that you do not need, or that are not used by your chosen journal.

Before you put too much time into your research project, do a literature search. Check your own reference files, and find the current edition of the most comprehensive, respected, relevant textbook. This is your baseline data information. You may or may not use and reference this source; peer reviewed journals don’t like textbooks being used as references. They prefer you to use the original publications. Search PubMed for your key words. Use chemical or botanical
names, and species name such as “canine” to produce the most relevant articles. If you only have access to the abstracts, how important are they? Copy and save the abstract or make a list for later use. Can you access their complete content at your local university library or through your nearest veterinary college? As you do your literature search, make notes under various subheadings, especially for the introduction and discussion. Always include the reference source.

Decide on your inclusion and exclusion criteria – this is very important. These criteria may change once you start examining and collecting individual patient data, but your criteria must be applied to all patients. Defining exclusion criteria can be quite difficult and are subject to researcher bias. Be clear. For example, define non-compliant owner and/or patient, or lost to your minimal time of follow-up, or comorbidities. If you do need to change the criteria, especially exclusions, you may need to re-start your patient record search or your patient record keeping.

Confounding factors are the bane of clinical trials. They are often the deal breaker that results in trials either not being conducted, or not being statistically significant or peer accepted. As holistic veterinarians, we know that nutrition is intrinsically associated with the animal’s health and disease problems, and that herbs have many beneficial effects. All veterinarians know that the body condition and exercise level affect each pet’s health, wellbeing and the outcomes of numerous diseases. We also know that diseases progress over time, many wax and wane. These most common confounding factors (food, treats, chews; herbal or other supplements; body condition as assessed by the same veterinarian; exercise level as recorded by the owner; and time) as well as other changes that owners make without consulting us, or even informing us, must always be considered, recorded and taken into consideration when assessing and reporting the results of clinical trials. For example, approximately one third of epileptic dogs responded to a placebo, as reported in a small meta-analysis.10

Confounding parameters do not negate doing a clinical trial but the principal researcher must take them into account when making the plan, otherwise the trial will be meaningless. As an example, if you were going to study whether a phosphate binding powder added to the food of patients with chronic kidney disease is effective in lowering the serum phosphorus level to that recommended by the International Renal Interest Society (IRIS), you would need to:

- Enact those food and supplement changes that you usually recommend (confounding factors),
- After 2 – 4 weeks, repeat the serum phosphorus level and any other relevant parameters,
- Have the owner add the phosphorus binder into each meal,
- After 2 – 4 weeks, repeat the serum phosphorus level and any other relevant tests.

Waiting 6 months is a problem as the patient may have changed its food preference, the owner may no longer be adding the correct amount of powder (compliance issues), and/or the kidney function may have changed (confounding factors).

The same considerations affect every prospective clinical trial and are what make retrospective studies of therapies so problematic to interpret.

Be wary of choosing a condition that varies over time. These conditions are very difficult to study objectively, and trials must include hundreds of patients over many years, and have a clear
benefit. These trials are open to challenge: correctly. Approaches to multiple sclerosis in people are a prime example. In our dogs and cats, arthritis can be variable, affected by numerous factors, so too are behavioral problems, anal gland impaction and chronic pain. And always, tincture of time must be taken into consideration.

**Recording patient data.** Medical diagnoses and therapeutic responses are not simple or clear cut. If they were this type of study would be simple. I suggest you use a spreadsheet table, such as Excel, with one line or several for each patient:

- This allows you to add columns anywhere in the table as you need them;
- You can delete columns that become redundant; or change the order of the columns;
- You can add lines, or move them around; and there are an unlimited number of lines;
- You can record each group and your patient exclusions on another ‘sheet;’
- You can change the order of the sheets and rename each sheet.

**In a retrospective study,** now you can start on the BIG JOB of going through your computerized, individual patient records that include your key words. You will need to go back at least 5 year, but possibly 10-20 years. If this is not a BIG JOB, then you probably don’t have enough patients to produce a worthwhile article. Diagnostic criteria need to be defined from at least 100 patients. Therapeutic efficacy needs to be compared with either the standard historical approach or placebo in at least 20 patients in each group, and preferably over 50 in each group. Six cases, uncontrolled, does NOT prove that a therapy is effective, and is within the category of case reports – the lowest level of scientific medical evidence, and subject to chance. When you are recording data, do include the patient medical record identifier, just in case you need to revisit any specific patient records for clarification or additional information. You don’t want to have to search all your records again.

**In a prospective study,** set up a system that works for you, enabling you to identify patients to be included, and for all the relevant information to be collected – now or in the future. Prospective studies may require 3–5 years before you have sufficient data for the results to be significant. Don’t be put off by the time-line. Yours will be the only study, and without your work we will not have evidence of effectiveness or lack thereof. We need to know.

**Making progress.** There will be periods of time when you are too busy to pay attention to your research project, due to practice demands, personal issues, social joys or illness. And that is okay. But then back to a few patient files or a reference article on most days. Every few files eventually results in a completed project. **Review your thesis,** your patient numbers and outcomes. Does your thesis hold up to this objective scrutiny? Do you have sufficient numbers for statistical significance? Talk to colleagues, rewrite, edit. And all of a sudden, the various piles of paper decrease, and its time to do the statistical analysis and look at the results objectively.

**The statistics** often scare clinicians away from such projects. Mostly, the statistics required are quite straightforward, such as standard deviation and confidence intervals with p values, even t-tests or null hypothesis or analysis of variance. We should all understand these concepts in order to objectively access published articles. There are a number of books and articles available that explain simple to medium level statistical analyses.
Statistics are a numerical way to measure the question: is there a difference between treatment A and therapy B? Because it is based on numbers, the answer must be couched in numbers.9 Tracking results such as “improved” or “less lame” or “feels better” is not enough when doing a statistical analysis. The answer should include a number – such as “how much improved, on a scale of 0 to 5?” And the scale should be constructed so that it is easily defined.3 The actual calculations are performed by inputting your data into a computer program. The latter are available online, from an engineering or math savvy friend, or from your university.

Once you have collected and analyzed your patient data, performed the statistical analysis and completed writing your article, you are not quite finished. Put the article aside for a week or two and then re-read, correct and edit. Have a colleague critique your work. Ask a veterinarian who has published in the major veterinary journals to critique your effort. Check that your reference numbers in the text refer to the correct article in your reference list. At least one of the journal reviewers will check your references. Make sure your article is formatted exactly for the journal to which you will be submitting. Then submit your precious effort to your first choice journal. If your work is valid the editor will want to work with you to get the best possible product published – that is the editor’s job. If your article is rejected, take it personally, for one week only, and then, using the reasons given, move on, improve your work, and submit it to the next journal on your list. Don’t forget to format it to the next journal’s requirements.

You are published. Congratulations. Now you can get on with your life, plan your next project, and apply to present a lecture at the next AHVMA conference. You have increased our objective knowledge of the holistic approach, and improved the respect awarded to complementary medicine by the general veterinary profession. What is most important, you have improved the care of our patients.

References
Biofield, Water, and Cell Biology – A Paradigm Shift in Medicine
Odette Suter, DVM, CVA, CVSMT, COT, MA

Objectives
- To learn about the latest findings on the mystery of water and biofields.
- To gain new insights from biophysics regarding the interaction of the animal’s biofield with the 4th phase of water and cell function.

Introduction
The discoveries in the areas of biofields and water are turning some more commonly accepted concepts upside down and propose an entirely new paradigm on how the body functions and interacts with the environment. They also shine a different light on interconnectedness of everything.

In this lecture, we will explore an emerging paradigm shift in medicine from a biochemical view to a biophysical and energetic exploration of life and health and its implications for our animal patients and the way we practice medicine.

The Crude Art of Medicine
“What the Bleep Do We Know?”
My observation as a practicing veterinarian is that we use a rather crude and somewhat haphazard approach to healing based on a finite knowledge of an enormously complex body that is influenced by a seemingly infinite number of factors. Surprisingly, some of what we offer our patients results in a positive outcome. Yet, if we are honest with ourselves, do we really know what we’re doing and what truly occurs in our patients? What really created the change? Is it simply time or a “higher force” that allowed the body to heal? Is it our intention or was it the therapeutic agents that did the trick? My guess is that we’ll never know for sure, but that’s what keeps life interesting.

Science and Water
Even though water covers 2/3 of our planet and makes up 2/3 of an animal’s body, it is poorly understood and mostly remains a mystery.

The very thing that allows us to live and thrive has been shunned by many researchers due to early flops in science that have led to discreditation of scientists (Water Memory Debacle and Polywater Debacle).¹ The mystical state surrounding water as well as the assumption that everything about water is already known has further pushed the subject into the fringe science category shared with UFO’s and subtle energies.

Scientists and pioneers such as Gerald Pollack, PhD and Drs. Emoto and Montagnier among many others have bravely tackled the challenge to explore the “unknown” and expand our view and understanding of water and all the “wonders” it offers, though leaving us with more questions than answers.

Water Mysteries
“Discovery consists of seeing what everybody has seen and thinking what nobody has thought.”
Here are just a few such water mysteries that have researchers scratching their heads:

- How does adding water to sand make the sand cornels stick together? After all, water is not a glue.
- Why does ice float while every other substance sinks in its solid state?
- What draws water to flow all the way to the top of a 30-foot tree?
- Knowing that concrete is hard, how does a little plant crack through it?
- Why don’t we find a puddle of water on the floor after a penetrating injury?

What’s New?
The molecule of water has been extensively explored, yet its social behavior with others of its kind as well as other molecules is what modern science is trying to uncover.

Gerald Pollack, PhD and his team have discovered a 4th phase of water that takes on a consistency more akin to gelatinous egg white. This gel is known by many names including gel phase, colloidal phase, structured and ordered water. Pollack termed it Exclusion Zone (EZ) water because it excludes most solutes as a result of the tight molecular arrangement.

A Little Bit of Physics to Understand EZ water
Just like making Jell-O, EZ water builds when water molecules come in contact with a hydrophilic surface (gelatin for Jell-O). Adding radiant energy – or heat in the case of Jell-O – unfolds proteins in the hydrophilic surface to allow water molecules to bond and start the process of reordering and building EZ water’s honeycomb-like sheets that grow into the remaining “bulk” water.

Because EZ water is H$_3$O$_2$ instead of H$_2$O, it is negatively charged. The cleaved off leftover H$^+$ ions combine with adjacent H$_2$O to form positively charged hydronium (H$_3$O$^+$) molecules. These moving superconducting protons are thought to be responsible for fast intercommunication within the body, possibly associated with acupuncture meridians.

The result of the charge separation with the negatively charged EZ water layer adjacent to positively charged bulk water enables it to perform like a battery and drive cellular processes.

Because the EZ water layer contains a significantly higher number of moving electrons than regular water, its conductivity is 100,000 times higher than that of water.

This of course has implications with regard to signal transmission within the body. One explanation of how local anesthetics work is through destroying EZ water, which results in interruption of signal conduction within neurons.

EZ’s Fundamental Properties
EZ water contains an infinite number of binding sites for all sorts of chemicals including hormones and other biologically important molecules as well as those that impair cell function (toxins). Emotions and thoughts are also believed to affect intracellular EZ water structure.
All subtle changes in EZ configuration are translated into a specific action by the cell. For example, if blood glucose levels increase, that glucose affects the intracellular gel of pancreatic beta cells. The resulting small change of the gel structure facilitates the unfolding of the DNA sequence that codes for insulin. And voila… insulin is made.

According to Mae-wan Ho’s research, there is a structural lineup present over vast regions of the body by means of water. Thus, a small change of EZ configuration in a cell can create a far-reaching instantaneous change.¹²

Overall, EZ water differs from regular water in many ways including light wave length absorption, viscosity, infrared absorption and emission and pH. As such, it hardly resembles liquid water.¹³

**EZ Water in The Cells**

Nuclear resonance imaging shows that healthy cells contain a crystallographic or “structured” cytoplasm, whereas unhealthy cytoplasms show more of a disordered, random arrangement of hydrogen and oxygen that resembles lower energy bulk water.¹⁴

An unhealthy cytoplasm can affect:

- **Bodily functions** including energy level, nutrient absorption, inflammation, mood, etc.
- **Spatial orientation of cells** due to mostly negatively charged cytosol and resulting repelling forces between cells that dictate tissue organization.
- **Protein folding** which is optimal in healthy EZ cytosol and results in misfolding and pathology in its absence (dementia, cataract, amyloidosis, prions).¹⁵

**Biofield**

We have all experienced the unexplainable such as knowing exactly who is at the other end of the line when our phone rang or our animal companions announcing the return of a family member even though there are no physically perceivable sign of them yet. Many of us also use applied kinesiology to access the ‘intelligence’ of our patient’s body. Energy therapies such as PEMF, “laying-on-of hands,” homeopathy and acupuncture present other examples of the mysterious. To take it a step further, how does radiating love help an animal relax and bring a smile to their faces?

As much as I enjoy the unknown and the mystery, there is emerging research available to help explain some of these phenomena.

Biofield physiology is one of them and isn’t new. In fact, many spiritual and medical traditions explain the function of the body based on energy and the flow or lack of flow of energy. Through the study of biofields we can find explanations for these mysterious wonders from a more scientific vantage point.

Biofields are defined as biologically generated fields such as can be measured through electroencephalography (EEG) and electrocardiography (ECG). The term was first coined by a committee assembled by the National Institutes of Health (NIH) Office of Alternative Medicine.
in the early 1990s to describe “a massless field, not necessarily electromagnetic, that surrounds and permeates living bodies and affects the body.”¹⁶

Biofield physiology encompasses electromagnetic, biophotonic, and other types of energy fields that result from physiological processes within the body as part of self-regulation and organization. In other words, biofields allow communication of cells from one end of the body to work in harmony with cells on the opposite end, not unlike a well-rehearsed orchestra producing exquisite music.¹⁷

Since biochemistry is unable to provide insights in this regard, we can draw on biofield and quantum theory for explanations on how instantaneous change can occur in a surrogate’s muscle tone when using applied kinesiology for example.

**EZ Water and Biofields – Connecting Physics with Quantum Theory**

Of course, a lot of the internal communication can be viewed and explained via biochemical processes such as the production and release of neurotransmitters. However, the speed of nerve conduction for example is much slower than that of electromagnetic wave propagation, which can occur at up to 50-99% of the speed of light (3x10⁸ m/s) compared to 120 m/s within nerves.¹⁸ Again, using the example of applied kinesiology, there is an instantaneous response to placing a substance into an animal’s biofield. Thus, the research on biofields comes in handy with regard to explaining the “mysterious.”

Biofields affect or influence the body through phenomena involving resonance and impedance matching.¹⁷ Three categories of biofield receptor have been examined: molecular-level receptors, charge flux sites and endogenously generated electric or electromagnetic fields.¹⁹,²⁰

Fascia, which connects all parts of the body as a continuous network, has also been implicated as a receptor system for endogenous and exogenous biofields.²¹ Transmembrane bridging molecules called integrins connect the loose extracellular network with the interior of the cells.²²

Because EZ water lines this network, it is speculated that signaling occurs through EZ water generated protons whose rapid movement is a way of energy transmission.

Quantum coherence of water molecules is another theory to explain creation and effects of biofields on an organism. Magnetic resonance imaging for example uses this concept to gain information on the state of health of cells.²³ This further solidifies that even very weak, nonionizing EMFs have biological effects.

**The Future of Medicine**

This newer knowledge deepens the understanding as well as opens doors to finding and utilizing therapeutic options that our cat friends for instance may deem acceptable as compared to the ‘poisonous’ concoctions we try to infuse into their mouths in the name of healing. It may also provide ways of addressing pathology in more elegant and all-encompassing (holistic) ways rather than being at the mercy of guessing what any given body is missing.
A focus on using external biofields and “re-aligning” endogenous fields may end up simplifying treatment of a very complex organism. Instead of focusing on individual trees, we may be able to take a step back even further and see a bigger forest. Even though this is the premise of holistic medicine, it is nevertheless not an easy feat when presented with a sick animal. Thus, healing may become much simpler, more elegant and less invasive for our animal friends with the aid of emerging technologies.

References
An Integrative Approach to Pain  
Susan O Wagner, DVM, MS, ACVIM (Neurology)

Objectives
- To understand the four categories of pain.
- To learn pharmacologic and complementary pain treatments.

Introduction
Loosely defined, pain is an unpleasant sensory experience. Current understanding of pain mechanisms groups it into four categories: Nociceptive, Inflammatory, Neuropathic and Functional.

Nociceptive
Nociceptive is what we commonly think of as a pain response. A stimulus with enough intensity to damage tissues produces afferent activity from the peripheral nervous system (PNS) to the central nervous system (CNS) for processing. The pain will vary accordant to the amount, quality and duration of stimuli. Transduction occurs with the translation of the stimulus into electrical activity through sensory receptors. Modulation of the electrical activity occurs through neurons in the dorsal horn of the spinal cord. Modulation is either facilitatory or inhibitory. Conduction is the process of sending the modulated signal to the CNS.

Three types of pain fibers occur in the PNS, each conducting a different type of sensation. Alpha Beta fibers are the fastest because they are fully myelinated. These conduct touch, pressure, vibration and proprioception. Alpha Delta fibers are thinly myelinated, and therefore slower. Alpha Delta fibers conduct sharp physiologic and acute pain. C-fibers are large and myelinated, which makes them relatively slow conductors of dull, chronic pain.

Once the signal reaches the CNS, relay nuclei in the thalamus send information to higher centers of the brain, including the limbic system and amygdala. These areas are involved in emotion, so it’s no wonder that anxiety and anger worsen pain. I always make sure I include anxiety disorders in my history taking. Adding an anti-anxiety approach to patient care may improve pain outcomes.

Inflammatory
If the sensation can’t be controlled by the nociceptive system or removal of stimulus, trauma to the tissues occurs and inflammatory pain takes over. If excessive inflamed tissue occurs, a “soup” of inflammatory and bioactive mediators creates a constant barrage of excitatory neurotransmitters, cytokines, prostaglandins, histamine and bradykinin in the dorsal horn. This can up regulate calcium and sodium channels, cause receptor phosphorylation, and lead to increased excitation to normal stimulation. So, the goal of managing inflammatory pain is to reduce it without impairing the healing process. However, we don’t want to inhibit the normal nociceptive process.

Neuropathic Pain
Neuropathic pain occurs with direct injury to the PNS or CNS, and is categorized in the following manner:
- Hyperpathia is a painful response to noxious stimuli
- Hyperesthesia is increased sensitivity to noxious stimuli such as heat, cold, or mechanical. This is also called hyperalgesia.
- Paresthesia is an unusual, but not always painful sensation such as a limb “falling asleep”
- Dysesthesia is an unpleasant, often painful sensation such as itching, burning or tingling
- Allodynia is pain caused by stimuli that shouldn't be painful

Neuropathic pain may cause a reorganization of neural circuitry which then creates chronic pain. Up to 70% of human spinal cord patients will have chronic neuropathic pain, and many of our patients may experience this at a level we are not able to detect. We have identified several types of neuropathic pain in animals related to trauma or disease of a nerve root such as peripheral nerve sheath tumor (PNST), nerve entrapment due to disc disease, and trigeminal neuralgia. Diabetes Mellitus causes paresthesia and dysesthesia in humans, and most likely creates a similar issue in our patients. Syringohydromyelia or other spinal cord disorders can create CNS pain syndromes. In humans, complex regional pain syndrome (formerly reflex sympathetic dystrophy) is a chronic, often debilitating state which causes pain disproportionate to the original injury. It begins in the injured area, then may spread to the entire body.

**Functional or Maladaptive Pain**

Functional pain syndromes may begin with an injury. The more recent term of Maladaptive Pain Syndrome is currently being described. This is pain that has no biologic benefit and becomes an entity until itself. Maladaptive syndromes include fibromyalgia, chronic fatigue, chronic chest pain, pelvic pain, and irritable bowel syndrome. There is mounting evidence to suggest that cats with Feline Interstitial Cystitis (FIC) can have comorbidities similar to maladaptive syndromes in humans. Also, Feline Hyperesthesia Syndrome is thought to be a type of seizure or behavioral disorder by some. It may eventually be discovered to be a maladaptive pain disorder. Likewise, Cavaliers with syringohydromyelia may progress to maladaptive pain. Further research is ongoing to better categorize these disorders.

Whether it is nociceptive, inflammatory, neuropathic or maladaptive, all pain shows plasticity, meaning pain pathways can remodel. This has been documented at every level of the pain pathway. The result can be a heightened and prolonged response that can be permanent in terms of conventional medical treatment. It’s important to treat pain early and maintain therapy such that it doesn’t allow pain to resurface. Pain is harder to treat once it has been established.

Pain can be treated with peripheral sensitization, such as what is seen with lidocaine. (This is not safe in cats due to cardiovascular depression.) Another approach is to work centrally with medications such as non-steroidal anti-inflammatory drugs (NSAIDS), ketamine, and gabapentin. We can also influence CNS inhibition of pain with opioids, GABA agonists such as baclofen, and SSRIs (selective serotonin reuptake inhibitors).

Another central mechanism for treating pain is by influencing the NMDA (N-methyl-D-aspartate) receptor in the dorsal horn of the spinal cord. Prolonged C-fiber firing causes a release of glutamate, which acts on the NMDA receptor. Constant activation increases sensitivity to pain, and NMDA antagonists such as amantadine and ketamine can disrupt this mechanism.
Opioids work both centrally and peripherally. They work well with inflamed tissue by preventing neurotransmitter release and pain sensitization. Centrally, they modulate neurotransmitters in the dorsal horn, specifically where C-fibers terminate. Finally, opioids blunt the perception of pain in the cerebral cortex. Tramadol and buprenorphine are the most common opioids used in practice; however, morphine is also available in oral form. Fentanyl patches and continuous rate infusions can be extremely effective. These medications are controlled substances, so this enters into their usage as well.

Alpha 2 agonists such as medetomidine and dexmedetomidine exert their effects on the locus coeruleus (LC). The LC is an adrenergic structure that sends output to all aspects of the nervous system. Its activation provides analgesia at the level of the dorsal horn. Sileo, an oromucosal gel formulation of dexmedetomidine, is being marketed for noise anxiety, however, its effect on the LC could be beneficial for pain.

Gabapentin also works at the level of the LC, in addition to blocking calcium channels at the spinal level. Gabapentin is also being used more and more for its anti-anxiety effects. It may be a good choice for the anxious, painful animal - especially the post-surgery, hospitalized patient. Gabapentin can be used long term, however, tapering it is advisable, as severe rebound pain can occur.

NSAIDS work peripherally as anti-inflammatories, as well as having effects at the spinal cord level. NSAIDS block pain by activation of glutamate and substance P receptors. They may also be beneficial in trauma, as CNS injury causes and increase in COX-2 expression.

**Complementary Pain Relief**

Complementary modalities and botanicals have been extremely helpful in managing acute or chronic pain in many patients. The following information is by no means a complete list of all the choices available today. Excellent courses in herbal medicine, as well as training in modalities such as acupuncture and chiropractic, are readily available. I chose options that may not be widely discussed but are easily accessible. All of these can be adjuncts to conventional medications but may also be used alone or in combination with each other.

Several herbs have been found to alleviate pain, including Boswellia serrata, Corydalis yanhusuo, and Devil’s Claw. While studies often focus on musculoskeletal pain, these herbs have also been shown to help with other types of pain. Bromelain is an enzyme found in pineapple that has also been studied in various types of pain such as arthritis, wound, and traumatic pain. Its activity is believed to be mediated through kinin and arachidonic acid pathways. Veterinary supplements are now available that contain these botanicals. They are safe to use with both NSAIDS as well as other conventional pain medications.

Homeopathic and homotoxicology preparations containing arnica can also be added safely to a patient’s pain management protocol. I find them very easy to administer, even for cats. They can be dissolved in a small amount of water and mixed with moist food or put directly in the water bowl. Most studies have focused on musculoskeletal pain; however, they have been found to be helpful in other types of pain, including that seen with cancer. I’ve found them to be useful for intervertebral disc disease, chronic pancreatitis, and feline interstitial cystitis.
The nrf2 enzyme is a master regulator of anti-inflammatory and antioxidant pathways.\textsuperscript{9} While most nrf2 synthesizers are synthetic, an herbal formula exists for both humans and animals. Because enhancing the nrf2 pathway takes time, these formulas are best utilized for chronic pain. It can take 2-4 weeks to see an effect.

The endocannabinoid system (ECS) is vitally important in the modulation of pain, so it is no surprise that phytocannabinoids continue to be extensively studied in pain research. Phytocannabinoids are plants that have an effect on the ECS. Common phytocannabinoids include turmeric, green tea, echinacea and cannabis. Cannabis strains that have less than 0.3\% tetrahydrocannabinol (THC) are called hemp.

Veterinary hemp formulations are coming to market at an increasing rate. Factors to consider when choosing a hemp based phytocannabinoid are bioavailability, whether it is full spectrum, amount of THC, growth and manufacturing processes, and certification. A Certificate of Analysis from the phytocannabinoid company will give information on all these factors, as well as pesticide and heavy metal content.

Phytocannabinoids are useful for pain therapy, as they effect all areas along the nociceptive pain pathway. They are also potent anti-inflammatories. Phytocannabinoids have been studied in laboratory animals and humans for chronic pain, mucositis, and musculoskeletal issues.\textsuperscript{10-12} Good data suggests that a deficiency in the ECS may lead to Maladaptive Pain Syndromes such as fibromyalgia, migraine, and irritable bowel.\textsuperscript{13} Moreover, the calming effect of some phytocannabinoids may enhance pain relief by reducing anxiety.\textsuperscript{14} A study in dogs with osteoarthritis revealed increased activity and decreased pain in the treatment group.\textsuperscript{15}

Essential oils can be helpful additions to a patient’s pain regimen. They have anti-inflammatory and anti-anxiety properties.\textsuperscript{16,17} Care must be given with oils that are commonly used topically for pain in humans, such as eucalyptus and blue tansy. These can cause distress if the patient licks the area. Frankincense and lavender are useful for inflammation and calming, and can be ingested, as long as they are not synthetic. Copaiba is an essential oil that also has anti-inflammatory properties and works well in connection with other oils.\textsuperscript{18} It is also safe to ingest.

Rehabilitation therapy, including underwater treadmill, massage, land exercises and laser therapy are very effective in maintaining quality of life, including pain management. Laser therapy has been shown to decrease PGE2 and COX2 concentrations, as well as having effect on pain receptors peripherally.\textsuperscript{19} I’ve seen patients have immediate pain relief with laser, in addition to chronic pain control. Lasers are a form of energy medicine.

Energy medicine is based in the detection and manipulation of the energy field by the practitioner. It has been shown to be helpful for various types of pain, including chronic headaches and cancer pain.\textsuperscript{20,21} Energy therapies are increasingly becoming utilized in the hospice setting, as well as for self-care among health professionals.\textsuperscript{22} Please refer to \textit{The Energy of Life: Our Quantum Connection} for more information on energy medicine.
Energy therapies can also be performed by using electromagnetic field pulse generators (pEMF). These devices are becoming more sophisticated and are now available for our veterinary patients. Care must be used when treating animals, as they may be sensitive to the frequencies. If the patient squirms or moves away from the delivery system, let it gain some distance. Turn down the power or place the patient away from the device. Sensitive animals may eventually be able to tolerate being closer to, or totally on, the mechanism.

Acupuncture is becoming a popular modality in veterinary medicine. Many easily accessible continuing education lectures and programs are currently available, so we won’t go into depth on the subject here. I did want to mention that acupuncture is an ancient and effective energy modality that has rigorous research to support its use in the management of many types of patients. It has been shown to release endorphins, as well as other neuropeptides, which makes it particularly useful for pain management.

By using an integrative approach to pain management, we can reduce risks associated with some medications, while gaining more effective pain relief. I hope this lecture gives you reliable and safe options to enhance the quality of life for your patients.

References


Herbals for Immune-Mediated Diseases: Studies
Huisheng Xie, DVM, MS, PhD

Objectives
- To understand how to search the evidence-based studies on Chinese herbals for the treatment of immune-mediated diseases.
- To understand the mechanisms why Chinese herbals can treat immune-mediated diseases.

Introduction
Atopic dermatitis and other immune-mediated diseases can be the very challenging problems in veterinary practice. Recent studies indicate that acupuncture and herbal medicine are useful for the treatment of these conditions.1-8 For example, research studies indicated that herbal medicine had effects including inhibiting production of IgE and increasing cAMP concentration to inhibit the release of mast cell contents.9-12 Clinical studies have also shown that many herbs have significant effects relevant to the treatment of atopy and other immune-mediated diseases.13-17 This review will include studies on Chinese herbs for the treatment of atopic dermatitis, autoimmune skin diseases, autoimmune hemolytic anemia (AIHA), immune-mediated thrombocytopenia (ITP), immune-mediated polyarthritis, or polyarthropathies.

Atopic dermatitis (Atopy)
It is estimated that 10-15% of dogs suffer from atopic dermatitis (AD). AD is involved in the production of IgE antibodies in response to exposure to allergens that are absorbed through the skin.18-20 In the traditional Chinese veterinary medicine (TCVM) perspective, AD is caused by Wind, Wind Toxin (Heat) and associated with Wei Qi, Lung, Spleen and Kidney disorders.14-17 Cassia angustifolia (Fan Xie Ye), Rheum palmatum (Da Huang), Coptis chinensis (Huang Lian), Phellodendron amurense (Huang Bai) and Scutellaria baicalensis (Huang Qin) significantly inhibited the edema induced by exposure to 12-O-tetradecanoylphorbol-13-acetate.4 Tea tree oil, with a fresh camphoraceous odor, is well known for its broad antibacterial and antifungal activity.5 Fifty-seven dogs with pruritic skin lesions, skin fold pyodermas and other forms of dermatitis were randomly allocated to two study groups: tea tree oil cream (n=28) and control cream group (n=29). All subjects were treated twice daily with a blinded topical preparation. After 10 days of daily topical treatments, the success rate for the tea tree oil cream was 71%, that was significantly better than 41% of the success rate for the control cream (p < 0.05).5 Sophora flavescens (Ku Shen) and Cnidium monnieri (She Chuang Zi), significantly inhibited the serotonin (5-HT)-induced itch-related response (scratching) and the spontaneous scratching in mice.6 A randomized and double-blinded, controlled trial of a traditional Chinese herbal medicine was conducted in 50 canine cases of atopic dermatitis.7 After the herbal treatment, 9 of 24 dogs (37.5%) had improved in the itching score while only 3 of the 23 dogs (13%) improved in the placebo group.7 The possible mechanisms included anti-inflammation, inhibition of airway smooth muscle contraction, and immunomodulation (but not overall immune suppression).8 Oral administration of water extract of Phellinus linteus (Song Gen) inhibited the drug-induced, systemic anaphylaxis-like reaction and the anti-dinitrophenyl IgE-mediated passive systemic and cutaneous anaphylaxis, while increasing the level of intracellular cAMP and significantly inhibiting the drug-induced cAMP reduction in rat peritoneal mast cells.9 A retrospective study
on patients with atopic dermatitis was conducted at the Chang Gung Memorial Hospital in Taiwan between 2002 and 2011. Of the 4145 patients included in the study, (8.8%) received traditional Chinese medicine therapy between 2002 and 2011. Among them, 2841 (68.54%) chose TCM only and 1304 (31.46%) chose to combine TCM and western medicine (WM) therapies. The most commonly used therapeutic principles of herbal formulas and single herbs were releasing exterior (20.23%) and clearing heat (41.93%), respectively. In a different study, another herbal mixture significantly reduced IgE production and expression of AD-associated pathogenic cytokines such as IL-4, IL-5, IL-10, IL-13, IL-17, TNF-α, and IFN-γ by lymphocytes isolated from AD-induced mice. Topical application of Catalpa ovata stem bark (Zi Pi) was used for dermatophagoides farinae-induced AD in a NC/Nga mouse AD model. This herbal therapy significantly inhibited serum total IgE, Th2 cytokines IL-4, IL-5 and IL-13, pro-inflammatory cytokines IL-1β, IL6 and TNF-α, the Th2 chemokine TARC and the pro-Th2 cytokine TSLP. Cudrania tricuspidata (Zhe Hua Guo) inhibited the development of AD-like skin lesions, reduced skin dermatitis scores and inhibited the histological changes induced by repeated application of D. farinae. In addition, C. tricuspidata inhibited the increases in plasma concentrations of mTARC, histamine and IgE induced by D. farinae. Xiao Qing Long Tang had been found to alleviate the syndromes of atopic dermatitis and allergic rhinitis. Yu Ping Feng San decreased the recurrence of atopic dermatitis. A modern herbal formula was successfully used for the treatment of a one year old female Dalmatian-cross dog for flea allergic dermatitis. Another Chinese herbal formula had a significant effect on AD and allergic rhinitis. Modern pharmacological research has shown that Chinese medicines Jing Jie (Schizonepeta), Ku Shen (Sophora), Bai Xian Pi (Dictamnus), Chan Tui (Cicada), Cang Er Zi (Xanthium), Di Fu Zi (Kochia) had obvious anti-allergic function, could inhibit or directly antagonism the release of histamine, slow-reacting substance and other allergic substances. Cang Er Zi (Xanthium) and Xi Xin (Axarum) increased the content of Ts cells; Gan Cao (Licorice) had corticosteroid-like, antiinflammatory and anti-allergice effects. Guo Min Jian significantly decreased serum IgE in an asthma model, and inhibited the allergic inflammation associated with asthma. Ge Gen Tang satisfactorily treated circumscribed scleroderma in 28 cases. Among 105 cases of circumscribed scleroderma, during either the development period or recurrence period, the modified Pu Ji Xiao Du Decoction induced clinical recovery of 31 cases.
and a curative effect in 65 cases. Sodium feralate can increase the number of circulating endothelial cells of patients with systemic scleroderma and significantly improve the clinical symptoms of systemic sclerosis. The modified Shen Ling Bai Zhu powder had significant curative effects on 88 cases of Pemphigus. Jin Gui Shen Qi pills, in combination with a glucocorticoid, had an improved therapeutic effect on bullous pemphigoid compared to treating with glucocorticoid alone.

Autoimmune Hemolytic Anemia (AIHA)
Chinese herbal medicines were widely used for the treatment of AIHA in both people and dogs. Ligustrazine extracted from Ligusticum (Chuan Xiong) promoted bone marrow hematopoietic reconstitution after bone marrow transplantation in mice. Quercetin and kaempferol from the root of Aster (Zi Wan) are potent anti-hemolysis and anti-superoxide radical generation agents. Si Jun Zi Tang stimulated the production of both red and white blood cells.

Immune-Mediated Thrombocytopenia (ITP)
Patients with ITP can benefit from using Chinese medicine treatment for the disease. Gui Pi Tang seems a very promising herbal medicine for the treatment of both ITP and AIHA.

Immune-Mediated Polyarthritis
Tripterygium hypoglaucum, Polygonum cuspidatum (Hu Zhang), Cissus assamica and other herbs were often used for treatment of rheumatoid or immune-mediated arthritis. Adjuvant arthritis (AA) in rats is an immune-mediated, inflammation model. Total anthraguinone of Rubia Cordifolia L. reduced serum concentrations of IL1, IL2, IL6, and TNF, resulting in anti-inflammatory and anti-rheumatic effects in AA rats. Triptolide is considered to be one of the most important anti-inflammatory and immunosuppressive ingredients. Triptolide’s effects included induction of apoptosis and inhibition of angiogenesis. Oxymatrine significantly suppressed secondary paw swelling, normalized the decreased IL-1β and TNF-α joint concentrations and reduced joint pathology. Panax notoginseng saponins had its therapeutic effect on AA rats via inhibiting the release of inflammatory cytokines TNF, IL-1β by peritoneal macrophages.

Conclusion
Immune-mediated disorders is a most challenging disease in dogs and cats. The most commonly seen diseases include immune-mediated hemolytic anemia (IMHA), immune-mediated thrombocytopenia (IMT), immune-mediated polyarthritis (IMP), myasthenia gravis (MG), inflammatory bowel disease (IBD), Immune-mediated skin disease (IMSD), granulomatous meningoencephalitis (GM), keratoconjunctivitis sicca (KCS) and glomerulonephritis. The conventional treatment of these immune-mediated disorders frequently involves managing immune responses with immunosuppressive pharmaceutical drugs. Side effects, incomplete resolution and relapses are common sequelae. A tremendous amount of studies indicate that Chinese herbal medicine offers additional treatment options to improve clinical signs, mitigate undesirable side effects, and address underlying environmental and intrinsic causes.
References
3. Qin L. Mild moxibustion at Xuehai (SP 10) for senile pruritus. Zhongguo Zhen Jiu 2011; 31(9):849. [In Chinese]

18. The list of the rest references 18-81 are available from the author.
Herbals for Immune-Mediated Diseases: Applications
Huisheng Xie, DVM, MS, PhD

Objectives

- To understand when to integrate Chinese herbals to treat immune-mediated diseases.
- To understand how to select herbal recipes to treat immune-mediated diseases.

Many Chinese herbal formulas have been proven to be useful for the treatment of immune mediated diseases including atopic dermatitis\(^1\), autoimmune skin diseases\(^2\)\(^-\)\(^3\), immune-mediated hemolytic anemia (IMHA)\(^4\)\(^-\)\(^5\), immune-mediated thrombocytopenia (ITP)\(^6\)\(^-\)\(^7\), and immune-mediated polyarthritis (IMPA)\(^8\)\(^-\)\(^9\). This presentation will include when and how to integrate Chinese herbs for the treatment of these immune-mediated diseases in dogs and cats.

Atopic Dermatitis
In Traditional Chinese Veterinary Medicine (TCVM), the Lung is related to the body surface, also known as *Pi-mao* ("skin-hair"), which includes the skin, hair follicles, hair coat and sweat glands. Physiologically, *Pi-mao* needs the abundant nourishment of *Jing* (Essence), *Qi*, Blood and Body Fluids that are associated with the Kidney, Spleen, Liver and Heart in addition to the Lung. Therefore, skin conditions are very complicated as they can be associated with either of Five Zang Organs. The Lung governs the skin and hair of the whole body, and patients with Lung *Yin* Deficiency usually present with generalized dry hair, alopecia, or itching. The Spleen holds organs and hair in place, so patients with Spleen *Qi* Deficiency lose hair easily, which is often presented in canine cases of hypothyroidism. In addition, the Spleen transports Dampness, so the therapeutic principle of strengthening the Spleen can be used for the treatment of Damp-Heat Skin cases characterized by excessive moisture. The Kidney Essence (*Jing*) nourishes the growth of long hair (the head and genital areas in people), and the long hair is considered an outward manifestation of the Kidney. In this sense, alopecia of these regions with unknown reasons might be caused by Kidney *Jing* Deficiency. The Liver stores the Blood and maintains the smooth flow of *Qi*, and hair is often considered as the surplus of Blood. So, itching and skin lesions at the scrotum and/or hypochondrium/flank, ears, medial thigh and feet where the Liver is in charge or where the Liver/Gallbladder Channels pass through are often associated with Liver Blood or/and *Yin* Deficiency, Liver *Qi* Stagnation, or Liver/Gallbladder Damp Heat. The Heart dominates the Blood and houses the *Shen* (Spirit/Mind). So pruritus associated with the behavioral issues such as excessive grooming and lick granuloma are usually attributed to Heart Blood/*Yin* Deficiency.

Even though skin conditions may have a relationship with all five Zang Organs (Lung, Spleen, Heart, Kidney and Liver), it is more important to differentiate the 3 Excess Patterns (including External Wind, Wind-Heat, Damp-Heat), 2 Deficiency Patterns (Blood Deficiency and *Yin* Deficiency), and 2 mixed Patterns of Deficiency and Excess (Blood Deficiency with Heat, and *Yin*/Blood Deficiency with Damp Heat) to achieve better results. How to diagnose and treat these 7 most commonly seen Patterns of atopic dermatitis is summarized in Table 1.
<table>
<thead>
<tr>
<th>Pattern Type</th>
<th>Clinical Signs</th>
<th>Acupuncture/ Herbal Medicine*</th>
</tr>
</thead>
</table>
| **External Wind** |  • Atopy, contact dermatitis  
  • Flea allergic dermatitis  
  • IgE-mediated hypersensitivity  
  • Pruritus @ face, neck, ear  
  • Tongue: Red or slightly dry  
  • Pulse: Wiry or fast | GV-17/20, Da-feng-men,  
  GB-20, BL-10, BL-12  
  SP-10, BL-17  
  LIV-3, GB-31  
  External Wind (Qu Feng Zhi Yang) |
| Wind-Heat |  • Warm skin surface  
  • Erythema  
  • Small vesicles on the surface  
  • Pruritus  
  • Tongue: Red  
  • Pulse: Floating and forceful | GB-20, Da-feng-men,  
  BL-10/12  
  LI-4, LI-11  
  Er-jian, Wei-jian  
  Wind Toxin (Xiao Feng San) |
| Damp Heat |  • Thick, yellow discharge on the surface with strong odor  
  • Scab formation  
  • Lesion: thigh, feet, abdomen  
  • Itching and restlessness  
  • Scratching and rubbing  
  • Alopecia  
  • Tongue: Red with greasy coating  
  • Pulse: Fast and forceful | GV-14, LI-4/11  
  ST-44, LI-2, LU-10, LU-5  
  Wei-jian, Er-jian  
  SP-6/9, ST-40  
  Damp Heat Skin  
  Qing Shi Re Tang  
  Long Dan Xie Gan  
  Si Miao San |
| Blood Deficiency |  • Dandruff, or dry skin/haircoat  
  • Alopecia, dry or cracked paw pads/hooves  
  • Tongue: Pale and dry  
  • Pulse: Deep, thin, weak | BL-17, SP-10/6/9, ST-36,  
  BL-20/21  
  GB-39, KID-10  
  Si Wu Xiao Feng |
| Blood Deficiency with Heat |  • Dry skin, or alopecia with red or warm skin  
  • Dry or cracked paws with redness or warmth  
  • Panting or cool seeking  
  • Tongue: Pale and dry  
  • Pulse: Fast, thin, weak | BL-17/18/20/23  
  SP-10/6/9, GV-14, LI-4/11, GB-31  
  Ku Shen Si Wu |
### Yin Deficiency
- Itching worse at night or in summer
- Hyperactivity at night
- Cool-seeking behavior
- Tongue: Red, dry
- Pulse: thin, fast

<table>
<thead>
<tr>
<th>TCM Formula</th>
<th>Acupuncture Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>LU-9, BL-13</td>
<td>Fei-men/pan, BL-23, SP-6, KID-3, BL-18, SP-10</td>
</tr>
</tbody>
</table>

*Yin/Blood Deficiency with Damp-Heat*
- Dry skin/haircoat, or alopecia with red skin
- Smelly and itching
- Panting, cool seeking
- Tongue: Pale or red and dry tongue
- Pulse: Fast, thin, weak

<table>
<thead>
<tr>
<th>TCM Formula</th>
<th>Acupuncture Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL-17/18/23, SP-6/9/10</td>
<td>KID-3/7/10</td>
</tr>
<tr>
<td>GV-14, LI-4/11</td>
<td>Wu Shen San</td>
</tr>
</tbody>
</table>

*All these herbal medicines are made by Jing-Tang Herbal. (Disclosure: Dr. Huisheng Xie is one of the owners of Jing-Tang Herbal, Inc.)*

**Case Example:** Baxter, a six-year-old castrated male Shih Tzu, presented with chronic alopecia, pruritus, and dandruff. His hair was dry overall and had alopecia with crusts and dandruff in the flank and back. He chronically rubbed around the eyes and flank area (around LIV-14/GB-24). His tongue was pale and dry with a thin and weak pulse. Hair loss, dry hair and dandruff, pale and dry tongue, and thin and weak pulse indicate Blood Deficiency. The Liver is the storage place of Blood and opens to the eyes and flank. Thus, the final TCVM Pattern for this case was Liver Blood Deficiency. Treatment included dry-needling acupuncture at GB-20, BL-17, BL-18, BL-23, Shen-shu, KID-3, KID-7, SP-6, SP-10 and LIV-8. The following Chinese herbal formulas were prescribed: *Bu Xue Xi Feng* and External Wind, 0.5 grams of each twice daily. Baxter had a normal haircoat after four acupuncture sessions (one session per month) and four months of dietary therapy and herbal medication.

**Autoimmune Skin Diseases**
The most commonly seen autoimmune skin diseases in dogs and cats are pemphigus vulgaris, pemphigus foliaceus and lupus erythematosus. The top two TCVM Patterns are Blood Heat and Qi-Blood Deficiency with Heat. Pattern differentiation and treatments are listed in Table 2.
Table 2: TCVM Pattern Diagnosis and Treatments of autoimmune skin diseases.

<table>
<thead>
<tr>
<th>Pattern Type</th>
<th>Clinical Signs</th>
<th>Acupuncture/Herbal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Heat</td>
<td>• <em>DLE, SLE,</em> and other autoimmune-mediated diseases</td>
<td>GB-20, <em>Er-jian,</em> <em>Wei-jian,</em> LIV-3, GB-34, BL-17, SP-10</td>
</tr>
<tr>
<td></td>
<td>• Depigmentation, crusting, or erythema</td>
<td>Blood Heat Formula <em>(Qing Re Liang Xue)</em></td>
</tr>
<tr>
<td></td>
<td>• Ulceration of the planum nasale or skin, erosions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tongue: Red or purple</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pulse: Surging and Fast</td>
<td></td>
</tr>
<tr>
<td>Qi and Blood Deficiency with Damp Heat</td>
<td>• Depigmentation or crusting</td>
<td>BL-20/21/24, LI-4/11</td>
</tr>
<tr>
<td></td>
<td>• Bleeding ulceration</td>
<td>SP-6/9, ST-36</td>
</tr>
<tr>
<td></td>
<td>• Erythema, or erosions</td>
<td><em>Han Lian Cao</em></td>
</tr>
<tr>
<td></td>
<td>• Tongue: Pale and dry</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pulse: Deep and weak</td>
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</tbody>
</table>

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**Immune-Mediated Hemolytic Anemia (IMHA)**

IMHA, also called Autoimmune Hemolytic Anemia (AIHA), is one of the most common immune-mediated diseases in dogs. In TCVM, IMHA is caused by the fact that *Wei Qi* misreads the markers on the RBC cell surface and recognizes them as "non-self" leading to hemolytic anemia. It can be triggered by infectious disease, cancer, blood parasites, heavy metals (lead and zinc), levamisole, and certain antibiotics or Dilantin (phenytoin). The main IMHA clinical signs include weakness, lethargy, anorexia, icterus/jaundice, an increase in the heart rate and respirations or heart murmurs, pale and dry tongue, and weak pulse. The primary TCVM Pattern is *Spleen* Qi Deficiency + Blood Deficiency, that is often effectively treated by *Gui Pi Tang*. It may be combined with three other Patterns. Severe Blood Deficiency should be added with *Dang Gui Bu Xue*. Yin Deficiency (hot/panting signs) should be combined with Rehmannia 6. With Damp Heat (jaundice), *Yin Chen Zhu Fu* should be combined.

The general integrative medical principles are: 1) blood transfusion as needed for emergency; 2) give prednisone initially for 1 month and wean off with TCVM herbal medications; and 3) give herbal medicines for 3-6 months, and then gradually wean off herbal medicines. The TCVM Pattern Diagnosis and treatment are summarized in Table 3.
Immune-Mediated Thrombocytopenia (ITP)
In TCVM, the pathology of ITP is that the Wei Qi misreads and destroys thrombocytes (platelets) leading to ITP. Its clinical signs are bruising or purpura, prolonged hemorrhage or excessive bleeding following trauma, hematuria, and/or hematochezia, pale tongue and weak pulse. The primary TCVM Pattern is Spleen Qi Deficiency and Blood Deficiency. High dosage of Gui Pi Tang effectively treats ITP initial being combined with prednisone. Integrative Medical principles are: 1) Prednisone initially for 1 month; 2) Continue TCVM and gradually wean off prednisone; 3) Gui Pi Tang with High Dosage, First 2 months: 2-3 grams per 10 kg body weight, and then a maintenance dosage of 1 gram per 10 kg.

Immune-Mediated Polyarthritis
IMPA is part of Bi Syndrome (pain and stiffness). When the initial primary signs are Pain and Stiffness, IMPA is divided into two patterns: Wind Bi with Damp Heat and Stagnation with Blood Heat. Wind Bi with Damp Heat is often presented in canine rheumatoid arthritis cases. The main clinical signs are shifting leg lameness, soft-tissue swelling around involved joints, trabecular bone loss with time, progressive cartilage erosion, red or purple tongue, sometimes dry and rapid full or wiry pulse. It can be treated with Bai Hu Si Miao San or Si Miao San. Stagnation with Blood Heat is presented in IMPA or idiopathic polyarthritis cases. The clinical signs include antibiotic-unresponsive fever, malaise, anorexia, stiffness or lameness, mild or non-existent radiographic changes, red tongue, and rapid, empty pulse. This pattern should be treated with Mu Dan Pi.

Conclusion
Immune-mediated disorders is a most challenging disease in dogs and cats. The conventional treatment of immune-mediated disorders frequently involves managing immune responses with immunosuppressive pharmaceutical drugs. Side effects, incomplete resolution and relapses are common sequelae. Chinese herbal medicine offers additional treatment options to improve clinical signs, mitigate undesirable side effects, and address underlying environmental and intrinsic causes.

References


Using "Where" and "What" in TCVM Diagnostics
Huisheng Xie, DVM, MS, PhD

Objectives
- To use western medical diagnosis to determine TCVM pattern.
- To understand how to make a final TCVM pattern.

Introduction
In any medical system, effective treatment of disease hinges upon an accurate, complete diagnosis. This places Bian Zheng, the diagnostic system of Traditional Chinese Medicine (TCM) and Traditional Chinese Veterinary Medicine (TCVM), as the most important part of medical practice. There are at least eight Bian Zheng systems which include: Eight Principles, Zang-Fu Patterns, Six Channel Patterns (Six Phases), Four Stages (Four Levels), San-Jiao Patterns (Tripler Heater Patterns), Pathogen Patterns, Qi-Blood-Body Fluid Patterns and Meridian Patterns.1 These often present a challenge for the novice TCVM clinicians or students to learn. Is there a simpler and easier method to achieve Bian Zheng? Based on my 30-years of clinical practice and teaching experience, I have created the 2 W’s TCVM Diagnostic System which should simplify TCVM Pattern diagnosis for clinicians.2

First W – Where Is the Problem?
Five Element System
Where is the lesion/disease located in the TCVM system? This is a very important and relatively easy question to answer. There are 5 TCVM medical systems that are associated with the Five Elements and Zang-Fu physiology and pathology. 3 A veterinarian can use the conventional diagnosis to place the disease in one of 5 TCVM systems. For example, epilepsy would be placed in the Liver system. Hive p dysplasia and Intervertebral disc disease should be placed in the Kidney system. Separation anxiety goes to the Heart system while inflammatory bowel disease is placed in the Spleen system.

When the conventional diagnosis is not available, a veterinarian can simply use the main complaint to place the clinical disease in one of the 5 TCVM systems. For example, cough belongs to the Lung system while diarrhea goes to the Spleen system. The rear weakness is placed in the Kidney system while behavioral change goes to the Heart system. There can be some overlap between the Spleen, Kidney, and the Liver, in terms of the origin of endocrine and metabolic pathologies. In addition, the nervous system can have several Zang-Fu organ categorizations based on the clinical signs. Cognitive dysfunction can signify problems with the Shen/Heart or Kidney,4 whereas seizures are usually classified as an Internal Wind Syndrome in the Liver system. Pathologies involving the spinal cord (e.g., fibrocartilaginous embolism or intervertebral disc disease) are most often associated with the Kidney. Nervous system disorders brought about by a tumor (e.g., menigioma, nerve sheath tumor) can be associated with Blood Stagnation or Phlegm and may signify an imbalance in the Spleen. In this manner, it is crucial to individually evaluate the evidence in each case in order to accurately label the underlying Pattern, and not rely solely on broad, generalized categorizations or a Western diagnosis.
**Second W – What Is It?**

**Eight Principles**

The fundamental basis of *Bian Zheng* is Eight Principles, that consist of four pairs: Yang vs. Yin, Excess vs. Deficiency, Exterior vs. Interior and Heat vs. Cold. Within each pair, one term is more Yin and the other is more Yang, as determined by the principles in *Yin-Yang* theory. Exterior, Heat, and Excess belong to Yang, while Interior, Cold and Deficiency belong to Yin. Thus, the 1st pair of Eight Principles is not as meaningful or useful in veterinary practice.

The second pair determines the location and depth of the disease, more Interior (internal organs) or Exterior (signs mostly on the surface). Exterior Patterns tend to be more acute, less severe, and Pathogen-associated. Interior Patterns tend to be more chronic, severe, and Deficiency-associated. In modern veterinary practice, the majority of TCVM cases belong to the internal medicine (Interior Pattern) while the acute onset of respiratory infectious cases (Exterior) are rarely seen by the TCVM clinician.

The question, “Is the animal patient too Hot or too Cold?” is answered by the third pair. To assess this accurately, we must determine Excess or Deficiency first to differentiate Excess (True) Heat, Deficient (False) Heat, Excess (True) Cold, Deficient (False) Cold. In other words, we can use the fourth pair to answer the Hot vs. Cold question much more accurately and precisely (discussed in detail below). Therefore, the core or most critical part of Eight Principles to determine is Excess versus Deficiency.

**Excess or Deficiency**

“Is this animal showing signs of a Deficiency or Excess?” This is an important question a TCVM practitioner should consider when evaluating a patient. When the body is not able to balance the extremes it experiences, disease follows. Consider the following analogy illustrating the experience of balance versus an Excess or a Deficiency.

There is a small café in a college town that was designed to optimally seat and feed about twenty people during a normal weekday lunch hour. Usually the café nicely accommodates this number, and the patrons enjoy the delicious food and pleasant atmosphere until they return to work. This is the balanced state. In the late afternoon business slows down, so there are only one or two people who are eating, and the café is very quiet and subdued. The patrons feel uncomfortable in the too-quiet environment. This scenario would represent a Deficiency of patrons, as there are fewer people and lower activity levels than normal. Conversely, during lunch on a Saturday with a football game occurring in town, over forty people crowd into the café. The patrons are hungry and irritated about having to wait, and they do not enjoy the noisy, crowded environment. This would represent an Excess, as there is much more activity than the café is equipped to handle.

The body is exhibiting a Deficiency Pattern when there are not enough resources to allow normal function. The body exhibits an Excess Pattern when it is functioning beyond capacity or is dealing with more than what it can accommodate. Deficiency Patterns occur in older patients or those that have chronic imbalances. In contrast, Excess Patterns are often seen in younger animals or those with traumatic injuries, infectious diseases, or acute pathologies.
Generally, Deficiency or Excess problems occur due to imbalances in the patient’s immunity, so these Patterns can indicate the Zheng Qi (the body's resistance to diseases) strength and the potential for Xie Qi (Pathogens) invasion. Frequently you will see an Excess Pattern when Zheng Qi first begins fighting the invading Pathogens and removes the Pathogens, with or without support from treatments. Deficiency Patterns appear when Zheng Qi becomes very weak and the Pathogens overcome the Zheng Qi and drain the body's resources. Sometimes combined Deficiency and Excess Patterns can occur when the Zheng Qi and organ Qi become weak and cannot prevent the Pathogen(s) from entrenching themselves and creating prolonged disruptions related to inefficient organ function.

The practitioner must go through a decision-making process to determine which of the four Deficiency Patterns is the most likely diagnosis. Let us walk through this process with a 15-year-old castrated male terrier mix presenting with a five-year history of progressive bilateral stifle osteoarthritis due to chronic medially luxating patellas. The first step in Pattern Differentiation is deciding if the illness is more related to an Excess or Deficiency. The chronic disease and dog’s old age indicate this is a Deficiency Pattern. Having established this as a Deficiency Pattern, the next step is to figure out the kind of Deficiency by finding any imbalances in Qi, Blood, Yin or Yang. Since this old dog had severe exercise intolerance, had weak and deep pulses (weaker on the right), felt slightly cool to the touch, and had a pale tongue, the TCVM diagnosis was specified as a Qi Deficiency. Like the quiet, empty café, Deficiency signs generally reflect a decrease compared to normal, such as emaciation, lethargy, exercise-intolerance, weakness, or a diminished, weak pulse. After identifying the Deficient substance (Qi, Blood, Yin, or Yang), the next step is to add one of the 5 TCVM medical systems (the 1st “W” Where). Osteoarthritis falls under the TCVM medical system for the Kidney. Thus, the final TCVM diagnosis is Kidney Qi Deficiency based on 1st W=Kidney and 2nd W=Deficiency (Qi).

The same decision-making process produces a very different diagnosis if we now consider a two-year-old Thoroughbred filly presenting with an acute onset of high fever, red tongue with yellow coating and a fast, forceful pulse. In this case, the practitioner decides that an Excess Pattern is a more logical choice given the patient’s young age and acute clinical signs. Furthermore, the high fever, red tongue with a yellow coating, and fast, forceful pulse suggest Excess Heat. The TCVM diagnosis of Lung Excess Heat would be based on 1st W=Lung and 2nd W=Excess (Heat). Excess Patterns are frequently characterized by the presence of a Pathogen, such as Heat; and, the culprit might be any one of the Six Exogenous Pathogens: Wind, Cold, Dampness, Summer Heat, Dryness or Fire/Heat. Generally, Excess Patterns present as hyperfunctional states, such as high fever, tachypnea, hyperactivity, and an excessive or surging pulse.

Excess and Deficiency Patterns are not mutually exclusive. In fact, certain Excess Conditions can result from Deficiency Patterns. For example, Food Stasis and Phlegm are Excess Patterns that occur secondarily to problems like a Spleen Qi Deficiency. Blood or Qi Stagnation is a common Excess Pattern which could be secondary to a Deficient condition.

**Excess Heat vs Deficient Heat**

Heat is divided into Excess Heat (True Heat) and Deficiency Heat (False Heat). Excess Heat is mainly caused by the invasion of Wind Heat, Summer Heat, or Dry Heat. It is sometimes caused secondarily from an interior disease process and can for example occur with the Stagnation of
food that turns into Heat, or as a consequence of prolonged Internal Heat from Liver Qi Stagnation. An Interior Heat that is caused by a Deficiency is due to Yin Deficiency. This can arise after a prolonged course of Excess Heat (Pathogenic and/or environmental) or based on combinations of diseases in susceptible individuals.

**Excess Cold vs Deficient Cold**

Cold can also be divided into Excess Cold (True Cold) and Deficiency Cold (False Cold). The Excess Cold Pattern is often caused by the deep invasion of Cold into the internal organs, such as a progressive respiratory virus. On the other hand, it can be caused by internal Cold infiltration from deep environmental penetration, such as the ingestion of ice-cold water. The cause of the Deficiency Cold Pattern is due to a Yang Deficiency, an imbalance that worsens with age and disease progression. It is important to note that even a Cold imbalance that begins with an Excess Cold can over time damage the Yang energy, which leads to Yang Deficiency and becomes False Cold.

**How to Use “2 W’s” TCVM Diagnostic System**

*A Diagnostic Map*: This system is made up of 2 basic diagnostic steps.

**Step 1: Where is it?** Locate where the problem/lesion/disease is. Even beginning practitioners can easily map out the various clinical signs onto a figure of the Five Medical Systems and determine the primary system(s) involved based on the pathological manifestations and physiological functions of the Zang-Fu organs.

**Step 2: What is it?** Determine if the animal has an Excess or Deficiency Pattern. It is relatively easy to figure this out. Generally speaking, Deficiency Patterns occur in older patients or those that have chronic imbalances. In contrast, Excess Patterns are often seen in younger animals or those with traumatic injuries, infectious diseases, or acute pathologies.

If it is an Excess, TCVM clinicians can use the clinical signs and medical history to determine if it is a Primary Pathogen (Wind, Cold, Heat, Summer Heat, Dryness and Cold) or Secondary Pathogen (Stagnation, Stone, Phlegm and Food Stasis). In general, the invasion of Primary Pathogens is often associated with seasonal changes, epidemic episodes or travelling to a new environment. Secondary Pathogens are often caused by emotional stress, abnormal food intake, and other chronic illnesses. If there is a Deficiency, TCVM clinicians can assess the clinical signs to figure out which substance(s) are affected (Qi, Blood, Yin or Yang).

In summary, the 2 W’s Diagnostic System consists of Where and What. The first step is to figure out “Where” the illness is located (5 Element TCVM Medical System) using the main complaint or western diagnosis. The second step is to determine What the Pattern is by using the TCVM clinical data including tongue and pulse. In this manner, the 2 W’s Diagnostic System is used as a TCVM diagnostic map especially for the novice TCVM practitioner.

Even though only Yin Organs (Liver, Heart, Spleen, Lung and Kidney) are used as the title of each TCVM Medical System, Yang Organs (Gallbladder, Small Intestine, Stomach, Large Intestine and Bladder) can be used in the diagnosis especially for Excess Patterns. A rule of thumb for beginners is if it is determined there is a Deficiency present in the case, then that
Deficiency is usually attributed to the *Yin* organ of the affected TCVM Medical System. In contrast, if it is an Excess Pattern, then the TCVM diagnosis can be related to the *Yin* organ or the *Yang* organ. Remember, as a general rule, as there can occasionally be Deficiencies in *Yang* organs (such as Stomach *Yin* Deficiency), and more often, Excess conditions in *Yin* organs. For example, the Liver as a *Yin* organ can be associated with Deficiencies, such as Liver Blood or Liver *Yin* Deficiency but it can also be prone to Excess problems such as Liver Heat, Liver Damp Heat and Liver *Qi* Stagnation. There can be other exceptions to this rule, but it can be helpful when beginning to choose logical TCVM Patterns.

Using the “2 W Diagnostic System” to evaluate a case of a 15-year DSH spayed female cat who presents with a 1-year history of urinary incontinence. Her rear limbs are weak. She has deep and weak pulses, a pale and wet tongue. Her urinary analysis is within normal limits. The presenting complaints (urinary incontinence and rear weakness) are classified in the Kidney medical system (Water Element). This cat has *Qi* Deficiency because of weakness, tongue and pulse character. Therefore, since this cat has a Deficiency in the Water Element, it is a Kidney *Qi* Deficiency (the Kidney is the *Yin* organ of the Water Element). On the other hand, if it is a young cat that acutely presents with stranguria, hematuria, with a red tongue and rapid pulse, this represents an Excess in the Water Element with signs of Excess Heat. Therefore, this TCVM diagnosis of Excess is most commonly seen in the *Yang* Organ in the Water Element which is known Excess Bladder Heat, or Bladder Damp Heat. This general rule can help novice practitioners navigate the complicated TCVM diagnostic process and formulate simple, but accurate TCVM Patterns.

**Case Example**

A thirteen-year-old spayed female German Shepherd named Maxine was diagnosed with lumbosacral stenosis and right coxofemoral osteoarthritis from chronic hip dysplasia, based on radiographic findings. She had shown weakness of her back, as well as rear limb lameness and weakness for three years. The owner reports that this had worsened recently. Her tongue was pale and wet. Her pulse was very weak, slow, and deep, with the right side weaker than the left. She preferred to sleep in warm places, such as lying in the sun. Her body felt very cold to the touch, especially her pelvic limbs and *Bai-hui* region.

The first step (1st *W*) is to figure out the location, (the Where in the TCVM Medical System or Element) using Maxine's western diagnosis and main complaints (lumbosacral stenosis and right coxofemoral osteoarthritis from chronic hip dysplasia), which are easily mapped into the corresponding System/Element-Kidney. The Kidney controls the bones, and the lower back is the house of the Kidney.

The second step (2nd *W*) is to determine What the pattern is (Excess or Deficiency) using the Eight Principles. Maxine's advanced age, chronicity of disease, character of her pulses and weakness all suggest a Deficiency Pattern. When assessing what is Deficient, her preference for warmth, the chronic nature of the illness, and the pale tongue all indicate that Maxine’s condition is due to a *Yang* Deficiency. It could be argued that a *Qi* Deficiency is also present in Maxine based on her age and character of her pulse and tongue. However, because of the extreme Cold signs present, a *Yang* Deficiency is her primary Pattern currently, and likely represents a progression of her *Qi* Deficiency. *Yang* Deficiency is usually a sequela from a long-standing Deficiency of *Qi*. Thus, the final diagnosis for Maxine was Kidney *Yang* Deficiency.
Conclusion
Using the 2 W’s TCVM Diagnostic System, organizing a complicated TCVM Pattern can be simplified. This system should be particularly helpful to veterinarians new to TCVM as it allows the user to quickly grasp the basics of effectively arriving at a TCVM diagnosis for their patients and therefore to institute correct treatment.

References
Objectives

- To understand the dosage of acupuncture.
- To understand how to enhance the acupuncture stimulation.

Introduction

Acupuncture has been used in horses for thousands of years.\(^1\) Studies indicate that acupuncture can be used for the diagnosis and treatment of lameness in horses.\(^2\)-\(^4\) Like a pharmaceutical drug, effects of acupuncture may depend on its dosage. The dosage is associated with size of needle, technique methods, numbers of acupoint used, duration, and frequency. Three tips to improve acupuncture results are also discussed.

Dosage of Acupuncture

Acupuncture is defined as the stimulation of specific point(s) on the surface of the body by insertion of a filiform needle resulting in a therapeutic or homeostatic effect.\(^5\) From a TCVM standpoint, the aim is to allow Qi (vital energy or life forces) to flow harmoniously, which for a Western practitioner can be seen as a stimulation of the nervous system. Studies have revealed that acupoints are located in areas of sensitive neuroimmune modulation.\(^6\)-\(^7\) Acupuncture analgesia is associated with the release of the neurotransmitters including beta-endorphin\(^8\) and serotonin\(^9\), and its anti-inflammatory effect is produced by regulating proinflammatory factors including interleukin-6 (IL-6) and cyclooxygenase-2 (COX-2).\(^10\)-\(^11\) These effects are closely associated with what is referred to as the De Qi responses, or the “arrival of Qi.” De Qi responses are often clinically observable myofascial or muscle fasciculations as the needle reaches the acupoint upon its insertion. Also associated are ear movement, lip movement, urination or bowel movement, and/or when the patient, sensing a neurogenic response, looks at the needle or veterinary acupuncturist. The Ling Shu book of the Huang-di-nei-jing (Yellow Emperor’s Classic of Internal Medicine) emphasizes, “The most important thing about acupuncture treatment is that the effect comes only with De Qi.”\(^12\) This basically means “No De Qi responses, no clinical results from acupuncture treatment.” These De Qi responses can be measured as the dosage of acupuncture that includes size of the needle, the depth of the needle insertion, number of acupoints used, the length and frequency of acupuncture stimulation.

The Size of Needles and the Depth of the Needle Insertion

Acupuncture treatment involves the insertion of thin sterile needles with a certain size (gauge) (Table 1) and length (Table 2) depending on species and location of acupoints.

Size and Length of Needles

The most commonly used sizes and lengths of acupuncture needle vary depending on species (Table 1). To simplify the practice, author recommends using 28 gauge for all large animals including horses, cattle, llamas and camels while 30 gauge for miniature horses, goats, sheep, alpacas and pigs.
Table 1: Acupuncture Needle Gauge, Length And Application

<table>
<thead>
<tr>
<th>Gauge</th>
<th>Millimeters</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>0.22</td>
<td>All small animals: cats, rabbits, small dogs, avian and small exotics</td>
</tr>
<tr>
<td>32</td>
<td>0.25</td>
<td>Goats, sheep, Alpacas, dogs</td>
</tr>
<tr>
<td>30</td>
<td>0.30</td>
<td>Goats, sheep, Alpacas, dogs, horses, cattle, llamas, pigs</td>
</tr>
<tr>
<td>28</td>
<td>0.35</td>
<td>All large animals: horses, cattle, llamas, pigs, elephants, Camels</td>
</tr>
<tr>
<td>26</td>
<td>0.40</td>
<td>All large animals: horses, cattle, elephants, Camels</td>
</tr>
</tbody>
</table>

Studies have indicated that many acupuncture points can have specific effects on the body, based on depth of stimulation. For example, acupuncture stimulation at ST-36 induced a decrease in sympathetic renal nerve activity (RNA) and mean arterial blood pressure (MAP) in rats under deep anesthesia. However, acupuncture stimulation at just the level of the skin of ST-36 did not induce any change of MAP and RNA. This suggests that the anatomic structures and physiologic effects of acupuncture points lies in the deeper tissues beneath the epidermis. Hence, the depth of the needle insertion impacts the De Qi and therefore the outcome of acupuncture treatment, as mentioned above. The most commonly used lengths of acupuncture needle depend on the location of each acupoint and species (Table 2). For equine practice, the most commonly used needles are 1, 2 and 3 inch. One inch needles are often used for the acupoints located at foot, lower limbs, face and tail, 2 inch used in the area of the neck, back, shoulder and stifle, and 3 inch used for the hip acupoints.

Table 2: Acupuncture Needle-Length And Application

<table>
<thead>
<tr>
<th>Millimeters</th>
<th>Inches</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>0.5</td>
<td>Goats, sheep, alpacas, pigs: Head, feet, lower limbs, ears, tail, front-mu (alarm) points Horses, cattle and llamas: ears/eyes, feet</td>
</tr>
<tr>
<td>25</td>
<td>1.0</td>
<td>Goats, sheep, alpacas, pigs: neck, shoulder, limbs back-shu (association) points Horses, cattle and llamas: feet, lower limbs, head, tail, front-mu points</td>
</tr>
<tr>
<td>40</td>
<td>1.5</td>
<td>Goats, sheep, alpacas, pigs: hip, shoulder Horses, cattle and llamas: back-shu points, limbs</td>
</tr>
<tr>
<td>50</td>
<td>2.0</td>
<td>Goats, sheep, alpacas, pigs: hip Horses, cattle and llamas: neck, shoulder, stifle, lumbosacral, hip</td>
</tr>
<tr>
<td>75</td>
<td>3.0</td>
<td>Horses and cattle: hip</td>
</tr>
<tr>
<td>100</td>
<td>4.0</td>
<td>Horses and cattle: hip</td>
</tr>
<tr>
<td>150</td>
<td>6.0</td>
<td>Horse: hip</td>
</tr>
</tbody>
</table>
Tip one: Do not use needles that are too small; they won’t induce good results, as they cannot generate enough De Qi Response. It is the authors’ recommendation to use 28-gauge acupuncture needle of varying lengths, depending on the location of acupoints in horses.

**Number of Acupuncture Points, Duration of Each Acupuncture Session and Frequency of Acupuncture Treatment**

In general, 10 to 20 acupoints are selected for each session of acupuncture treatments, and each session lasts about 10 to 30 minutes.\textsuperscript{14-16} Unlike the “I want to see results now” mindset of many of our clients, usually three sessions of acupuncture are needed for the treatment of clinical conditions.\textsuperscript{14-17} Hence, acupuncture often takes time to see significant improvement, especially since it is commonly used for chronic diseases.

Tip Two: Acupuncture takes time and usually three sessions are needed for the resolution of lameness in horses.

**Common Methods of Veterinary Acupuncture and Indications**

Two patients having the same disease process as diagnosed by western medicine may be diagnosed as having two distinctly separate “Pattern” diagnoses in TCVM. This is because a TCVM disease “pattern” is based on a patient’s specific personality type or “constitution”, their behavior, environmental and dietary impacts, as well as clinical presentation and pathologies. Therefore, each patient would be treated differently with TCVM according to its specific disease pattern, whereas in western medicine they would be treated identically based solely on their clinical signs.\textsuperscript{18} Four main patterns include 2 pairs - Excess vs Deficiency, and Heat vs Cold. Excess and Deficiency Patterns refer to the opposing forces between the body’s resistance and pathogenic factors during the course of a disease. As an example, an Excess pattern could present as erythema with a serous exudate, whereas a Deficiency pattern may present as dry flaky skin. Cold and Heat Patterns are used to determine the nature of a disease through the clinical signs of an imbalance of the body’s warming and cooling powers.\textsuperscript{19} For an example with these patterns, intuitively a Heat pattern would present as localized or systemic pyrexia, often with cool seeking behavior; and a Cold pattern as inadequate blood flow in the extremities, such as cold ears and legs, with heat seeking behavior. Some acupuncture methods are good at treating Excess or Heat, while others are good at Deficiency or Cold.

**Dry Needle (DN)\textsuperscript{12}**

DN is the most commonly used technique and involves the insertion of fine, sterile needles into specific anatomic areas of the body ("acupoints"). Mechanical stimulation can be applied to the needles manually if electro-acupuncture is not available and if the patient tolerates it.

*Indications:* DN is one of the oldest acupuncture methods and can be used in treating any pattern.
Cautioned and Contraindication: Caution is warranted in placing needles in the acupoints around the abdomen, as they are not easily accessed in horses and are often associated with reflexive kicks. In addition, in pregnant mares BL-67, SP-6, ST-36, ST-40, LIV-3 and LI-4, as well as the points around abdomen, should be used with judgement and skill.

**Electro-acupuncture (EA)**

EA involves the use of a mild electrical current by attaching electrodes and applying a mild electric current to the needles. EA enables deeper penetration of electric energy into the percutaneous and muscle tissue and promotes a more profound local and systemic analgesic response.

*Indications:* EA is often used for Heat patterns such as high fever; for Excess patterns including pain management, lameness, colic, and impaction; and for Deficiency patterns including diarrhea, infertility, and facial or radial nerve paralysis.

*Cautions and Contraindications:* Caution is needed in using EA in cases with seizures, neoplasia, a pacemaker or pregnancy. It is also a time-consuming protocol, thus may not be the first choice for a busy equine practitioner.

**Aqua-acupuncture (AA)**

Aqua-acupuncture, sometimes called pharmacopuncture, involves the injection of sterile liquids into acupuncture points in order to stimulate the point. AA may provide a prolonged stimulus at the point. Mildly caustic or autologous substances (i.e. blood) can also be used. Commonly used substances include saline, polysulfated glycosaminoglycans, Vitamin B Complex and Vitamin B-12.

*Indications:* AA is often used for myofascial or muscle pain, muscle atrophy, anorexia, diarrhea.

*Cautions and Other Comments:* Since AA is simple, relatively quick, with easy access, it is one of the most popular acupuncture methods used in the equine practice.

Tip Three: If aqua-acupuncture which is the most convenient, cannot produce the desired result, electro-acupuncture can be the back-up method in equine practice.

**Moxibustion**

This involves the heating of either an acupuncture point or a needle inserted into an acupuncture point with moxa, a type of bundled herb consisting of *Artemesia* (mugwort). Modern research indicates that the mechanisms of moxibustion mainly relate to the thermal, radiation, and pharmacological effects of moxa and its combustion products at the acupoint.

*Indications:* Moxibustion is good for Cold and Deficiency Patterns such as chronic arthritis, back pain and poor digestive and absorptive conditions.

*Cautions and Contraindications:* Moxibustion should not be used for a Heat pattern.
Low-level impulse Light Amplification by Stimulated Emission of Radiation (LASER)

This is the stimulation of an acupuncture point using a low-level impulse LASER.

**Indications**: It is effective for open wound or non-healing wound. It can be used in the acupoints in the area such as feet where the skin is thin, and horses hate to be needled.

**Cautions and Other Comments**: The results for the acupoints near the area where skin is dark colored or thick may not be as desired, in that the Laser may not be able to penetrate deeply enough. However, the penetration may be improved if the skin is pre-cooled with ice or clipped.

**Conclusion**

Acupuncture is relatively safe and effective for the treatment of lameness when practiced by skilled, accredited practitioners. Its clinical results depend on dosage of acupuncture (number of acupoints, depth of needle insertion, frequency, and duration), type of the acupuncture methods and pattern diagnosis.

**References**

How to Improve Acupuncture Results in Horses: Part 2
Huisheng Xie, DVM, MS, PhD

Objectives
- To understand top five indications of acupuncture in equine practice.
- To understand why the western medical diagnosis can improve acupuncture result.

Introduction
As the use of acupuncture has increased over the past few decades in countries where modern Western medicine is the foundation of health care, there has been increasing scientific effort to evaluate this ancient medical modality for objective evidence of efficacy.1-4 This paper will review the top acupuncture points for commonly seen lameness along with case examples.

There are over 300 transpositional and over 150 classical acupuncture points in horses.5 In TCVM, a western medical diagnosis may present different patterns due to differences in a patient’s personality, constitution, environmental and dietary impacts. Therefore, each patient should be treated differently according to a specific pattern. However, it takes a lot of training to be capable of differentiating each pattern based on the TCVM examination including tongue and pulse diagnosis. The information below is in a cookbook style outline of suggested acupoints for various disease entities with the intent to introduce a simple protocol for the listed clinical condition. To provide a more refined treatment with maximal effect, veterinarians should consult a certified veterinary acupuncturist (CVA) or certified TCVM practitioner for more accurate or detailed pattern differentiation and treat each patient with acupuncture and Chinese herbal medicine accordingly.

Acupuncture for Foot/Hoof/Heel Pain5,6
DN or EA at Top 5 local points: PC-9, Qi-ti-men, LI-3, SI-3 and TH-1 (Figure 1)
Add DN LU-11 when BL-13 is sensitive
Add DN LI-4 if LI-18 still sensitive
Hemo-acupuncture (HA) LI-1, SI-1 and TH-1 for acute laminitis

Acupuncture for Shoulder Pain5,6
DN: SI-1, SI-3, TH-1 and LI-3 (Figure 2)
AA: GB-21, TH-15, LI-16, Shen-shu, BL-11
EA: LI-15+TH-14, PC-1+GB-21, SI-9 + SI-10
AA or PA at Gong-zi or any muscle atrophy areas
Acupuncture for Cervical Stiffness Pain\textsuperscript{5,6}

\textit{DN}: SI-3, TH-1 and LI-3 (Figure 2)

\textit{AA or EA}: Jing-jia-ji, GB-20, GB-21, BL-10, BL-11, Jiu-wei (Figure 2)

Acupuncture for Back Pain\textsuperscript{5,6}

\textit{DN}: BL-67, BL-65, BL-60, Wei-jian (Figure 2)

\textit{AA or EA}: Hua-tuo-jia-ji, BL-20, BL-23, Shen-shu, BL-40

Acupuncture for Sacral and Hip Pain\textsuperscript{5,6}

\textit{DN}: BL-67, GB-44

\textit{AA or EA}: BL-23, Shen-shu, Shen-peng, Shen-jiao, Ba-jiao, BL-53, BL-54, BL-40

Acupuncture for stifle pain\textsuperscript{5,6}

\textit{DN}: ST-45, GB-44, BL-18, BL-20 (Figure 2)

\textit{AA or EA}: BL-40, ST-34, ST-35, ST-36, GB-32 and GB-34

Acupuncture for hock pain\textsuperscript{5,6}

\textit{DN}: BL-67, GB-44, BL-62 (Figure 2)

\textit{AA or EA}: BL-54, Shen-shu, BL-40, BL-60, KID-3, KID-7, GB-39
Case Study

Case example 1

A 10-year-old Thoroughbred gelding presented with acute onset of laminitis of both forefeet one week after prosthetic laryngoplasty. He had a history of white line disease in both front feet. Radiographic evidence showed that the distal phalanx of both thoracic limbs had rotated by roughly 10 degrees. The horse was pyrexic and was being treated with 2 grams Phenylbutazone* PO BID. On examination, the gelding's constitution was Wood. He was 4/5 lame on the left thoracic limb, and 5/5 lame on the right thoracic limb. His tongue was dark purple and his pulse wiry. The acupuncture points LI-17, LI-18, PC-1, and BL-13 (5/5) were sensitive bilaterally. A TCVM diagnosis of both front feet was Qi-Blood Stagnation and Liver Damp Heat, based on his history, his dark purple tongue, wiry pulse, and sensitivity on diagnostic points. Treatment for this case included the following:
Acupuncture:

*Phenylbutazone Powder

a. DN: Bai-hui
b. HA: TH-1, LI-1, SI-1 with 25-gauge hypodermic needles
c. EA: 20 Hz 20 minutes at the following 7 pairs of points, one session per week for 3 weeks:
   Shen-shen, bilateral
   bilateral GB-21 + BL-11
   bilateral Qian-ti-men + LI-3
   bilateral PC-9 + SI-3

Outcome: The gelding became less lame (lameness 2/5 in both front limbs) and was comfortable enough to move around in the pasture after 3 weekly acupuncture treatments. The horse was totally sound and galloped in the pasture after another 3 biweekly acupuncture treatments, using DN and EA at the same points described above. Since then the horse has become a pleasure riding horse and has had no foot lameness for the past 11 years at the writing of this chapter.

Tip Four: Aggressive, as in multiple sessions per week, acupuncture treatment can be used effectively for the treatment of acute laminitis in horses.

Case Example 2

A 20-year-old Quarter Horse gelding presented with chronic back pain of one-year duration. While being ridden, he would swing his right pelvic limb laterally and kick out. He had a history of right hock osteoarthritis. Corticosteroid injections into the hocks did not appear to improve the condition. The referring veterinarian had also diagnosed equine protozoal myeloencephalitis (EPM) based upon analysis of the cerebrospinal fluid. After three months of EPM medication, the horse seemed more alert, but he would still side-kick during rides. Extensive massage (each session lasting several hours) of his back and hip provided mild relief. Saddle changes gave no relief. The horse was a typical Earth constitution and tolerated well any type of treatment well (e.g. dental work, injections, shoeing, acupuncture needling). He had remained generally healthy his entire life, except for this side-kicking issue. As a pleasure riding horse (jumping and trotting) he was ridden about three times a week for about an hour each time. On TCVM examination, the gelding appeared alert with good Shen (mentation). His tongue was purple, and his pulse was deep and fast. On acupuncture point palpation (“scanning”), he was very sensitive (4/5) over points BL-13 through BL-21 on both sides. The points BL-38, BL-39, BL-53 and BL-54 were mildly sensitive (2/5) on palpation. The TCVM diagnosis for this gelding was Qi Stagnation of the back and secondary Stagnation in the pelvic limbs. Treatment included the following:
Acupuncture: 1 session every 3 to 5 weeks for a total of 3 treatments

DN: Bai-hui, BL-67, GB-44, BL-60

EA (at 20 Hz for 20 minutes) at the following 6-point pairs: Shen-shu + Shen-shu; BL-15 + BL-15; BL-18 + BL-18; BL-21 + BL-21; BL-40 + BL-40; BL-54 + BL-54

AA (5 milliliters of vitamin B5 per point): Hua-tuo-jia-ji along BL-17 to BL-21

Oral herbal medicine: Modified Shen Tong Zhu Yu Tang at 15 grams twice daily for 45 days

Outcome: After two acupuncture treatments and seven weeks of daily herbal medication, the horse's back pain and side-kicking behavior were 80% improved. After one further acupuncture treatment, these problems were clinically resolved. The previous rider and horse owner (her body weight was around 250 lb.) had been encouraged and sent this horse to her niece (weighed about 100 lb.) as a pleasure riding purpose. Subsequently the horse enjoyed 8 more years of pleasure riding and had no recurrent back pain before being retired to pasture as a sound horse.

Tip Five: Back pain can be caused by a rider, or saddle. These factors must be considered as part of your diagnosis and treatment of a sore back in horses.

Case Example 3
A 16-year-old Thoroughbred broodmare presented with severe pelvic limb lameness. During her racing career 10 years earlier, she had had a history of a hip fracture and tendonitis. After her retirement from racing, she produced three foals from normal pregnancies. On TCVM examination, the mare's lameness grade was 4/5 in her right hind limb. On her right side, BL-54, BL-53, Lu-gu, Huan-tiao and Huan-hou were very sensitive (4/5) on palpation. Her constitution was Earth. Her tongue was purple, swollen and wet and her pulse was deep and weak. The mare had desirable genetic traits; therefore, the goal was to make her sufficiently comfortable and prepared for the next breeding season. The TCVM diagnosis was Qi-Blood Stagnation of the hip with Kidney Qi Deficiency. Treatment included the following:

Acupuncture: 1 session per month for a total of 3 treatments

DN: ST-45, BL-67, GB-44, Bai-hui

EA (at 20 Hz for 20 minutes) at the following 6-point pairs: Shen-shu + Shen-shu; BL-54 + BL-54; BL-40 + BL-35 bilaterally; Left BL-38 + SP-5; Right Lu-gu + GB-29

Oral herbal medicine: Modified Shen Tong Zhu Yu Tang at 15 grams twice daily for 3 months

Outcome: The mare became pasture sound after three acupuncture treatments and three months of daily herbal medication. At this point, treatment of the infertility due to Kidney Qi Deficiency was initiated. The mare was prescribed Sheng Jing San (Epimedium Formula) at a dose of 30 grams orally twice daily for two months. As a result, the mare
went on to produce a further six foals before she was retired to pasture at the age of 23 years.

Tip Six: Infertility in mares might be caused pain. Pain must be resolved first before considering the fertility.

**Case Example 4**
An 11-year-old Dutch Warmblood gelding used for dressage and jumping competitions presented with significant lameness of the right pelvic limb. Four months earlier he had run into a tree injuring this right hind limb but had appeared to recover after four months of rest. However, when the rider started to train the horse again the lameness recurred. Initially, oral phenylbutazone (Phenylbutazone Powder) relieved the lameness, but six days later the horse presented to a conventional veterinarian with a grade 3/5 right pelvic limb lameness being unresponsive to the drug. Injections of local anesthetic into the right hock joint did not improve the lameness and no abnormalities could be detected via radiography, MRI or scintigraphy. The gelding was then referred for acupuncture. On TCVM examination, the horse was assessed to have a Wood constitution with adequate quality Shen. His pulse was wiry and his tongue purple. His caretaker described him as a good athlete who loved to run and compete, also as being dominant and aggressive towards other horses. On the left, LI-15 to 18 (3/5), BL-13 to 21 and BL-54/Lu-gu (2/5) were sensitive. On the right, BL-13 to 21, BL-39 (2/5) and BL-54/Lu-gu (4/5) were sensitive. The horse's TCVM diagnosis was therefore Qi and Blood Stagnation of the right hip and back. Treatment included the following:

**Acupuncture:**
DN: BL-67, GB-44, left LI-1, left LU-11

EA (at 20 Hz for 20 minutes) at the following 5 point pairs: Shen-shu + Shen-shu; BL-54 + BL-54; Shen-jiao + Lu-gu; Right BL-53 + BL-35; Right Da-kua + Xiao-kua

AA (5 milliliters of vitamin B5 per point): BL-18, BL-19, BL-40, BL-53, Lu-gu

**Oral herbal medicine:** Modified Shen Tong Zhu Yu Tang at 30 grams twice daily for two weeks followed by 15 grams twice daily for two months

**Outcome:** This horse received only one acupuncture treatment. Six weeks later, he had returned to work and the lameness was 95% improved. Later, the horse had a colic episode that was resolved by TCVM. He also had an episode of anhidrosis, which too was resolved by TCVM. After which the horse with his owner was 100% sound for a high-level competition.

**Conclusion**
Acupuncture stimulation, especially electro-acupuncture, can release neurotransmitters such as 5-HT and endogenous opioids including β-endorphin, which appear to be the main pathways in which acupuncture relieves pain. Although the strength of the clinical trials cited above vary, acupuncture has been shown to be a viable integrative treatment for back pain, foot pain, cervical stiffness, laryngeal hemiplegia and infertility in horses.
Acupoint sensitivity on palpation may be useful for the assessment of lameness along with conventional diagnostics in horses.

References
Like everyone else, I sometimes wonder these basic philosophical questions: Who am I? Where do I come from? And how did I get here? The key to these questions may originate from an experience in adversity I had during my first job.

I studied veterinary medicine at the Sichuan College of Animal Science & Veterinary Medicine, Rongchang, Sichuan Province, China. My college was one of the smallest veterinary schools in China at the time. During the 1980s in China, every college graduate was guaranteed a job, but it was assigned by college leaders based on student performance, not by the graduate’s choice. Immediately after receiving my veterinary medicine degree in the summer of 1983, I was dispatched to Beijing Agricultural University (BAU), the most popular university in China in the field of veterinary medicine (which has recently changed its name to China Agricultural University). I was so happy and felt I had the best of luck, not only because I went to the best veterinary medical school to teach, but also because I had never been to a big city or taken a train. Beijing was the biggest city and capital of China, and 2000 km far away from my hometown Tongnan. There were three main transportation methods during the 1980s: bicycle, bus, and train, and there was no way to travel to Beijing by bus or bicycle then. My train ride was exciting, as it was my first time experiencing a moving toilet and it was much faster than the bus, even though it took 50 hours to finally arrive in Beijing.

I liked my first job as a staff veterinarian and junior faculty member assisting senior professors/clinicians at the Department of Traditional Chinese Veterinary Medicine (TCVM), College of Veterinary Medicine BAU. The experience taught me a lot about how to treat patients, how to talk to clients and how to teach students. I had never realized I loved teaching until I delivered my first lecture for the TCVM Internal Medicine course to veterinary medical students. Even though my shirt was soaked with sweat due to nerves by the time the talk ended, I completed it and it went well! Since then, teaching has NOT been my job, but has been my love, passion, and hobby. I was recognized twice as the best teacher by the university. Life was so wonderful and colorful, not to mention that I also met a lovely young lady who soon became my wife during that time on campus.

I was even more excited when I heard that there was an opportunity open to junior faculty members to go to the University of Oxford in the UK to receive PhD training fully funded by the Ministry of Education, China. However, there was a problem: there was only one ticket available, and there were dozens of junior faculty members. In Chinese, we have an expression: “few bones, too many dogs.” Fortunately, I was a very lucky dog, as I was selected by college leaders as one of two finalists based on performance, including teaching and researching. I was from the department of TCVM, and my challenger represented the department of western veterinary medicine (WVM). The tiebreaker was simple and seemed fair, at least initially: whoever got a higher score on the English Proficiency Test (EPT), which the Department of Education had been using to select Chinese scholars to be sent abroad, would go to the UK. We had three months to prepare for the EPT. That was the first time I had studied English as hard as I did the TCVM, maybe even harder. To my surprise, my EPT score was 77 and my opponent only scored 63. I always felt my English was not very good compared against faculty
members from the department of WVM, as they had studied WESTERN medicine and their English should, therefore, be excellent.

I was so proud of myself and the entire Department of TCVM faculty celebrated for me. Everybody was so pleased that the TCVM department finally defeated the WVM department! In the end, however, the opportunity turned sour. The dean made the final decision and chose the other finalist from WVM. I was disappointed and very angry, so I confronted him to ask why. I never forgot his demeanor: his entire body was very calm and still, even his face and eyes, when he said so peacefully, “Huisheng, what would you learn from the PhD training in the UK, as your major is TCVM? We sent Mr. F.G. to get an infectious diseases training, which was the obvious and fair decision.”

I felt that this was not fair at all. I was cheated. My dream of going abroad disappeared from underneath me. I hated my dean. I hated BAU. I felt powerless and useless. I was even disappointed in myself. Why did I choose to learn TCVM in the first place; why didn’t I choose to pursue WVM?

As you can imagine, I was very angry, irritable, sad, and depressed every day. My life was miserable until I ran into one of my college friends in the street two weeks later. We had not seen each other since we graduated. He told me that he was currently a PhD candidate at the University of Minnesota and was on a summer vacation visiting Beijing. I learned from him that the basic tickets to enter a U.S. PhD program are the TOEFL and GRE. Yes, the TOEFL and GRE were the only things I needed to complete to go to school in the USA. Forget about the University of Oxford; forget about the UK. I was going to America!

When one door was closed for me, another door was clearly opened, and that was going to the USA for PhD training. I studied English very hard once again. I did well on the TOEFL and GRE. But the only way for me to receive a visa to enter the United States at that time was to get a full scholarship. After several years failing to find a university to sponsor the scholarship, Dr. Asquith, a great equine veterinarian and faculty member from the University of Florida (UF), was interested in my background and provided the needed scholarship. I finally arrived at Gainesville, Florida in 1994 for my own PhD training. I learned so much about immunology, molecular biology, neurology, and pain physiopathology. Before I received my PhD diploma in 1999, I became the UF faculty member specifically in charge of veterinary acupuncture services to both large and small animals. This veterinary acupuncture faculty was the first one of the veterinary medical schools in all western countries. Then I created the first veterinary acupuncture internship program in the world, along with offering acupuncture rotations to DVM students. There was initially a strong resistance to acupuncture at UF, but now we have four faculty members running the acupuncture and integrative medicine service and see over 20 cases daily.

Many years have since passed, and I now look back at the adversity I experienced at BAU with appreciation for my dean. It was he who changed my life greatly in a positive way. I am so happy to be where I am. If he had sent me to Oxford to get a more serious WVM training, I would probably have given up TCVM, and I would never be in the USA. F.G received a PhD from Oxford. He is a great scientist and world expert in virology. He is an academician of the
Chinese Science Academy and now is the director of Chinese CDC to lead to have contained this terrible COVID-19 outbreak in China.

My story was simple. Every one of us will experience failure or adversity sooner or later during our lifetime. When one door is closed to you, it is ok because that door was meant for others, and another door (often a better one) will open for you. If there is one thing to remember from this talk, in the face of adversity, take a deep breath in, smile, and look around you. Often the better door is right around the corner.
Black Box Theory - Philosophic Base for TCVM
Huisheng Xie, DVM, MS, PhD

Objectives
- To define what the Black Box Theory is
- To use Black Box to make a TCVM pattern diagnosis

History of Black Box
The initial idea of black box can be traced to two-port networks (quadripoles) that were created by a German mathematician, Franz Breisig, in 1921. In 1941, twenty years later, Wilhelm Cauer, another German mathematician and scientist, applied this idea in electronic circuit theory. Norbert Wiener, an American mathematician and philosopher, defined a black box to be an unknown system that was to be identified using the techniques of system identification in 1948. Since then, the Black Box theory has been widely applied to philosophy and science.

What is the Black Box?
A black box is a system or object which is purely external or phenomenological and its internal constitution and structure is unknown or irrelevant to being opened for inspection. The opposite of a black box is a white box, that is a system where the internal constitution and structure can be viewed. A white box is also referred to as a clear box, transparent box, or glass box.

As illustrated in Figure 1, a white box is transparent, like glass, as we can see all that is inside the box. On the contrary, we cannot see what is inside the black box. How the black box functions internally, however, can be tested and defined in terms of its "stimuli inputs" and "output reactions" (Figure 2). In other words, an observer or investigator is able to figure out how the black box functions internally by the relationship between the exterior appearance of something to its characteristics and behavior within (interior/inner).

For example, the school of behaviorism sees the human mind/brain as a black box in psychology. Since the brain cannot be opened to be examined, a psychologist can design a series of questions for a patient (input), and the responses from a patient (output) are analyzed to decipher the type of behavior issues present. Another example is that the earth can be treated as a black box when undertaking oil exploration. After exploration tests are conducted on the surface of the Earth (input), the signals from the surface (output) are analyzed to determine potential oil field locations.
White Box and Medicine
With a white box, we can see what is inside the box (Figure 1). All modern diagnostic devices including MRI, CT scan, radiographs and ultrasound help clinicians visualize the interior of the body and give an accurate diagnosis (bony changes, fracture, neoplasia and other pathologic changes); thus, they are the white box approach. Another example is exploratory laparotomy. The abdominal exploratory surgery is often used to investigate an inconclusive mass or other gastrointestinal disease in veterinary medicine. After the abdomen is surgically opened, a veterinarian is able to view pathological changes (such as masses), and a biopsy sample is collected when necessary for further diagnosis.

The Traditional Chinese Veterinary Medicine (TCVM) Diagnostic System
When TCVM diagnosis was developed several thousand years ago, ancient healers did not have modern diagnostic tools such as laboratory tests, radiography, ultrasound, scintigraphy and magnetic resonance imaging (MRI). Instead, the ancient medical practitioners could only rely on their senses to gather information about a patient’s condition. The practitioners visually evaluated a patient’s behavior and body appearance to identify abnormalities. They used their hands to feel the pulse and palpate the body. Their senses of hearing and smell allowed them to identify abnormal noises or odors coming from the patient. Over generations, TCVM practitioners established Si-zhen (“four diagnostic methods”) which provided a systematic method for collecting clinical data (external information from the patient) in order to make the correct diagnosis (Table 1).6 The theoretical principle behind Si-zhen is that changes occurring within the Interior of the body will be evident on the Exterior due to the connections among the organs. Thus, a practitioner can examine the Exterior signs to understand the condition of the body’s Interior Zang-Fu organs. This is well documented as "To know the inside by examining the outside" in the ancient traditional Chinese medical classical text Huang Di Nei Jing (Yellow Emperor’s Classic of Medicine). 7 For example, redness and swelling of the eyes may indicate a Liver Heat Pattern because eyes are associated with the Liver and redness and swelling correspond with Heat or Fire. The characteristics of Heat or Fire tend to ascend; thus, their pathological damage is not only in the Liver, but also in the eyes that are the Exterior portion of the Liver System. TCVM practitioners, therefore, can predict that the condition is Liver Heat or Fire (interior) when they see redness and swellings of the eyes (exterior).
Table 1: The Four Diagnostic Methods (Si-Zhen)

<table>
<thead>
<tr>
<th>Si-zhen</th>
<th>TCVM examination</th>
<th>Western Medicine counterpart</th>
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<tbody>
<tr>
<td>Inspection</td>
<td>Wang</td>
<td></td>
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<tr>
<td></td>
<td>• Examine the tongue characteristics and color patterns</td>
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<tr>
<td></td>
<td>• Observe the <em>Shen</em> (the Mind-state)</td>
<td>Observation</td>
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<tr>
<td></td>
<td>• Observe the general body condition</td>
<td></td>
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<tr>
<td></td>
<td>• Evaluate the quality and luster of the hair and skin</td>
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</tr>
<tr>
<td></td>
<td>• Listen to the voice quality (weak, muffled, strong and/or robust)</td>
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</tr>
<tr>
<td>Hearing</td>
<td>Smelling Wr.</td>
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</tr>
<tr>
<td></td>
<td>• Listen to breathing</td>
<td>Auscultation</td>
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<tr>
<td></td>
<td>• Auscultate heart and lungs</td>
<td>Olfaction</td>
</tr>
<tr>
<td></td>
<td>• Note odors from the body, breath, ears</td>
<td></td>
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<tr>
<td></td>
<td>• Question owner about medical history</td>
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</tr>
<tr>
<td></td>
<td>• Question owner about temperature-preferences, diet, personality, activity, clinical signs</td>
<td></td>
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<tr>
<td></td>
<td>• Feel the pulses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Palpate the Meridians</td>
<td></td>
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<tr>
<td>Palpation</td>
<td>Qie</td>
<td>Palpation</td>
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<tr>
<td></td>
<td>• Palpate the back-<em>Shu</em> (association) points and front-<em>Mu</em> (Alarm) points for sensitivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Palpate abdomen, lymph nodes, joints</td>
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</tbody>
</table>

Other examples of exterior observation revealing internal TCVM Patterns include gingival bleeding/ulceration with Stomach Fire, tongue ulcers with Heart Fire, nasal discharge with Lung disorders, diarrhea with Spleen Qi Deficiency and congenital disease with Jing Deficiency. In the first 2 exterior observations, the redness and swelling associated with gingival bleeding or ulceration and tongue ulcers corresponds to Heat or Fire. Since the Stomach Channel runs through the gingiva and the Heart opens into the tongue, the interior TCVM Patterns associated with these external clinical signs is Stomach Fire and Heart Fire, respectively. The nose is the opening for the Lung, therefore, nasal discharge/congestion (exterior) is associated with Lung disorders (interior). A watery, loose stool (exterior) is a diagnostic sign for Spleen Qi Deficiency (interior) as the primary function (*Qi*) of the Spleen is to digest/absorb food and move fluid. Deficient Spleen *Qi* fails to digest/absorb food and move fluid, leading to excessive dampness and watery diarrhea. Finally, a young white kitten born deaf, suggests a Kidney problem (hearing functions are associated with the Kidney), specifically a Kidney Jing Deficiency.

**Clinical Application of the TCVM as a Black Box**

Identifying relevant clinical signs is a common task in Western medical diagnosis; however, the concept of Zheng (Pattern of disease) is a much more formalized system in TCVM. In TCVM, the diagnosis is the TCVM disease Pattern (Zheng). A particular TCVM diagnosis is assigned to
specific combinations of clinical signs resulting from particular imbalances within the patient. A Western medical disease diagnosis analyzes significant clinical signs, laboratory tests and diagnostic images to find the underlying cause. Although Western practitioners do acknowledge that some diseases can produce stereotypical physical manifestations, such as Cushing’s disease in dogs; these disease patterns are less specific than in TCVM. The same Western medical diagnosis may correspond to different TCVM Patterns. Consider the following two examples:

Case Example One
A Western medical practitioner diagnosed two horses with bloody diarrhea as having Salmonella colitis because fecal cultures were positive for Salmonella species. The first horse was a two-year-old Thoroughbred filly who presented with profuse hemorrhagic diarrhea which had begun three days prior to presentation. She had a red tongue and rapid pulse. The second horse was an eighteen-year-old Thoroughbred mare who presented with a twenty-one-day history of bloody diarrhea. The mare had a pale tongue and weak pulse. Although both horses were diagnosed as having Salmonella colitis, their TCVM diagnoses differed; the first horse had an Excess Heat Pattern because of the red tongue, rapid pulse, young age and acute onset, while the second horse had Spleen Qi Deficiency based upon her pale tongue, weak pulse, old age and chronic diarrhea.

Case Example Two
A Western medical practitioner used allergy testing to diagnose two dogs with atopic dermatitis. One dog was a friendly and high energy two-year-old castrated male Labrador retriever with a Fire personality. He presented with constant pruritus and showed Heat signs (red tongue, a bounding pulse and cool-seeking behaviors) without Deficiency signs (weakness). The second atopic dog was a thirteen-year-old spayed female bichon frise that has had chronic allergies since she was young. She seemed less itchy as a geriatric dog but was weaker overall and still developed pyoderma and pustules on her ventrum. Her tongue was pale and dry. Her owner reported that she preferred comfortable places, drank a lot of water, and her body was slightly warm to the touch. From a Zheng perspective, these two dogs have two different Patterns of diseases, even though they both have the same Western diagnosis. The young Labrador showed signs of Excess due to an invasion of Wind-Heat, whereas the older dog had a Kidney Yin/Liver Blood Deficiency. Thus, for an effective Chinese medical treatment, the TCVM practitioner must accurately identify the signs indicating the kind of imbalance and not rely solely on the Western diagnosis.

Conclusion
The TCVM approach is like the black box. External information (clinical signs) displayed by patients is used to diagnose the correct TCVM Pattern which enables the veterinarian to select an appropriate treatment correctly matched to the pattern. It is a very useful approach, especially in clinical cases when a Western diagnosis is not available or is unable to pinpoint the etiology of a disease.

References
7. Chapter 47 of *Ling Shu (Miraculous Pivot), Huang Di Nei Jing* (Yellow Emperor’s Classic of Medicine). (In Chinese, originally published in 475-221 BC)