INTRODUCTION

Integrating Conventional and Complementary Therapies

Integrative veterinary medicine (IVM) blends the use of conventional therapies such as surgery and pharmaceuticals with diet, nutraceuticals and botanicals to address health conditions, as well as to optimize wellness in patients. Health conditions that can be treated with IVM range from the acute onset problems such as diarrhea and vomiting to chronic degenerative conditions such as osteoarthritis and renal disease to cancer.

In most cases, pharmaceutical therapies can be used concurrently with nutraceuticals or botanicals quite effectively. In some cases the use of nutraceuticals and botanicals can help to mitigate some of the side effects of pharmaceuticals. One example of that would be the use of milk thistle extracts to protect the liver from the potentially toxic effects of pharmaceuticals such as phenobarbital, prednisone or carprofen.

In other cases the use of nutraceuticals can help to enhance the effectiveness of pharmaceuticals, resulting in lower effective dosing. An example of this is the use of licorice root or EPA/DHA concurrent with prednisone to reduce the dosage of corticosteroid needed to create adequate anti-inflammatory effectiveness. Another example would be the use of grapefruit juice to help maintain therapeutic levels of cyclosporine compounds.

An example of an instance when the concurrent use of nutraceuticals would not be indicated would be with the use of fish oil at high doses in a patient who has a coagulopathy, is on anti-coagulants, or who will be having surgery soon (peri-operatively). High doses of fish oil can increase clotting times, and thus in some patients the value of their use needs to be closely examined.

More veterinarians are becoming involved with prescribing and dispensing dietary supplements in their practices. More companies are providing increasingly larger ranges of nutraceutical and botanical products. This is making the choices that veterinarians need to make in selecting products and applying them in clinical protocols much more complicated.

Not every veterinarian will become expert in the use of these novel clinical tools. Some will find one or two supplements that work for them and not expand their usage beyond that. Others will find their use of these supplements to markedly augment their clinical practice and will be continually upgrading their repertoire of supplements on their shelves.

This last section will provide some integrative protocols to help one get started in the clinical use of these new tools. These protocols have been used very effectively in this author’s clinical practice, but are by no means the only protocols available for use in the treatment of veterinary patients. One should try them clinically, and adopt those aspects of these protocols that work the best for each practitioner’s style of medicine.

The table below lists common chronic and degenerative veterinary diseases in the far left column along with their conventional therapies in the middle column; in the column
to the far right are suggested complementary therapies that can be used in combination with or (when appropriate) as “stand-alone” therapies for these conditions.

**TABLE A: INTEGRATING CONVENTIONAL AND ALTERNATIVE RXs**

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>CONVENTIONAL RX</th>
<th>ALTERNATIVE RX</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADDISONS DISEASE</td>
<td>Gluco- and mineralo- corticoid supplementation</td>
<td>Licorice root and adrenal extracts</td>
</tr>
<tr>
<td>LIVER DISEASE</td>
<td>Ursodiol, prednisone, antibiotics</td>
<td>Diet, milk thistle, NAC, ALA, SAMe, EPA/DHA. B complex, phosphatidylcholine</td>
</tr>
<tr>
<td>ARTHRITIS</td>
<td>NSAIDs, steroids</td>
<td>GAGs, MSM, AP, lifestyle changes, anti-inflammatory herbs, EPA/DHA</td>
</tr>
<tr>
<td>CANCER</td>
<td>Surgery, radiation, chemotherapy, euthanasia</td>
<td>Diet, EPA/DHA, arginine, glutamine, probiotics, medical mushrooms, transfer factors, IP6, Ozone, AP, Homeopathy, cell wall fractions, orthomolecular IV therapy</td>
</tr>
<tr>
<td>ALLERGIES</td>
<td>Steroids, antihistamines, hyposensitization, hypoallergenic diets</td>
<td>EPA/DHA, AOX, Homemade diets, homeopathy, AP, herbal therapies, immune balancing agents, addressing “Leaky Gut” with probiotics and glutamine</td>
</tr>
<tr>
<td>PHARMACEUTICAL TOXICITY</td>
<td>Discontinue pharmaceutical such as phenobarbital, NSAID, corticosteroid, chemotherapy agent</td>
<td>Milk thistle, EPA/DHA, probiotics, AOX, NAC, ALA, SAMe, addressing “Leaky Gut”, CoQ10, carnitine, taurine</td>
</tr>
<tr>
<td>CARDIOVASCULAR DISEASE</td>
<td>Digitalis, lasix, enalapril, benazepril</td>
<td>EPA/DHA, taurine, carnitine, CoQ10, hawthorn, magnesium, potassium, herbal diuretics</td>
</tr>
<tr>
<td>RENAL DISEASE</td>
<td>Modified protein diet, fluid therapy, phosphate binders</td>
<td>EPA/DHA, B complex, probiotics, NAC, glutamine, arginine, AP, TCM herbs, homeopathy</td>
</tr>
<tr>
<td>BEHAVIORAL DISEASE</td>
<td>Psychopharmaceuticals, behavioral modification training, euthanasia</td>
<td>Thyroid status, B complex, phosphatidylcholine, DHA and EPA, tryptophan, theanine, SAMe, kava, hypericum, TCM formulas, AP, Flower Essences, TTouch</td>
</tr>
</tbody>
</table>
INTEGRATIVE PROTOCOLS FOR SELECTED VETERINARY CONDITIONS

Diarrhea

Acute Diarrhea Protocol
1. Fecal examinations for micro-organisms and for parasites
   a. Multiple fecal exams may be necessary until pathogen is eliminated
2. Diarrhea Management therapy
   a. Appropriate conventional therapy based on fecal exams
      i. Amoxicillin
      ii. Metronidazole
      iii. Tylosin
      iv. Loperamide
   b. Rice Water fast or dietary white rice
   c. Probiotics
   d. Montmorillonite clay to adsorb toxins and stop diarrhea
   e. L-glutamine 500-1000 mg/kg SID-BID (Plumb’s 6th edition)
      i. Empiric dosage: 250-1000 mg BID-TID usually effective in this author’s experience; higher doses are non-toxic and may help if lower doses do not
   f. TCM herbals
      i. Huo Xiang Zheng Qi San
      ii. Shen Ling Bai Zhu San
      1. best with impaired pancreatic exocrine function

Chronic Diarrhea Protocol

Same therapeutics as Acute Diarrhea protocol with the addition of:
1. Food allergy panel and/or Elimination diet
2. “4-R” Program to improve intestinal mucosal barrier function

Diarrhea Management Therapies
1. Rice Water Fast
   a. Boil 1 cup of white rice (not minute rice!) in 6 cups of water, decant when liquid becomes creamy. Can re-boil the rice as many times as needed to produce more rice water.
   b. Rice water has been recommended by the WHO for use to treat diarrhea in developing nations. It’s mechanism of action is via a compound that is released when the rice is boiled that affects the chloride channel in the colon, causing it to re-absorb chloride ions, which carry with them sodium ions and water, which then dries out the stools, thus reducing water loss and diarrhea. (1)

2. White Rice and Chicken Baby Food Modified Fast
   a. Cook white rice (not minute rice) into a gruel like oatmeal with 1 cup of rice and 2.5 cups of water
   b. Dogs tend to inhale their food, so cooking it this way predigests it for them, and releases more of the rice which helps to control the diarrhea. The baby food is used to flavor the rice and add some protein for patient convalescent nutrient needs.
c. Fast animal for 24 hours, only allowing water, rice water and rice balls with baby food that contain medication and supplements. The medication is placed inside the rice ball with baby food and given to the pet as a treat. This medicates the pet and also allows a digestive system that is not working properly to have a chance to rest a little, by feeding a small amount of bland food, but at the same time provides supportive nutrition to the pet.

d. Intestinal protectants such as ground psyllium seed, slippery elm, marshmallow root powder, okra powder, aloe vera juice or extract, and licorice root all are helpful in reducing inflamed bowel mucosa.

3. Calcium Aluminosilicate (an evidence-based form of montmorillonite clay)
   a. Adsorbs toxins
   b. Helps to improve intestinal barrier function
   c. Helps to stop diarrhea
   d. In a clinical trial of dogs with intractable diarrhea following chemotherapy treatment for cancer, improvement in 75% of the patients with intractable diarrhea was observed. (2)

4. TCM Herbals for Diarrhea
   a. Huo Xiang Zheng Qi San (Pogostomom and Perilla Formula)
   b. Shen Ling Bai Zhu San (Ginseng and Atractylodes Formula) (helpful for EPI or borderline EPI patients—personal experience)

5. 4 R Program for Chronic diarrhea and Increased Intestinal Permeability
   a. REMOVE pathogens allergens and toxins.
      i. By lowering the “total load” (the body’s burden) of these troublesome substances, the immune system and liver do not need to work as much in processing them. This makes more energy available to these systems to direct toward re-establishing healthy patterns. Removal can be by elimination from the diet or environment, or by the use of agents such as antimicrobial agents to reduce the population of pathogenic organisms.
   b. REPLACE digestive factors that are inadequate or absent.
      i. Inadequate pancreatic or intestinal enzyme production leaves digesta only partially broken down, thus altering the environment in the bowel, providing opportunity for pathology to develop. The beneficial bacteria that produce short chain fatty acids (SCFA) from soluble fiber in the bowel need a narrow range of temperatures and pH, as well as adequate substrate for their activity. When food is only partially digested, the intermediate breakdown products of the ingested food that result is not conducive to the normal function of these probiotic species.
   c. REPAIR damaged intestinal mucosal barrier
      i. The use of the free form amino acid l glutamine has been found to reduce bacterial translocation, and to increase the protein synthesis of the enterocytes which enables them to increase their rate of self-repair. The phospholipid-rich compound lecithin, and the omega
three fatty acids commonly found in fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are also integral to the repair of intestinal mucosa damaged from disease, stress or diet. Antioxidants reduce ROS damage to intestinal mucosa. Zinc and Vitamin B5 (pantothenic acid) are involved in the mucosal repair process. Soluble fiber promotes SCFA production which provides nourishment for repair of damaged lower bowel mucosal cells. Rice protein solids have been found to reduce intestinal secretions and improve reabsorption of water from colonic digesta. This is why the Rice Water Fast has been recommended for treating diarrhea in developing countries by the WHO.

d. **REINOCULATE** w/probiotic microflora cultures and accessory nutrients to create a healthy bowel ecology
   i. Normal indigenous GI bacterial flora are an extremely important factor in maintaining the healthy GI mucosal barrier. Anaerobes are the most numerous bacteria in the bowel. These commensal beneficial microorganisms compete with potential pathogens for nutrients and for attachment sites to the mucosa, and thereby inhibit bacterial overgrowth by the pathogenic gram negative bacteria. Antibiotics can upset this balance between the good bugs and the bad bugs. H2 blockers, as well as hyperosmolar enteral diets can result in bacterial overgrowth and colonization of the stomach.

**Atopic Dermatitis Protocol**

1. Thorough history and examination including a diet history
2. Allergy testing and Immunotherapy
3. Thyroid testing if warranted
4. Antihistamine use recommended
5. Diet changes based on findings
6. Topical therapies
7. EPA/DHA
8. Probiotics

Pet allergies are usually very complicated and can be quite frustrating cases. There are no “magic bullets”, unfortunately, in either conventional or alternative therapies. But there are a few evidence-based uses of nutraceuticals and botanicals that can help the allergic patient to feel better. This author’s approach to Atopy blends the best elements of conventional therapies with the best elements of alternative therapies to create the best possible position for a successful outcome in the allergic patient.

Allergies in pets can come from immunologic reactions to food, or inhalants or contact allergens. It is important to figure out which of these are involved in a given patient’s allergic dermatitis. Most pet-owners are told at the pet food store that food allergies are very common, which gives the pet food store the opportunity to sell a variety of different diets, as a solution to the misery the pet is suffering through with its allergies. This benefits the sales figures for the pet food store, but may not be helpful at all to the pet.
Veterinary dermatology research has determined that food-allergic patients only constitute 15% of all allergic animals. That figure could be as high as 25%. But food is one thing we can change. We can’t always move the cedar tree that has been growing in the front yard for the past 50 years.

For that reason, this author always starts with taking a diet history and seeing if there are any correlations between diet changes and improvements or “deprovements” of the allergic symptoms. This empirical-historical data can help with the selection of a hypoallergenic diet, or in the designing an elimination diet. Food should be selected that does not contain any of the ingredients that were in any prior diet fed that seemed to increase allergic symptom expression.

Although most veterinarians are more comfortable recommending manufactured pet food diets, home preparation of the pet’s diet can be taught to the client in a way that is effective, balanced, complete and nutritious. This author has been counseling clients for the past 25 years in the preparation of wholesome diets for their pets with a great deal of success and very few problems, except for the extra time it takes to do the nutritional consultation.

Veterinary fees should reflect the increased time and expertise on the part of the veterinarian who is providing nutritional counseling. There are several websites and veterinarians (both board certified and not) who offer this advice for a fee. (See resource list below) This can be a good compromise for the client whose pet would benefit from home prepared meals and a veterinarian who is open to that but who doesn’t know where to start.

By the way, home prepared diets do not need to be raw to be nutritious. Cooking at regular kitchen temperatures does not adulterate the food the way the high temperatures and pressures associated with the manufacture of commercial foods can.

If in taking a thorough history of the atopic patient it becomes evident that there is a seasonal nature to the allergic symptoms, then the suspicion that it might be an inhalant allergy becomes possible. If symptoms increase in the winter, we think about dust mites and mold and other allergens from the indoor environment as being the possible culprits.

On the other hand, if the symptoms increase during the growing seasons, then it might be related to grasses or trees or flowers. If the symptoms continue basically unchanged throughout the year, it could be both indoor and outdoor environment, or it could be neither and might be related to diet. There is no reason why a patient would have either dietary allergies or inhalant allergies but not both. One study suggests that upwards of 20-30% of patients may have allergies to both food and inhalant allergens. (3)

For this reason this author tries to convince the client to see a board certified dermatologist for a work up which may include serology or may involve skin testing and an elimination diet. If they don’t want a referral, then allergy testing is highly recommended for both food, indoor and outdoor allergens.

Current food allergy serology testing technology is based on an evaluation of serum for IgE specific to individual food ingredients has been evaluated by the American College of Veterinary Dermatology Task Force and found to have a number of problems associated with its reliability as a testing standard. (4)
In this author’s experience, the results of the IgE food allergy serology can be used as a starting point when designing an elimination diet, although strict adherence to the findings is not advised. It is one additional factor to take into account when developing a hypoallergenic diet. Elimination diets are considered the gold standard by dermatologists for determination of allergenic food ingredients.

Recently, a new food allergy serology test using saliva has become available based on IgA and IgM responses. Preliminary studies suggest that this testing methodology should yield highly accurate results, thus reducing the time it takes to develop a truly hypoallergenic diet. (5) (6) (7)

Using the results of the allergy testing, combined with a thorough diet history, a hypoallergenic diet can be selected or prepared at home, and immunotherapy can be initiated. Often success rates as high as 75% (or higher) can be achieved with immunotherapy combined with dietary changes and the use of appropriate pharmaceuticals and dietary supplements.

This author also recommends thyroid testing to include the use of Free T4 as well as checking for autoantibodies to rule in or rule out autoimmune thyroiditis. If the patient is hypothyroid, supplementation with the appropriate dosage of thyroid hormone will improve the patient’s condition substantially.

This author has a client handout of OTC antihistamines and suggests that the client try a number of them until they find the one or ones that are most effective for their allergic pet. Sometimes a pet will get used to the same antihistamine over time. By alternating the use of the antihistamines that have shown efficacy for that patient when the effectiveness of one is attenuated, increased relief of symptoms may occur. Reducing the long term use of steroids is very important to the success of immunotherapy. The side effects of steroids can be as bad as the effects of the allergic symptoms. Substituting antihistamines can be a good solution. Using a very low dose of steroid combined with antihistamines at higher doses can also be very helpful in relieving the debilitating symptoms of atopy when antihistamine use alone is not sufficient.

The use of cyclosporine compounds (Atopica™) have been shown to have some efficacy in treating atopic patients. These compounds are costly, but can help to relieve the debilitating symptoms of atopy in many patients. Side-effects are few and rarely more serious than vomiting or other GI effects. These compounds blunt the T cell activity that underlies the atopic response, thus relieving or reducing the severity of atopic symptomology.

Topical products can be very helpful. The selection of the product depends quite a bit on the type of dermatitis being treated. Shampoos that have benzoyl peroxide are good for cleansing the hair follicles if the pathology is involved with that anatomical structure. Shampoos with oatmeal are emollient and can help with dry hair and skin but should not be used if an allergy to oatmeal is suspected. Shampoos that have tar and sulfur in them can be very effective for reducing seborrhea and reducing pruritis. Some of these shampoos have been altered due to concerns with the use of pine tar.

Conditioners can also be very helpful. This author has used a leave on conditioner that contains 1% hydrocortisone that can be used to cover large areas of rashes or hot
spots, or can be used as a whole body rinse with a great deal of efficaciousness, sometimes for as long as a week’s worth of relief.

For patients whose dermatitis is the result of a staph infection or for whom the staph infection is secondary to the dermatitis, the pulsed used of cephalaxin is very helpful. If this treatment is effective and if the staph infections are recurrent, then by giving the cephalaxin for 2 weeks on or 4 weeks on and then 2-4 weeks off is one way that the staph dermatitis and the strong pruritis that it causes can be best managed.

All of the above therapies would be considered to be “conventional” in nature. Yet many veterinarians only will use steroids for these miserable atopic patients. Steroid use is effective but comes with a cost in terms of the liver, the adrenal glands and the skin hair coat when iatrogenically cushingoid.

EPA/DHA

Two studies that support the effectiveness of EPA in the treatment of atopic dermatitis are described below. The dosage derived from the use of EPA combined with DHA as an intervention for atopic dermatitis by this author has been found to have benefit for many of these difficult-to-treat atopic patients.

In a double blinded placebo controlled washout study of 16 dogs with atopic dermatitis, one group was given EPA (180 mg) and DHA (120 mg) per 10 pounds of body weight (4.5 kg) daily for 6 weeks. The other group was given corn oil (570 mg Linoleic acid & 50 mg gamma linolenic acid) per 10 pounds of body weight daily for 6 weeks. Following a 3 week washout period, the treatment groups were reversed.

Statistically significant reduction in pruritis scores, alopecia and self trauma, and improved scores for coat character was found for the group receiving the high doses of fish oil. (8) This is a 40 mg/kg dose of EPA and a 27 mg/kg dose of DHA, or a combined dose of 67 mg/kg of EPA+DHA daily.

A 12 week randomized double-blind placebo-controlled multicenter clinical trial of 60 dogs with atopic dermatitis evaluated the steroid sparing effect of fish oil supplementation. These dogs were randomly assigned to receive a combination of borage seed oil (source of gamma linolenic acid (10.5-12.5 mg/kg)), fish oil (source of EPA/DHA (1-2 mg/kg EPA & 0.7-0.8 mg/kg DHA ) and linoleic acid (19-20 mg/kg) or a placebo consisting of medium chain triglycerides in addition to prednisolone. All dogs received the same basal diet.

A visual analog pruritis score was used by the dog’s owners to record daily findings. The dosage of prednisolone was established based on this pruritis score according to written instructions. The use of prednisolone during the test period was lower in the treatment group although it was not a statistically significant difference. It was found, that by day 64 in this study that the difference between the treatment group and the control group became statistically significant, and continued to increase as the study progressed.

At the end of the study, the pruritis score and the total clinical scores were lower for the treatment group. This study concluded that there is a steroid sparing effect of fatty acid supplementation in canine atopic dermatitis and that there is also a time lag before the effect is attained. (9)
The clinical significance of this study is that it takes 2-3 months for the full effect of fatty acid supplementation. Clients need to be counseled to be patient and continue to supplement with fatty acids for at least 3 months.

**Probiotics**

Studies of atopic pediatric patients have found that probiotics can serve as a primary intervention. (10) The development of the healthy microfloral ecology in the neonatal and pediatric patient plays an important role in the development of the healthy immune response and gastrointestinal function. The use of antibiotics in this developing ecology can create problems which the use of exogenous probiotic species administered orally can counteract. (11)

Most veterinarians will tell you that there is an epidemic of allergy cases. Perhaps some of this increase can be attributed to the indiscriminate use of antibiotics without concurrent use of probiotics. If veterinarians were to dispense probiotics with each dispensing of antibiotics, it is possible that this allergy epidemic could become significantly reduced.

It is thought that probiotics contribute to the healthy development of the immune system. The gastrointestinal system, with its large surface area exposure to the external environment of pathogens, antigens and toxins contains the majority of the immunocytes in the body (60-70%). This tissue is called the Gut Associated Lymphoid Tissue (GALT). Probiotics modulate the immune system by communicating with the GALT, and by preventing the colonization of pathogenic bacteria. (10)

Recent advances into understanding the role that probiotics play in the pathogenesis of atopy points to the early development of “tolerance” to foreign antigens due to the interaction of naïve T lymphocytes in the intestinal mucosa with probiotic species. When these T lymphocytes are exposed to probiotic species early in their differentiation they are less likely to become reactive to foreign antigens. It is in fact this increased intolerance to foreign antigens that underlies the development of atopy, along with genetic factors in the neonate. (12)

With early intervention by the exogenous administration of an adequate inoculum of the appropriate species of probiotics to the young and developing puppy or kitten, it may be possible to reduce the development of atopy in susceptible individuals. This is borne out by clinical research studies in atopic children (13). For this reason, in an attempt to help combat the rising epidemic of allergies alluded to in an earlier paragraph in this section, this author recommends the use of probiotics in his first examinations of puppies and kittens. This recommendation is as a preventative, with the hope that it will help to reduce the incidence of allergic dermatitis in our veterinary patients.

Probiotics are used as one of this author’s first interventions when addressing the problems of the atopic patient.

**Neoplastic Disease**

**Protocol**

- Accurate diagnosis is essential
- Establish goals of pet’s guardian
• Recommend referral to medical oncologist/radiation oncologist or surgical oncologist if one has not already been seen
• Work with therapeutics offered by oncologist
• “Cancer” diet
• Chemotherapy/Radiation adverse side-effect mitigation
• Chemotherapy/Radiation efficacy enhancement
• Protocols if not on Chemotherapy/Radiation or if in remission are different than Chemotherapy/Radiation protocols
• Recommended Daily Supplements (no interference with Chemotherapy/Radiation):
  o L glutamine (0.5 mg/kg/day divided BID-TID PO; can also be used as an oral rinse with radiation induced mucositis
  o DHA (30 mg/kg/d)
  o Probiotics (2-10 B CFU/d)
  o CoQ10 (2 mg/kg/d)
  o Carnitine (10 mg/kg BID)
  o Arginine (10 mg/kg BID)
  o Silymarin (15-25 mg/kg BID)
  o Green tea (Camillia sinensis) 10-20 mg/kg/d (standardized to 80% polyphenols and 55% EGCG) (14, p 576)
• Immune-Modulating Supplements
  o Beta glucans: Medical Mushrooms & Yeast extracts
  o Arabinogalactans
  o Astragalus (50-400 mg/kg divided TID PO) (Wynn p. 479)
  o Cell wall fractions (muramyl di- and tripeptides)
• Anti-Neoplastic Supplements
  o Neoplasene™ (topical or oral or intra-lesional injection)
  o PolyMVA™ (PO or IV)
  o Artemesinin
  o Vitamin A & Vitamin D
  o Ascorbic acid IV in very large doses (1 gm/kg/d IV q 3 consecutive days)
  o Ozone therapy (Rectal, IV, intra-lesional)

Cancer is on the rise. Cancer is the most common natural cause of death in dogs and cats that are older. In fact, cancer accounts for nearly 50% of pet deaths each year. Pet cancer rates are comparable to human cancer rates. (15) This also means that more of your patients will be presenting to your hospital for your help with cancer therapies or to deal with the side-effects of cancer or of cancer therapy. In spite of advances in chemotherapy and radiation treatments, the patient with cancer faces a number of challenges that simply removing the tumor does not address.

The multi-modal approach of blending conventional therapies with evidence-based complementary therapies and providing support for the cancer patient and their care-givers will create the best quality of life (QOL) for your patients. By acknowledging the emotional sides of a diagnosis of cancer, and by addressing it with whatever means are most appropriate, creates a positive attitude that can help both patient and client. The
details of this bond-centered approach to oncology have been published in Canine and Feline Geriatric Oncology by Villalobos. (16)

A recent survey of veterinary cancer patients at Colorado State University’s Veterinary Hospital found that 76% of 254 pets were receiving alternative therapies. Nutritional therapies were being used by 40% of these patients, followed by prayer (38%), diet (35%) and vitamins (30%). Perhaps the most important statistic from this survey, though was that 65% of these clients were not telling their veterinarians about their use of these therapies. (17) How many of your cancer patients are going to the internet or to non-veterinarian “Animal Holistic Consultants” to use alternative therapies and not telling you about it?

This author integrates evidence-based complementary therapies with conventional therapies into his everyday practice. One of the most common problem addressed by this approach in the author’s practice is cancer. It is not uncommon for clients to want to hide the fact that they were coming to this author for alternative therapies from their veterinary oncologist or regular veterinarian. These people are encouraged to give full disclosure of their visit to an integrative practitioner, and of their use of these complementary therapies.

This author sends standard referral letters to those veterinarians or oncologists who have referred their patients for an integrative approach. Veterinarians who are trained and skilled in integrative veterinary medicine are becoming more common. If this approach is one that you as a veterinarian are not comfortable with, there may be colleagues in your community, or nearby, or available by telephone or email who you can responsibly refer patients to for this integrative oncology approach.

**Diet and Cancer**

Nutritional support of the patient with cancer is very important to the QOL and to successful cancer therapy. Commonly, cancer will rob the body of its vital nutrients, leaving it in a weakened and cachexic state that allows the further progression of the cancer and reduces success of cancer therapies. Malnourishment and starvation are one of the most common causes of death from cancer. By feeding the cancer patient and not also feeding the cancer, one can improve the patient’s response to the cancer and to the cancer therapies. Many cancer patients become finicky about their food as a result of their illness. Their taste preferences may change, and the cancer or the cancer therapies can also alter their appetite. Many dogs and cats will start to turn their noses up at commercial kibble, and may even reject canned diets as well. For these patients, feeding a home prepared meal may improve their appetite and increase their food consumption and subsequently, help to maintain their healthy body weight.

**Home Prepared Food**

Fresh and wholesome home prepared diets, minimally processed, contain a much wider diversity of macro and micro nutrients than commercially manufactured diets. Home prepared meals are rich in food bound antioxidants and phytonutrients that have cancer chemopreventive properties. Balanced and nutritionally complete home-prepared diets are simple to prepare and can be easily modified to adapt to a patient’s individual needs. These diets, due to their increased palatability can also serve as vehicles to hide supplements or medication to facilitate the long term administration of medications and
dietary supplements that cancer patients often require. Another benefit of home prepared meals for cancer patients is the “bonding” experience that it creates. Many cancer patients are living out their last days/weeks/months, and for their human guardians to take the time to express their love for their animals by preparing their meals is a memorable experience that helps to reduce the emotional pain they are feeling over the incipient loss of their beloved pet.

**The “Cancer Diet”**

Research studies have found that the metabolism of the cancer cell is different than a healthy cell in many ways. Cancer cells take in large amounts of glucose and use anaerobic glycolysis which results in a small energy gain for the tumor, but with the byproduct of increased lactate levels in the cancer patient; the patient uses the Cori cycle to convert the lactate back to glucose. The net result is a loss of energy for the cancer patient. Thus, a cancer patients’ metabolism is not unlike that of a Type II diabetic having glucose intolerance, increased hepatic glucose production and insulin resistance. Dogs with lymphoma and with non-hematopoietic malignancies have elevated lactate, resting insulin and glucose levels. (18) (19)

In a study of 90 canine patients with non hematopoietic malignancies elevated lactate and insulin levels were measured which persisted even after all the cancer was successfully treated. (20) In another study, 32 dogs with Stage III or IV lymphoma were randomized to receive one of two diets supplemented with menhaden fish oil and arginine or an identical diet supplemented with soybean oil. Both groups of subjects were receiving doxorubicin chemotherapy and fed the diets before and after remission had been achieved. Dogs with Stage III lymphoma in this study that were fed the experimental diet had significantly increased disease free intervals and survival times, as well as lower lactic acid responses to intravenous glucose and diet tolerance testing (21). This study serves as the basis of the only veterinary specific diet in the market-place for cancer patients, N/D by Hills. An increase in proteins that are highly digestible (“comfort proteins”: “small molecules that passively and sometimes actively pass through the GI tract and cause the feeling of satiation and comfort and nourish the patient”) are beneficial to the cancer patient. (22) Diets that are higher in protein and fat calories (like the Atkins diet) help to improve insulin regulation, which, due to the altered metabolism of the cancer patient, can help to improve clinical outcomes as demonstrated in the Lundholm study where insulin was given to cancer patients and improved clinical outcomes resulted. (23)

**Recipe for Home Prepared Food**

Home prepared cancer diets use proportions of these macronutrients comparable to those used in the above study, with fish oil and arginine added. (CHO: 10%; PRO 50-75% for dogs 90% for cats; Veggie 10-30%; 1 capsule standard strength fish oil per 10 pounds of body weight daily; Lite Salt (KCL/NaCL) 1/8 tsp/20#/d; Calcium 10 mg/#/d; multivitamin; (24) Flax seed freshly milled 3T/25#/day or flax seed oil 1 T/25#/day). Increased fat calories in this diet are supplied not only by high doses of fish oil, but also by the use of flax seed oil or freshly milled flax seeds added to every meal. Flax oil is high in fat calories and also contains ALA which may have beneficial effects for patients with cancer. (25) (26)

**Fish Oil and Cancer**
The two biologically-active fatty acids found in fish oil have been intensely studied for the past 10-15 years for their benefit to cancer patients. Studies have found that fish oil does not interfere with the pharmacokinetics of doxorubicin when used in canine patients with lymphoma. (27) Fish oil, when fed in large amounts to canine patients diagnosed with lymphosarcoma Stage III who were also fed the “Cancer Diet”, had improved patient survival times, whether they were receiving chemotherapy or not. (21) It is thought that since the metabolism of patients with lymphoma and non-hematopoietic malignancies is similar, as based upon prior cited studies, that the same diet that showed benefit to lymphoma patients could also be beneficial to patients with non-hematopoietic malignancies. The studies are lacking but the evidence is suggestive of this. In one study it was found that the use of DHA with alpha tocopherol (isomeric form of vitamin E) reduced the effectiveness of doxorubicin in the treatment of mammary cancer in experimental animals. (28)

Studies into the use of fish oil use in cancer have found a benefit for patients with cancer cachexia (29). Piroxicam is used as an NSAID and COX-2 inhibitor, which can reduce the growth of cancer cells, particularly as regards osteosarcoma. A recent study has found that the concurrent use of fish oil with piroxicam creates a synergistic response. This is because the use of these two agent together enhances the apoptotic effect of the EPA. The cyclooxygenase enzyme is responsible for the conversion of EPA intracellularly, and it was unknown if the concurrent use of these two agents would reduce the effectiveness of EPA. In fact, piroxicam it seems to increase the effectiveness of EPA as an apoptotic agent. (30)

The recommended dose for fish oil for cancer, based on the prior cited studies is about 30 mg/kg/day of DHA. The EPA that is given along with the DHA with fish oil will help to improve patient outcomes. This will be a high dose of fish oil for many patients. To avoid diarrhea or pancreatitis, the fish oil should be introduced gradually. The use of fiber, both insoluble and soluble can help to dampen any GI reaction to that amount of oil. This author recommends flax seed meal to increase the fat content of the cancer diet with a healthy fatty acid, alpha linolenic acid, that has some evidence of benefit to cancer patients. Fiber will bind carcinogens, the lignans in flax seed competitively bind with estrogen receptor sites, thus reducing the adverse impact of toxic estrogens that come in food, pesticides and from our own bodies. This is a similar effect (competitive binding at estrogen receptor site) that soy isoflavones share with flax phytolignans.

**Antioxidant Use in Cancer Patients**

The use of antioxidants in the cancer patient concurrent with chemotherapy or radiation has been a controversial topic. Research supports both points of view, with the variables of which particular antioxidant, dose, cancer type, and type of cancer treatment creating either positive or negative results. Experimental modeling of complementary cancer therapies may not lend itself well to good measurements of the true benefit of dietary supplements, due to the complex nature of their biological activity. Epidemiological studies and clinical studies of phytochemicals’ influence on cancer has found that eating fresh wholesome antioxidant and micronutrient rich foods is chemopreventive in its effect on cancer. Quite a few studies have found a positive influence on improving patient response to cancer therapies and/or mitigating
chemotherapy side-effects associated with eating wholesome diets and taking dietary supplements. (31) (32) (33).

**Positive Studies of Antioxidant Benefits**

Antioxidants have been found to help mitigate the damage done by chemotherapy and radiation therapies, as well as mitigate the pathology of the cancer itself. Simone (34) (35) performed an extensive literature review and found overwhelming support for the benefits of supplementing with antioxidants concurrent to chemotherapy and radiation. Conklin (36) found benefits to patients receiving chemotherapy who also were taking antioxidant supplements. Salganik in his 2001 review of chemotherapy use with concurrent antioxidant supplementation urges for using the measurement of oxidative stress in an individual patient as the criterion for the safe and effective use of antioxidant therapies. He stresses that excessive amounts of antioxidants can have a pro-oxidant effect, or could negate the mechanisms of oxidative stress that chemotherapeutic and radiation therapies use to create their effects and side effects. He also mentions that a certain amount of oxidative stress is important to maintain the body’s normal homeostatic mechanisms. (37) The immune system uses oxidative stress to destroy pathogens and newly formed cancer cells that arise from carcinogenesis or mutation.

**Antioxidants Can Interfere with Cancer Therapies?**

The n-3 Long Chain Polyunsaturated Fatty Acid (n-3 LC-PUFA) Docosahexaenoic acid (DHA: c-22) has been found in a number of in vivo studies to enhance the effectiveness of chemotherapy and radiation cancer therapies. It is thought that there are a number mechanisms of action that enable this effect, including increasing oxidative stress, anti-angiogenic and pro-apoptotic mechanisms. (38). Recent research though has found that the administration of alpha tocopherol, one of the isomers of the naturally occurring vitamin E complex will reduce the beneficial effect of the high dose DHA as used in this study (1-1.5 grams/m). (39) (40).

Several different non-pharmaceutical formulas of nutraceuticals and botanicals have been developed to treat cancer. Simone and Simone, in their 2 article series, “Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival” (34) (35) proposes that antioxidants function in more ways than just as free radical scavengers, and that, due to the different metabolism of the cancer cell from healthy cells, neoplastic cells will accumulate excessive amounts of antioxidants which can shut down the oxidative reactions necessary for generating energy within the cell. These articles discuss the many other actions listed in this article that antioxidants use to generate negative biological effects on cancer cells.

Another 2007 study discovered that hypoxia inducible factor (HIF-1) levels are reduced with either supplementation by the antioxidants vitamin C or n acetylcysteine. HIF-1 is a transcription factor that is stabilized due to local tissue hypoxia. When it is activated by low oxygen tension it significantly contributes to the induction of VEGF (vascular endothelial growth factor) which leads to angiogenesis of the tumor, and progression of the cancer. The adaptation of the HIF-1 to the hypoxic tumor microenvironment results in increased glucose uptake, lactate production, and angiogenesis. The authors of this study believe that this mechanism of HIF explains the “anti-tumorigenic effect of antioxidants in general. (41)
What To Do Clinically?

Clinically, for those cases where DHA is being used at high doses for its lipid peroxidative effect to assist anthracyclines or other chemo agents and radiation that use oxidation for their effect, it would be wise to not use alpha tocopherol at all. However, many veterinarians and veterinary oncologists have taken this to mean no antioxidants with any therapies at all, an opinion that had been held prior to this study by many oncologists, both human and veterinary.

To completely eliminate the use of antioxidants for cancer patients may be doing a disservice to the patients, with the number of studies indicating that in many cases moderate levels of antioxidants can improve the effectiveness of cancer therapies. Also note, that for this study, it is the effect of alpha tocopherol on the effect of DHA on chemotherapy that has been studied. It may be safe to use plant based antioxidants like ECGC from green tea, or utilize the antioxidant benefit of whey protein inducing glutathione, or Co Enzyme Q10 for lipid peroxidation as well as to help protect the heart from the cardiotoxicity of anthracyclines. (34) (35)

PolyMVA™ for Pets

One of the better-researched of alternative cancer products; developed by a research chemist and dentist, it contains the rare earth palladium, complexed with lipoic acid, and containing n acetylcysteine and other antioxidants and B vitamins, this formula interferes with the electron transport in the mitochondrion of the cancer cell, thus depriving it of cellular energy to divide, thus resulting in cell death. It is administered by mouth or intravenously.

A veterinary oncologist tested this compound in a number of patients with a wide variety of conditions concurrently with his chemotherapy protocols. In these trials, the PolyMVA was given intravenously. PolyMVA is recommended to be given concurrently with CoEnzyme Q10 (1-2 mg/kg/qd) and with a milk thistle extract formula to help with the extensive detoxification necessary to help the body clear out dying cancer cells and their associated cancer toxins. It is quite expensive, but non-toxic. There are no side effects other than those associated with the death of the cancer cells.

It is suggested that patients who take the PolyMVA refrain from taking alpha lipoic acid specifically, and to avoid the use of other antioxidants like vitamin C and n acetylcysteine within 3 hours of taking the PolyMVA formulation. There may be an interaction among the different antioxidants resulting in a denaturing of the PolyMVA’s potency.

Ogilvie performed a study of the effects of PolyMVA in 2004 to evaluate its efficacy when given concurrently with standard chemotherapy and radiotherapy protocols. In osteosarcoma patients, PolyMVA was substituted for chemotherapy to compare its efficacy with that of current chemotherapy protocols for OSA; this is published in AMARC’s practitioner guide for the use of PolyMVA. (42) Use of PolyMVA is recommended concurrent with chemotherapy, radiation and/or surgery, although historically patients who had not received chemotherapy prior to PolyMVA treatment tended to “do better”.

The study found that this antioxidant compound was most effective with solid tumors such as STS, HSA, MCT, TCC, Lung cancer, anal sac carcinoma, renal
carcinoma, SCA, FSA, melanoma, meningioma, neuroblastoma, mammary adenocarcinoma, and OSA. This study found no significant difference in median survival time in patients amputated and put on PolyMVA versus amputation with chemotherapy.

Other than survival time, patients on PolyMVA showed improvement in weight, anemia, liver and kidney function. An owner quality of life (QOL) survey indicated an 86% improvement while on the PolyMVA.

Suggested oral dose: 1/4 ml per pound of body weight twice daily.

**Intravenous Orthomolecular Doses of Ascorbic Acid**

The use of pharmacologic doses of ascorbic acid intravenously has been associated with improvement in cancer patients. The doses recommended are 1 gram per kg BW intravenously daily for 3 days weekly. It is necessary to gradually ramp up the intravenous dose over several administrations to acclimate the patient to that high of a dosage.

A recent in vivo study found that a “hypoxia protein” labeled HIF-1 helped cancer cells to compensate in conditions of hypoxia. These researchers found that this protein was abundant in untreated cancer cells, but disappeared in mice treated with vitamin C. Some rapidly growing tumors consume enough energy to remove all of the available oxygen in their vicinity, which makes the HIF-1 critical for their continued survival. HIF-1 can only function if it has a supply of free radicals. Antioxidants remove these free radicals and stop HIF-1 and along with it tumor growth. Researchers were able to measure significant reduction in tumor size in treated animals. (41)

**Neoplasene™**

A proprietary formulation containing the herb sanguinaria (“blood root” is the common name for this western herb) complexed with other agents, developed by Buck Mountain Botanicals. The sanguinaria induces apoptosis in cancer cells, and is only mildly irritative to healthy tissue. Has been used for centuries as a folk medicine topical preparation called “Black Salve”. The Neoplasene, as provided by Buck Mountain Botanicals is available in a topical salve, an oral solution with 2 different strengths (75 mg/ml and 300 mg/ml) and an injectable solution complexed with DMSO. There are many anecdotal and case reports published on the use of this herbal anti-neoplastic agent, some of these cases were from oncologists. (43)

**Artemisinin**

Artemisinin is a compound extracted from the plant Artemesia annua L.(sweet wormwood, also known as the Chinese herbal *qinghao*) and is a sesquiterpene lactone. Artemisia annua has been used in China since AD 341 to treat febrile illness. In 1971, the active ingredient, artemisinin, was identified and isolated. Derivatives of artemisinin have been synthesized. These include: dihydroartemisinin (DHA), artemether, artesunate, arteether, and artelinic acid. These compounds have been packaged in different forms: tablets, capsules, suppositories and injectable. DHA, artesunate and arteether are relatively water-soluble, whereas the others are oil (fat) -soluble.

The artemisinin molecule contains two oxygen atoms linked together in what is known as an ‘endoperoxide bridge’, which could react with an iron atom to form free radicals. Artemisinin is toxic to malaria parasites because the parasite contains a high
amount iron in the form of heme molecules. Free radicals cause to macromolecular damages and kill the parasites. Artemisinin has been used as an anti-malaria in more than two millions patients. Compared to normal cells, cancer cells sequester relatively large amounts of iron, mainly in the form of holotransferrin. Artemisinin has been shown to cause rapid and extensive damage and death in cancer cells and have relatively low toxicity to normal cells.

Artemisinin has been analyzed for its activity against 55 cancer cell lines. It was most active against leukemia and colon cancer cell lines and active for melanomas, breast, ovarian, prostate, CNS, and renal cancer cell lines. A comparison of artemisinin's cytotoxicity with those of other standard cytostatic drugs showed that it was comparable to established anti-tumor drugs. These results and known low toxicity of artemisinin and its derivatives make them a promising novel candidate for cancer chemotherapy. (44)

In one study regarding the activity of 22 drugs on leukemia CCRF-CEM cells lines, artemisinin showed both anti-leukemic activity if applied alone and modulation activity in combination with daunorubicin in multidrug-resistant (MDR) cells. (45)

Artemisinin and its derivatives have been found to inhibit the proliferation of cancer cells and increased cytotoxicity of perarubicin and doxorubicin in P- glycoprotein-overexpressing, and in MRPI-overexpressing, but not in their corresponding drug-sensitive cell lines. (46)

One of the problems with artemisinin is its poor absorption and the fact that its effect is blunted by the presence of dietary iron, such as might be found in red meat. It therefore is recommended to be given away from meals at night. It has also been found that when given concurrently with sodium butyrate its absorption is markedly improved. Sodium butyrate is a short chain fatty acid produced by the microflora of the colon, but which is available as an encapsulated supplement. (47)

Although well-designed studies in dogs with cancer are lacking, anecdotal reports indicate some patients responding remarkably well to lower doses, and other patients responding to relatively higher doses of artemisinin. Sources of supply include Holley Pharmaceutical (www.holleypharma.com); and Allergy Research Group (www.allergyresearchgroup.com); injectable artesunate and artesunate tablets can be obtained directly from pharmacies in Singapore and Hong Kong.

**Beta glucans: Medical Mushrooms & Yeast-derived**

Medical mushrooms and yeast typically contain biologically active polysaccharides and other immune active compounds. Beta glucans are one such polysaccharide that contribute to the biological activity of both mushrooms and yeast. Yeast and mushrooms contain the β1,3 glucan. Some mushroom species will also have the β1,6 glucan, which could account for some of the differences in their activity.

Research studies have been conducted into the immune modulating properties of yeast, and have found it to be a potential intervention against anthrax. (48) Not all beta glucan preparations have the same potency. A recent study compared several different products containing beta glucans from both yeast and mushroom sources. This article also contains a good review of beta glucans and their beneficial influence on immune function. (49)
This author has used a considerable amount of the agaricus blazeii mushroom powdered extract of Japanese manufacture which has good supportive research performed on their product, including clinical work by two veterinary oncologists. Many other mushrooms are also quite potent, including ganoderma lucidum, cordyceps mushroom, grifola, and shiitake, to name a few. Each mushroom contains unique combinations of beta glucans and phytochemicals specific that define its specific activity. (50)

Clinically, the use of medical mushrooms as immuno-modulators has been very successful in this author’s experience for patients with neoplasia as well as for other problems that immune function can benefit. A Chinese in vivo study of the Agaricus mushroom found suppression of tumor growth and angiogenesis. (51) Patients with acute or chronic infections, such as chronic rhinitis/sinusitis, often will have those resolve more rapidly when placed on a medical mushroom extract. A Norwegian in vivo study also found a basis for the extract of the Agaricus blazei mushroom to protect against allergy. (52)

**Green tea (Camilla sinensis)**

One of the most popular drinks in the world has been touted for years for its health benefits. Studies have found green tea’s main active ingredient to be an anti-oxidant molecule named “epigallocatechin-3 gallate (EGCG). Green tea is a complex botanical material, and there are many other “active” compounds in this ancient beverage and medicinal drink. Many studies have found this common herb to be beneficial for a variety of diseases, including neoplastic conditions.

A study published in The Lancet, September 2004, found that ECGC promotes cancer cell apoptosis and death. It does this by interfering biochemically with VEGF function, inhibiting the activity of this bioactive protein. VEGF (vascular endothelial growth factor) is a potent angiogenic cytokine that is and is integral to the ongoing progression of cellular damage that are the symptoms of the disease process. (53)

The mechanism of action of the tea polyphenols on the cancerous cell is thought to be due to their promotion of apoptosis in the neoplastic cell, and their inhibition of angiogenesis or neovascularization. Promoting apoptosis, or programmed cell death, and inhibiting of the growth of new blood vessels (neovascularization) that support the increased growth of the tumorous mass, are two powerful ways that tea polyphenols have a negative effect on the growth of neoplastic cells.

Many epidemiological studies have been performed charting the improvement in general health patterns in a population that follow certain food and beverage preferences, such as drinking green tea, which is a common-place occurrence in Asia.

In a retrospective study published in the International Journal of Cancer; a large population of patients were enrolled in this study in Shanghai, China. These patients were diagnosed with cancer of the colon (931), rectum (884) or pancreas (451). (Controls = 1552 selected from Shanghai residents and frequency matched to cases by gender and age.)

This study, from the Division of Epidemiology, School of Public Health, Columbia University, New York City, NY observed an inverse association with each cancer with increasing green tea consumption in this study population. Rectal and
pancreatic cancers responded better to green tea consumption than did patients with cancers of the colon who were also taking green tea. The list of epidemiological studies finding positive benefits to the ingestion of is long and ongoing. A good summary of the benefits of green tea to the prevention of cancer and for patients who have cancer can be found at this link to the National Cancer Institute’s website (54)

SUMMARY
To conclude, in this author’s experience over the past 25 years, botanical and nutraceutical compounds are necessary and critical to the creation and maintenance of optimal health in veterinary patients. They can be used safely and as effective adjuncts to conventional veterinary therapeutics when used concurrently, and in many cases can effect therapeutic benefits when used as stand-alone therapies.

RESOURCES
Texts

List of sources of nutritional counseling
WEBSITES for FOOD PREPARATION
a. www.ACVN.org
b. www.petdiets.com
c. www.balanceit.com

ACADEMIC NUTRITION SERVICES
a. UC Davis 530 752 1393 (pet owners); 530 752 1387 (veterinarians)
b. University of Tennessee 865 974 8387
c. Michigan State University 517 432 7782
d. North Carolina State University; Dr Korinn Saker 919 513 6488
e. Angell Animal Medical Center 617 522 7282
f. Ohio State University 614 292 1221 or 292 3551
g. Tufts Cummins School of Veterinary Medicine 508 839 5395 X84696

REFERENCES
14. Wynn and Fougere eds. Veterinary Herbology
remission and survival time for dogs with lymphoma: a double-blind, randomized placebo-controlled study.

22. Ogilvie G. 2007 VIN Online course on Integrative Oncology


24. Wynn S 2007 VIN Online course on Integrative Oncology


34. Simone CB 2nd, Simone NL, Simone V, Simone CB. Antioxidants and other nutrients do not interfere with chemotherapy or radiation therapy and can increase kill and increase survival, Part 1. Altern Ther Health Med 2007 Jan-Feb;13(1):22-8.


42. www.polymva4pets.com www.polymva4vets.com
43. www.neoplasene.net