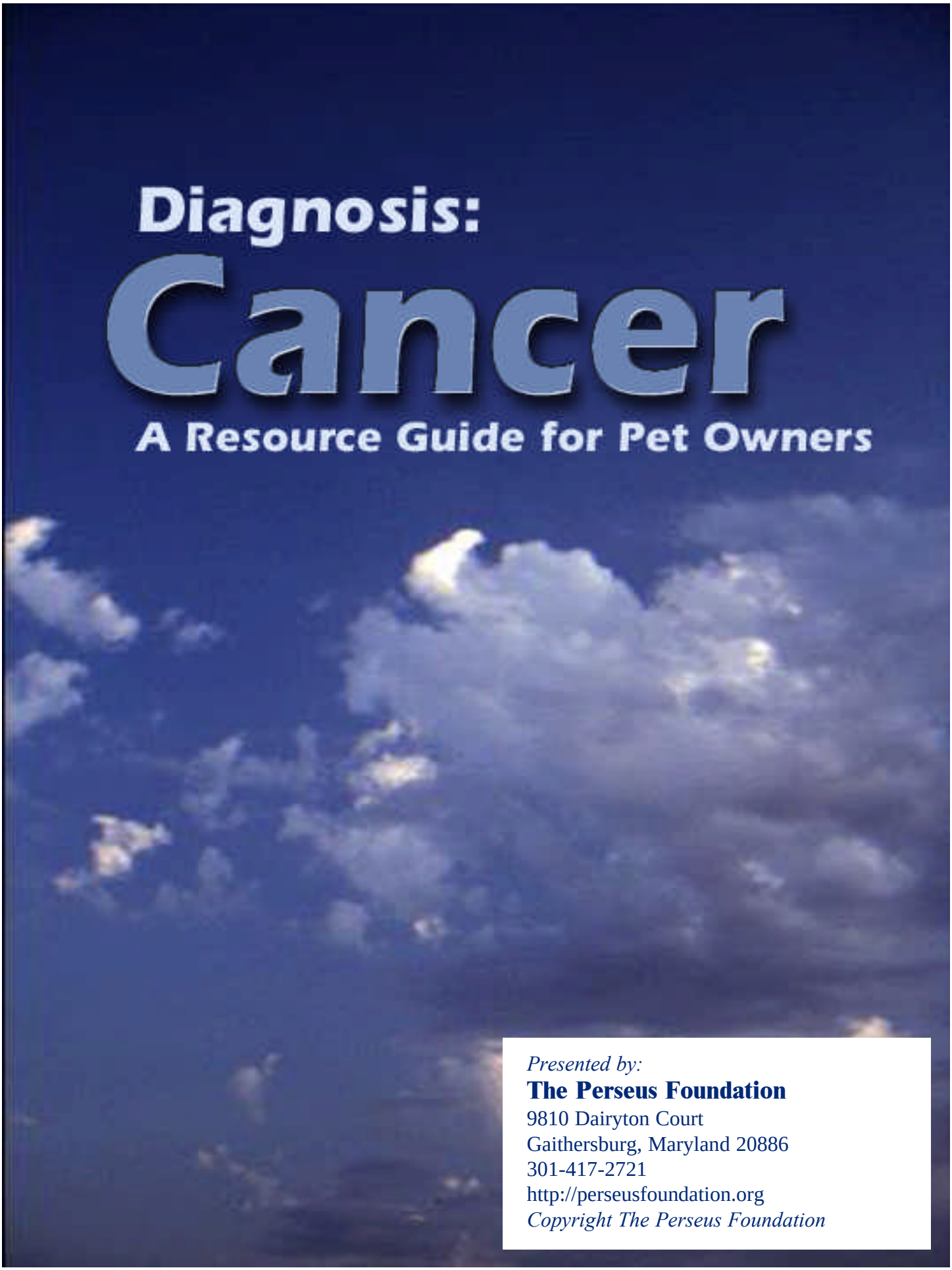

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Mission Statement

The Perseus Foundation, a not for profit organization 501(c)3, was established to operate exclusively for charitable, scientific and educational purposes.

Its goals include, but are not limited to, the following:
To educate the general public and promote public interest, in the United States and abroad, in cancer research, the search for a cure for cancer in animals, in particular those cancers that share a similarity to the cancers that afflict children.

To support, sponsor, encourage and disseminate knowledge of research on cancer, and particularly on cancer in animals, and to encourage institutions to conduct research leading to a cure for cancer in animals, especially that research which may be helpful in finding a cure for cancer in children.

The type of research that The Perseus Foundation will support in the future will directly help pet animals with cancer and as a result will be translated into better care of human cancer patients. Animals and humans with cancer will be the beneficiaries of this research.

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Foreword

It is with a great deal of enthusiasm that The Perseus Foundation introduces Diagnosis: Cancer, A Resource for Pet Owners. We sincerely hope you will find this handbook informative and useful as you engage in your battle against cancer. Even though cancer is a formidable enemy, information is a powerful weapon against it.

We ask that you please use this publication to better inform yourself, but not as a means of diagnosing or treating your pet. This handbook is not intended to replace medical advice. We urge you to please contact your veterinarian if you suspect anything may be wrong with your pet.

In closing, we wish you much success in your journey against cancer. There are many survivor stories to be told and we sincerely hope that yours holds the happiest of endings.

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What Causes Cancer?
Cancer Treating Modalities
Courtesy of Chand Khanna, DVM, PhD, Animal Cancer Institute, Columbia, Maryland
www.animalcancerinstitute.com

Staging Cancer - How Much? When? Why ?
Courtesy of Sarah Sheafor, DVM and South Paws Veterinary Clinic, Springfield, Virginia
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Overview of Biopsy Principles and Surgical Oncology
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An Overview of Common Type Tumors: Signs, Symptoms, Treatment Options
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When is Radiation Therapy Really Indicated?
By. Donald Thrall,
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Characteristics and Toxicities of Common Antineoplastic Agents
The following material has been excerpted and adapted from The Merck Veterinary Manual, Eight Edition, 1998. We are indebted to Merial and to Dr. Susan Aiello for kind permission to reprint.
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When Conventional Treatment is not Enough
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Understanding Canine Cancer: An Herbalist's Perpective
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A Visit with the Veterinary Oncologist

Once your veterinarian has confirmed the diagnosis of cancer in your animal friend, a consultation with a veterinary oncologist will be necessary.

On occasion, the primary care veterinarian can treat the cancer patient, but this should be done in collaboration with a veterinary oncologist. Your pet's veterinary oncologist will tailor a cancer therapy that is best suited for your pet.

Some facts and figures to take into consideration:

- Generally speaking, the cost of major surgical procedures will start at five hundred dollars.
- Chemotherapy will greatly vary depending on the size of your dog. It may range from about $500 upward for palliative care to over $5,000 for a three to six month period.
- Radiation therapy will range from $1500 to $5,000 depending on the type of radiation therapy and the facilities.

The questions listed below have been compiled from visitors to our site. They have our gratitude.

What are the objectives of this initial evaluation?

How will you evaluate my dog's tumor? Will it require a radiography? An ultrasonography? A biopsy?

Once a diagnosis has been obtained:

What direct effects will this tumor have on adjacent organs?

Is the cancer localized or has it spread? What are the chances of it spreading?

How is this cancer categorized? Please explain the definition of the stages and what the treatment options are for each one.

What are my treatment options: Biotherapy? Chemotherapy? Radiation? Surgery? Antiangiogenesic approaches?

Please don't feel as if you should know what these terms mean. Ask your veterinarian to explain these terms if you do not have a clear understanding.

If we decide not to treat conventionally, what is the prognosis?

Can we incorporate holistic methods in the treatment?

What type of diet would you recommend? Why?

Are there any clinical trials for this type of cancer?

Is there any documentation I can read on the success of specific treatments?

If treatments need to be delayed due to other health reasons, how will this affect the outcome?

How do I deal with vaccination issues now that my dog has been diagnosed with cancer?

If Chemotherapy is presented as an option, the following questions could be asked:

Which drug or combination of drugs does the oncologist recommend and why? Ask your doctor to explain how many treatments will be needed.

How will these drugs be administered?

What are the possible side effects? How can I prepare my pet for the treatments?

What can be done to limit side effects from the chemotherapy?

What do I need to watch out for when I take my pet home?

What signs should I look for to indicate my pet is coming out of remission?

What is the average remission time using this protocol? Ask your doctor where you can obtain copies of statistical studies of the findings.

What are our backup plans if one treatment fails?

How much will the treatment(s) cost? Can I pay in installments? Can I find the drugs somewhere else for a lesser price? Is this safe to do?

It is very important that you keep an open line of communication with your veterinarian and/or veterinary oncologist. When dealing with nonmainstream methods, you will be confronted with an enormity of choices. Please keep your veterinarian abreast of any supplementation or changes in diet as these may have an impact on the treatment.

We sincerely hope the questions will you help prepare for your visit. And please know you can always contact us directly for any research assistance you may need. We would be delighted to provide a helping hand.

What Is Cancer ?

By Chand Khanna, DVM, PhD, DACVIM (Oncology)

Cancer is strictly defined as an uncontrolled growth (or proliferation) of cells resulting in an abnormal accumulation of cells in a particular region of the body. This process is the result of aberrant activation of expression of a cell's genes. Cancer is always associated with a single or more commonly several genetic changes.

Cancers may be described as benign or malignant. Benign cancers, often referred to as benign tumors, tend to stay in their original location without spreading to other parts of the body. Conversely malignant cancers invade normal tissues and may spread to other parts of the body. The process of spreading from the original tumor location (the primary tumor) to another part of the body is referred to as metastases. The pattern of spread for many cancers includes the nearby (i.e. draining or regional) lymph nodes and then distant sites, i.e. the lungs.

Cancers may develop from normal tissues in any part of the body. The behavior of a particular cancer is largely dependent on the type of tissue from which that cancer developed and the underlying genetic changes that characterize a cancer. Malignant cancers that develop in epithelial tissues are called carcinomas, while malignant cancers that develop in connective tissues are called sarcomas. The name of a malignant cancer comes from a tissue identifying prefix combined with the term carcinoma or sarcoma. Benign cancers use the same tissue prefix but add the suffix oma for both connective and epithelial tissues.

e.g. squamous cell carcinom - malignant cancer of epithelium
osteosarcoma = malignant cancer of connective tissue

Cancers that are derived from bone marrow or blood cells follow a different naming system and are referred to as leukemias.

e.g. a leukemia of lymphocytes = lymphoid or lymphocytic leukemia
a leukemia of red blood cells = erythroleukemia

What Causes Cancer

Cancer is caused by genetic changes in the nucleus of the cell. The more important question then becomes what causes the genetic changes in the nucleus? The answer more often than not is that we do not know. We are learning more about the causes of cancer or more correctly, the risk factors for cancer. These risk factors are often environmental. Exposure to these risk factors does not necessarily cause the genetic changes associated with cancer, but exposure to these risk factors will increase the chance that a cell in our body will become damaged and then initiate a process that may lead to the development of a cancer. Some of the established risk factors for cancer include:

- smoking -> lung cancer, colon cancer, oro-facial cancer.
- diets high in red meats -> colon cancer and others.
- low exposures to estrogen -> breast cancer.
- exposure to UV light -> skin cancer.

In pet animals risk factors for cancer are less clearly defined:

- Feline leukemia virus -> lymphoma in cats
- Breed associations(e.g. Golden Retriever, Boxer)
- Exposure to lawn chemicals -> Dogs and lymphoma
- Obesity -> Dogs and bladder cancer
- Second hand smoke inhalation -> suggested by several lines of evidence

The cells in our body are always dealing with genetic damage. The cells can detect genetic injury and can stop the cell from dividing until the damage can be repaired or the cell can "decide" that the damage is not repairable and then enter a process of programmed cell death. Programmed death of a cell is referred to apoptosis. If a cell looses its ability to undergo apoptosis it will continue to divide without repairing the damage. It is these damaged cells which can then develop characteristics of cancer including the loss of control of growth, invasion into surrounding normal tissue and eventually spread to other parts of the body. Apoptosis is becoming a more and more important part of understanding why cancers develop and why they become so difficult to treat .

Modalities of Cancer Treatment

The goal of cancer treatment is to destroy the abnormal cancer cells and spare the normal healthy cells. All forms of cancer treatment attempt to exploit differences between cancer cells and normal cells to preferentially kill more cancer than normal cells. There are four fundamental modalities used in the treatment of cancer. These include **(1) Surgery; (2) Radiation Therapy; (3) Chemotherapy; (4) Biotherapy**. Advances in all of these cancer treatment modalities have developed over the last few years. These advances, as well as cancer prevention and early detection programs, have lead to the new sense of optimism that now exists in the treatment of several cancers.

Surgery. Surgery continues to be the most effective way to manage cancer. If a cancer cannot be managed with surgery alone the prognosis decreases dramatically. Surgery is most effective if a cancer exists in a localized region or single site and if a margin of surrounding normal tissue can be removed with the cancer to prevent it from re-growing. Having a margin of normal surrounding tissue is critical to the success of the surgical removal of cancers. The rule of thumb is to remove a margin of 3 cm in all directions around the cancer and to remove at least one tissue plane deep.

Radiation Therapy. Radiation sources can be used to treat cancer in a number of ways. Radiation damages and then kills rapidly dividing cells *(i.e. cancer cells)* to a greater extent than normal, slower dividing cells. In veterinary oncology, radiation therapy is commonly applied as teletherapy. Teletherapy delivers a radiation dose at a distance from the patient, similar to a x-ray machine. This unit emits high-energy radiation that can kill cancer cells rather than the low energy radiation that is emitted from diagnostic x-rays. Teletherapy can be used to treat cancer as the only modality *(primary therapy)* or can be used to clean surgical margins *(adjuvant therapy).*

Teletherapy radiation therapy is effective for the management of localized tumors that have not spread to distant sites. Once a cancer has spread from a primary tumor site to another location in the body, the curative role of radiation therapy is lost. Situations where radiation therapy is most likely to be effective include:

- a cancer type sensitive to radiation induced damage.
- mast cell tumor, soft tissue sarcoma, canine squamous cell carcinoma, nasal tumors
- oral melanoma, brain tumors.
- tumor localized to a single site without spread to distant sites.
- tumor location that will allow radiation without life threatening damage to surrounding tissues

Radiation is given in several small doses, called fractions, several times over a 3-4 week period *(usually daily)*. These small fractions are given to limit the side effects of radiation. The rationale for administering small fractions is that normal cells are better equipped to repair the genetic damage induced by radiation than are tumor cells. This allows more tumor cells to be killed than normal cells. Unfortunately side effects from radiation therapy still do occur. Side effects associated with radiation therapy are associated wtih damage to normal tissuse in the field of the radiation beam. Generalized illness *(radiation sickness)* is not seen in veterinary patients because radiation of the entire body is not commonly undertaken and the doses of radiation are less than those used in human patients. The normal tissues that are most likely to be damaged by radiation therapy are rapidly dividing *(i.e. skin, hair cells,*

lining of the oral cavity). These rapidly dividing normal tissues are damaged during the course of radiation, referred to as acute radiation effects. Supportive care for such acute radiation damage is often required for 5-7 days. Although acute effects can be uncomfortable for the patient, they are limited to the time that the radiation is given. It is uncommon for these acute radiation side effects to be life threatening. It is essential to prepare clients for the possibility of such radiation effects. Owners that are not prepared for such reactions may consider discontinuing radiation or may lose hope and consider euthanasia. Acute radiation effects will resolve.

Chemotherapy. Modern chemotherapy began in the 1940s with the treatment of leukemia using the alkylating agent nitrogen mustard. Drawing on previous experience with antimicrobials, the empirical use of chemotherapy continued through the 1950s. Since then, chemotherapy has become an integral and essential component of the management of cancer, especially in patients whose cancer has spread or is likely to spread beyond the control of the surgeon or radiation therapist. The progression from simple, single agent chemotherapy protocols to multi-agent and now multi-modality *(including chemotherapy with radiation therapy and other novel approaches)* has occurred in both human and veterinary oncology. The next decade will continue to see progression towards increasingly specific forms of chemotherapy that will target critical molecular alterations in cancers. Early experience with such targeted *(molecular)* therapies suggests significant anti-tumor effects with minimal toxicity. The result of these developments is the need for the veterinarian to be knowledgeable about conventional chemotherapeutic agents and the basic biology of cancer such that both conventional and novel targeted approaches for cancer therapy may be used appropriately.

How does chemotherapy kill cancer cells?

In general, conventional chemotherapy does not kill cancer cells preferentially over normal cells. The differential sensitivity of tumor cells compared to normal cells results from three basic differences: **(i)** a greater proportion of tumor cells are actively moving through the cell cycle than normal cells (see figure 1), a large proportion of normal cells are non-cycling and quiescent; **(ii)** normal cells are more able to respond and repair chemotherapy induced damage than tumor cells; and **(iii)** normal tissues are more capable of repopulation following chemotherapy exposure. Successive treatments, or cycles, of chemotherapy will result in enhancement of the differential killing of tumor versus normal cells.

Most chemotherapeutics act against cells that are actively progressing through the cell cycle. These dividing cells are dependent on organized synthesis of DNA, RNA and protein and on the coordinated activity of cellular organelles to allow the successful division of the cell. The target of the chemotherapy may be cellular DNA, RNA, protein, or organelle function. Irrespective of the target, the result of chemotherapy exposure is the generation of "defective" DNA. The defective DNA initiates a process of programmed cell death, also referred to as apoptosis, which results in cellular suicide. Apoptosis is essential part of a normal cell physiology (i.e. embyrogenesis, cellular senescence, immune regulation). It is important to note that the chemotherapy exposure does not kill the cell itself, rather the tumor cell recognizes the DNA damage, the cell stops moving through the cell cycle (arrests), and then commits suicide (apoptosis) (figure 1). The decision to arrest and then either repair or die (undergo apoptosis) is dependent on genes referred to as cell-cycle checkpoint genes. These genes survey the integrity of DNA and consider extracellular signals in the determination of whether a cell should continue to repair or undergo apoptosis. For this reason chemotherapy cytotoxicity is dependent on the proper function of the check point genes. Failure of proper checkpoint gene function may be a mechanism for chemotherapy resistance, as discussed below.

A cardinal rule of chemotherapy killing is that an inverse relationship exists between cell number and tumor curability. This rule is based on the chemotherapy log kill hypothesis. The log kill hypothesis states that a particular dose of chemotherapy will result in a fixed percentage of tumor cells (log kill) regardless of the initial size of the tumor. This means that the dose of chemotherapy required to take a tumor from 1 000 000 cells to 100 000 cells (destruction of 900 000 cells) is the same as the dose required to take that tumor from 100 cells to 10 cells (90 cells). In both cases 90% (1 log) of cells are being killed. The clinical relevance of this hypothesis is that small tumors are more likely to be cured than large tumors. More importantly the hypothesis explains the necessity of continued chemotherapy after the disappearance of a grossly detectable tumor. If a 1 cm tumor contains 109 cells, then 5 log kills will destroy 99.999 % of the tumor and make it grossly undetectable. However, 104 viable tumor cells (representing 0.0001% of the original tumor) will still remain and will need an additional 5 log kills before all viable tumor cells are destroyed. The log kill hypothesis does not take into account the development of resistance in tumor cells during therapy or the fact that all cells in the tumor may not be in active growth phase.

Chemotherapy Resistance. Given that death from chemotherapy requires an intact cell death program (apoptotic pathway) one mechanism for a tumor cell to resist chemotherapy may be through mutations in the regulators of this programmed cell death pathway (cell checkpoint genes). The p53 gene, the classical checkpoint gene, functions to arrest cells in the cell cycle between the first growth phase (G1) and synthesis phase (S) and to a lesser extent between the second growth phase (G2) and the mitosis phase (M) of the cell cycle. Mutations in p53 may prevent a tumor cell from appropriately arresting after DNA damage from chemotherapy and as such may allow the tumor to be resistant to the damage induced by the chemotherapy. P53 is the most commonly mutated gene in human cancers and has been found to be mutated in several canine and feline cancers (e.g. canine osteosarcoma, canine and feline lymphoma, feline soft tissue sarcoma, canine mammary carcinoma). P53 is also considered to be a tumor suppressor gene. Mutations or loss of function to a tumor suppressor gene like p53 may allow the dysregulation of cell cycle control and may be an important early step in the transformation of a cancer. Therefore mutations in p53 may initially contribute to the development of a cancer and may also allow a cancer to resist the damage induced by chemotherapy.

Loss of checkpoint function is a mechanism of resistance that may be relevant to all forms of chemotherapy and may or may not be associated with any prior exposure to chemotherapy. Conventionally, chemotherapy resistance has been associated with mutations that emerge during the treatment of a cancer cell with chemotherapy. The development of drug resistance is the most common cause of chemotherapy failure. The development of chemoresistant clones within a tumor is not thought to occur until a tumor has reached between 100 000 and 1 million cells. However, the risk for resistant tumor cell emergence increases exponentially after this critical size and suggests the importance of starting chemotherapy as early as possible. Mechanisms for resistance to chemotherapy may be common to several unrelated agents or specific to a particular chemotherapeutic class. A specific form of multi-drug resistance has been associated with the MDR gene and its protein product, p-glycoprotein. P-glycoprotein is a protein complex expressed on several normal tissues (e.g. intestinal mucosa, liver, brain) that functions to efflux a variety of macromolecules (including chemotherapeutics) from the cytoplasm of a cell to the extracellular space. The normal function of p-glycoprotein in these tissues may be to export potentially harmful toxins. Chemotherapeutic agents that induce p-glycoprotein expression include drugs that are natural products such as the vinca alkaloids (i.e. vincristine and vinblastine), anthracylines (e.g. doxorubicin), and glucocorticoids. The result of p-glycoprotein over-expression on a tumor cell may be the active pumping of these chemotherapeutics out of a cell before they can induce

their desired effects on the cell. Current investigation is underway with a number of agents to block or reverse MDR expression. Agents under investigation include cyclosporin, verapamil, and newer more selective MDR antagonists.

The Use of Chemotherapy .Induction chemotherapy refers to the use of drug therapy as the primary treatment of patients with advanced cancer or for which no other treatment options exist. The use of combination therapy in dogs and cats with lymphoma represents the most common example of induction chemotherapy in veterinary medicine.

Adjuvant chemotherapy describes the use of systemic chemotherapy following the control of the primary tumor using other modalities *(i.e. surgery or radiation therapy)*. The selection of a treatment protocol for adjuvant use is often based on initial observations of the responsiveness of a particular cancer in the induction settings. The use of platinum containing chemotherapy after amputation in dogs with appendicular osteosarcoma is an example of adjuvant chemotherapy.

Neoadjuvant chemotherapy denotes the use of chemotherapy as the initial treatment of a localized cancer for which other definitive treatment options exist. Neoadjuvant chemotherapy is often considered in the management of vaccine induced sarcomas prior to a definitive resection. The rationale for such an approach is that a more successful surgery may be performed following chemotherapy *(tumor shrinkage or sterilization of tumor margins)* compared to surgery on the untreated tumor.

Biotherapy. Biotherapy *(or biological therapy)* refers to a diverse group of therapeutic strategies for cancers. It is a treatment modality based on products of the cancer, products of the host response against the cancer, and products of the interaction between the cancer and the host. Biotherapy is the product of the dramatic increase in our understanding of the basic biology of cancer and cancer metastasis. It is safe to say that the next breakthrough(s) in the treatment of cancer will come from biotherapy. A number of forms of biotherapy are currently under investigation in the field of Veterinary Oncology. In many cases these therapies may become available to pet animals with cancer before they are available for treatment of human cancer patients. Increasing awareness of biotherapy strategies by the pet owning public has forced veterinarians to be knowledgeable about these novel forms of cancer therapy.

For the sake of discussion, biotherapy can be divided into four major *(non-mutually exclusive)* groups.

- Immunotherapy
- Agents that Inhibit Angiogenesis or Invasion
- Growth Factor Modulation
- Small Molecules (Inhibitors of signal transduction)

Each of these groups have evolved independently as forms of cancer therapy and have been subsequently grouped under the umbrella cancer biotherapy.

Immunotherapy. The belief that the immune system may play a role in the treatment of cancer has been held for over 100 years. Coley, a surgeon in the early 1900s, observed the spontaneous regression of large ovarian tumors in women following post-surgical bacterial sepsis. His belief that the fever associated with the sepsis was responsible for regression of the tumor led him to administer mixtures of bacteria to patients in the hopes of re-creating the fever and resultant tumor regression. These bacterial mixtures, referred to as Coley's toxins, were some of the first documented attempts at cancer immunotherapy. Since the days of Coley considerable progress in our understanding of the immune

response *(and lack of immune response)* against cancer has emerged. This understanding may be summarized in the following generalizations:

- Cancers differ in their sensitivity to immune recognition and destruction (immmunogenicity)
- The determinants for immune recognition of cancers are specific to each cancer type
- Cancers evade immune recognition by many different mechanisms
- The cell mediated immune recognition by many different mechanisms
- Cancer immunotherapy is likely to be most effective against small tumor
- Burdens (microscopic disease)

This understanding has lead to several promising strategies that use the immune system to first detect and then destroy cancer cells. Approaches to immunotherapy include the following:

Non-specific Immunotherapy. Where bacterial agents *(e.g. BCG, Corynebacterium Parvum)*, natural products *(Acemannan)*, synthetic compounds *(Muramyl tripeptide)*, chemical agents, and others, are used to stimulate an immune response. This approach is similar to that of Coley, and referred to as non-specific because the target for immune recognition in the cancer is not known. The most extensively studied form of non-specific immunotherapy in veterinary oncology is muramyl tripeptide *(MTP)* delivered in a long acting lipid encapsulated formulation. In randomized, controlled, and placebo-blinded trials, MacEwen et al has demonstrated the activity of MTP against canine osteosarcoma and canine hemangiosarcoma. Treatment of dogs with osteosarcoma or hemangiosarcoma using MTP plus chemotherapy resulted in significantly longer survival times compared to chemotherapy alone. The commercial availability of MTP is uncertain at this time; however, the recent demonstration of MTP activity in childhood cases of osteosarcoma may stimulate commercial interest in this form of immunotherapy.

Specific Immunotherapy. Attempts to generate a specific immune response against a known or unknown *(whole cell approach)* tumor antigen *(target)*. A tumor vaccine is the most common form of specific immunotherapy. Our understanding of the immune response against cancer suggests that the most effective tumor vaccines will stimulate cell-mediated responses against cancer. The use of autologous tumor vaccines based on genetically modified tumor cells *(using gene therapy)* or purified factors from the tumor *(heat shock proteins)* are currently under investigation in dogs and cats with cancer. Preliminary results from these trials and human clinical trials using these autologous tumor vaccine approaches are encouraging.

Adoptive Immunotherapy. Refers to the administration of parts of the immune system to a patient. Monoclonal antibodies raised against cancer represent adoptive humoral immnunotherapy. Advances in the design of monoclonal antibodies to prevent immune reactions against the antibody and to improve antigen recognition have raised the potential value of this type of therapy. The recent release of Herceptin®, an antibody that binds the epidermal growth factor receptor, to treat breast cancer in women is evidence of the progress that has been made in this field. In dogs, the canine lymphoma antibody MoAb221® has been approved for use in dogs. The activity in this antibody in randomized trials has not been demonstrated to date. The conjugation of monoclonal antibodies to chemotherapeutic agents or cellular toxins will be the next step in the evolution of this work. Adoptive cellular immunotherapy, where stimulated immune effector cells *(e.g. LAK - lymphokine activated killer cells)* are administered to

the patient, has not been extensively evaluated in dogs. Logistically, this type of therapy presents problems for both human and veterinary cancer patients.

Cytokine Immunotherapy. Refers to the administration of products of the immune system *(cytokines)* to stimulate or direct anti-tumor immune responses. Cytokines are released by leukocytes and function in the activation and regulation of the immune system. Cytokines such as interleukin-2 *(IL-2)* have been used to induce significant anti-tumor immune responses and objective tumor responses in dogs with osteosarcoma.

Growth Factor Modulation. Normal tissues utilize signals from growth factors to regulate specific cellular functions. In tumors the normal response to growth factors is dys-regulated. This may result in the abnormal dependence of a tumor cell on a growth factor or a growth factor pathway. In either situation the blockage of the growth factor/growth factor receptor pathway may prevent tumor cell growth or progression. As discussed above, the realization that many breast cancers were dependent on the epidermal growth factor receptor pathway resulted in the development of an antibody to block this growth factor receptor. The result of epidermal growth factor receptor blockade is a profound decrease in tumor cell growth and metastasis. Work is currently underway to identify tumors in dogs and cats that are dependent on the epidermal growth factor pathway, such that this antibody may be used in veterinary cancer patients. In osteosarcoma the insulin like growth factor *(IGF-I)* has been shown to be essential *(in both dogs and humans).* This growth factor appears to provide a life signal to osteosarcoma cells. This life signals prevents these cells from dying even after receiving normally lethal doses of chemotherapy. We have recently completed accrual of dogs with osteosarcoma to a clinical trial that evaluated the benefit of IGF-1 inhibition plus chemotherapy compared to chemotherapy alone. In this trial the inhibition of IGF-1 was well tolerated and did not increase the toxicity of carboplatin chemotherapy. Preliminary analysis of the data suggested improved survival in dogs receiving IGF-1 plus chemotherapy that approached statistical significance *(p=0.10)*. Further analysis of this data is expected by the fall of 2000. Feline vaccine associated sarcomas may share similar dependence on the IGF-1 pathway and may be responsive to therapies that inhibit IGF-1.

Agents that inhibit angiogenesis or invasion. Our understanding of the process of cancer progression and metastasis has increased dramatically. What is clear, is that tumor cells interact closely with their host and their immediate environment (microenvironment) and in many cases recruit host cells or enzymes to facilitate their spread. This understanding has lead to the development of two novel cancer treatment strategies, anti-angiogenesis and anti-invasion.

Angiogenesis describes the generation or recruitment of new blood vessels. It appears that new new blood vessel development is essential for tumor cells to grow beyond a size of 1mm. Because such therapies would be directed against blood vessels and not tumor cells, their use could be imagined against all cancers as opposed to a specific cancer type. Such therapies may lack normal tissue toxicity since most adult tissues do not require new blood vessel formation. Several human and veterinary clinical trials are currently underway to evaluate the activity of antiangiogenic agents. Endostatin® and Angiostatin® are the best known of these agents. Other antiangiogenic agents include thrmbospondins, thalidomide, and interleukin-12. Our preliminary experience with thalidomide as an anti-angiogenic treatment for dogs has been disappointing. Thalidomide treatments were undertaken in dogs with advanced disease (bulky tumors). The failure to see objective tumor responses in this trial speaks to the importance of evaluating these novel agents in animals with small if not microscopic tumor burden.

The process of cancer invasion within tissues and across tissue boundaries *(basement membranes)* is essential to cancer metastasis. The recent understanding of the determinants for invasion by cancer cells has lead to the development of a number of agents that inhibit cancer invasion. Matrix metalloproteinases *(MMPs)* have been identified as critical enzymes that facilitate tumor invasion. Natural and synthetic inhibitors of MMPS have been defined and developed as potential inhibitors of cancer progression. Several classes of MMP inhibitors are currently under investigation in pre-clinical models and in veterinary cancer patients. No data on the effectiveness of these agents is yet available.

Small Molecule. Describes a class of novel anti-cancer agents that target signaling pathways in a cell. Signaling pathways describe the biochemical pathways that are responsible for all cellular responses *(i.e. cellular growth, death, motility, adherence, invasion, etc)*. Small molecules interfere with biochemical pathways in a highly selective manner. The potential to target a specific biochemical pathway in a cancer cell carries great potential. The small molecule may be viewed as the "switch that turns the cancer cell off". Such selective therapies focus on the important basic differences in the biology of cancer cells and normal cells.

Progress that has been made in our understanding of the basic biology of cancer has uncovered several opportunities for the treatment of cancer. The improved knowledge of cancer biology has allowed differences between cancer cells and normal cells to be identified and has uncovered important interactions that occur between cancer cells the host. The cancer treatment strategies *(biotherapy)* discussed above specifically target cancer and as such are less likely to result in the tonicities that are associated with conventional cancer therapy. Effective and non-toxic cancer therapy is therefore the goal. Several forms of biotherapy, that share this goal, are now under investigation in the field of veterinary oncology. In the very near future we can expect biotherapy to be used in conjunction with conventional cancer treatment modalities *(surgery, radiation therapy, and chemotherapy) in the management of our* veterinary cancer patients.

Staging Cancer - How Much? When? Why?

By Sarah E. Sheafor, DVM, DACVIM (Oncology)

Often when we are presented with a patient with a "lump" or "cancer," we have to decide not only how to obtain a definitive diagnosis, but also how to determine whether the cancer has appeared. Depending on the type and location of the tumor, different staging protocols are indicated. The first rule of thumb is not to perform any test whose results will not change the diagnosis, prognosis, or therapeutic plan.

Mammary tumors: In both dogs and cats, chest radiographs, assessment of regional lymph nodes via palpation, and aspiration or biopsy of any enlarged nodes, as well as a complete assessment of all other mammary tissue comprises the minimal evaluation of a patient with mammary cancer. CBC and profile will give any assessment of overall biopsies performed - they should be excised completely (wide margins) and biopsied. Inguinal lymph nodes should be removed at the same time as the caudal inguinal mammary gland, and should be biopsied. Axillary dissection, in the face of no palpable axillary lymph node enlargement, is probably not necessary.

Perianal tumors: These tumors are common in dogs and exceptionally rare in eats. Chest radiographs, abdominal ultrasound to assess sublumbar node status, and serum chemistry to assess calcium values are the essential components of a staging workup of a patient with a large, ulcerated, or invasive perianal mass or with any anal sac mass. Anal sac tumors metastasize early to the sublumbar lymph nodes. If any enlargement of these nodes is noted on abdominal ultrasound, they can be aspirated or a plan can be made to have these nodes removed at the time of the definitive surgery for the anal sac tumor.

Lymphoma (dogs): The complete staging workup includes a CBC, profile, lymph node biopsy, chest radiographs, abdominal ultrasound or radiographs to evaluate the liver and spleen, and a bone marrow aspirate. The stage of canine lymphoma, however, is very rarely of prognostic significance in dogs with multicentric lymphoma. The academic benefits of a staging workup must be balanced against the costs of this evaluation in a dog needing life-long chemotherapy. A modified staging protocol that is practical for the majority of dogs with multicentric lymphoma is a lymph node aspirate for diagnosis, and a CBC and profile to assess overall health, and to have a baseline for chemotherapy planning. Should significant abnormalities be noted on history, physical examination, or on the lab work, additional testing to rule out concurrent diseases or organ dysfunction may be needed.

Soft tissue sarcomas: Chest radiographs are the minimal essential components of a staging workup for dogs and cats with soft tissue tumors. For certain patients, radiographic imaging or CT scanning of the primary tumor is helpful in planning an appropriate treatment of aggressive surgery and/or radiation therapy. These studies are helpful in finding out how extensive and invasive the tumors is, and can sometimes change therapeutic recommendations.

Cutaneous mast cell tumors (dogs): The ideal staging workup for dogs with cutaneous mast cell tumors depends on the grade of the tumor, as well as the type of therapy recommended. In cases of an incompletely-resected, grade I or II mast cell tumor, where the owners are contemplating extensive surgery or radiation therapy, regional lymph node assessment, abdominal ultrasound, +/- splenic and hepatic aspirates, buffy coat smear, +/- bone marrow aspirate are performed to try to be certain that the tumor is confined to the primary site. In dogs with grade III mast cell tumors, metastatic disease is expected, so chemotherapy should be recommended in addition to local therapy. A complete staging workup is not as essential in these patients, although routine blood work and buffy coat smears can provide helpful monitoring points.

Visceral mast cell tumors (cats): Cats with splenic mast cell tumors often have positive buffy coat smears. Once the spleen is removed, the buffy coat can become negative. There is no difference in survival times between cats with positive or negative buffy coat smears prior to surgery, but it can provide a useful monitoring test.

Staging evaluations should be individualized to fit patient and client needs, as well as the type and location of the tumor.

Overview of Biopsy Principles and Surgical Oncology

by Stephen Withrow

One of the most important steps in the management of the cancer patient is the procurement and interpretation of an accurate biopsy specimen. Not only will the biopsy provide a diagnosis but also it will help predict biologic behavior, which aids in determining the type and extent of treatment that should be afforded.

The common goal with any biopsy technique is to procure enough neoplastic tissue to establish an accurate diagnosis. Which procedure to use will often be determined by your goals for the case, site of the mass, equipment available, general status of the patient, and personal preference and experience. An accurate tissue diagnosis should be attained before treatment for the following two reasons:

If the type of treatment (surgery vs. radiation vs. chemotherapy, etc.) or the extent of treatment (conservative vs. aggressive resection) would be altered by knowing the tumor type. A biopsy is particularly important if the surgery is in a difficult location (e.g., distal extremity, tail, or head and neck) for reconstruction or if the proposed procedure carries significant morbidity (e.g., maxillectomy or amputation).

If the owners' willingness to treat their pet would be altered by knowledge of tumor type and therefore, prognosis, a biopsy is desirable before major therapeutic intervention.

General Guidelines for Tissue Procurement and Fixation

1. The proper performance of an incisional or needle biopsy does not increase the rate of metastasis. On the other hand, cancer cells may be allowed to contaminate the tissues surrounding the mass, making resection more difficult. The biopsy site should be planned so that it may be subsequently removed along with the entire mass.
2. Avoid biopsies that contain only ulcerated or inflamed tissues.
3. Several samples from one mass are more likely to yield an accurate diagnosis than a single sample.
4. Small biopsies should not be obtained with electrocautery, as it tends to deform (by autolysis or polarization) the cellular architecture.
5. If evaluation of margins of excision is desired, it is best if the surgeon marks the specimen (fine suture or ink on questionable edges) or submits margins in a separate container.
6. Tissue is generally fixed in 10% buffered neutral formalin with one part tissue to ten parts fixative.
7. Tissue should not be thicker than 1 centimeter or it will not fix deeply. Large masses can be cut into appropriate sized pieces and representative sections submitted or sliced like a loaf of bread, leaving one edge intact, to allow fixation. After fixation (two to three days), tissue can be mailed with a 1:1 ratio of tissue to formalin.
8. A detailed history should accompany all biopsy requests!

Biopsy Methods

The more commonly used methods of tissue procurement are needle punch biopsy, incisional biopsy, and excisional biopsy. All have indications depending on a number of variables such as tumor size, location, presence of ulceration, and likelihood of malignancy.

Interpretation of Results

The pathologist's job is to determine: 1) tumor vs. no tumor, 2) benign vs. malignant, 3) histologic type, 4) grade (if available and clinically relevant), and 5) margins (if excisional). Many pitfalls can take place to render the end result inaccurate. Potential errors can take place at any level of diagnosis and it is up to the clinician in charge of the case to interpret the full meaning of the biopsy result. As high as 10% of biopsy results are inaccurate in a clinically significant sense. If the biopsy result does not correlate with the clinical scenario, several options are possible:

1. Call the pathologist and express your concern over the biopsy result. This exchange of information should be helpful for both parties and not looked upon as an affront to the pathologist's authority or expertise. It may lead to:

   a. Re-sectioning of available tissue or paraffin blocks.
   b. Special stains for certain possible tumor types (e.g., toluidine blue for mast cells).
   c. A second opinion by another pathologist.

2. If the tumor is still present in the patient, and particularly, if widely varied options exist for therapy, a second (or third) biopsy should be performed.

   A carefully performed, submitted, and interpreted biopsy may be the most important step in management and subsequent prognosis of the patient with cancer. All too often tumors are not submitted for histologic evaluation after removal because "the owner did not want to pay for it." Biopsies should not be an elective owner decision. Because of increasing medicolegal concerns, it is not medical curiosity alone that mandates knowledge of tumor type.

Surgical Oncology

The vast majority of solid tumors in animals will be treated with surgery. Surgery can be used to prevent cancer (e.g., ovariohysterectomy in young dogs prevents later development of mammary cancer), diagnose cancer (biopsy), provide palliation (removal of necrotic oral tumor in a dog with metastasis), debulk a tumor to enhance response to radiation or chemotherapy, or surgery can be used with curative intent.

Just like radiation and chemotherapy, surgery can be administered by dose. The commonly used doses are intralesional (shelling out a lipoma), marginal (on the pseudocapsule, often leaves microscopic residual disease), wide (in excess of 1 cm margins), and radical (entire compartment, e.g., amputation). Tumor site, tumor grade, tumor stage, and species affected determine the needed surgical dose. If curative intent surgery has been performed, it is imperative to properly submit the entire specimen (fixed and inked) for assessment of grade and adequacy of removal (margins). Incomplete margins require immediate re-intervention with a second surgery, radiation, or chemotherapy rather than waiting for the inevitable local recurrence and possible metastasis. Aggressive surgical resection such as mandibulectomy, maxillectomy, orbitectomy, nasal planum resection, amputation, limb sparing, rib removal, and hemipelvectomy are generally tolerated well with acceptable cosmetic and functional outcomes. Proper attention to analgesia, anesthesia, and postoperative support are vital to a successful outcome.

An Overview of Common Type Tumors: Signs, Symptoms, Treatment Options

by Kevin A. Hahn, D.V.M., Ph.D., D.A.C.V.I.M. (Oncology)
Gulf Coast Veterinary Specialists

Editor's Note: As there is ongoing clinical research, protocols will be added or modified. Many factors are taken into consideration when choosing the appropriate one for your canine patient.

Acute Lymphoid Leukemias in Dogs

Common Clinical Presentation : Acute onset lethargy and anorexia; splenomegaly common; mild lymphadenopathy

Common Histologic Type(s): Lymphoblasts; differentiate from stage V lymphoma

Epidemiology and Natural Behavior: No age or gender predilection; large-breed dogs; rapidly progressive; pancytopenia due to myelophthisis

Prognostic Factors : None identified

Treatment Considerations:

Supportive Treatment: Antibiotics and transfusions of blood and blood products.

Chemotherapy: Use nonmyelosuppressive agents, at least initially (e.g., prednisone, vincristine, L-asparaginase) until normal neutrophil counts are obtained, then use standard lymphoma protocols; median survival is 120 days, with a 40% response rate to vincristine and prednisone

Acute Nonlymphoid Leukemia in Dogs

Common Clinical Presentation: Nonspecific, lethargy, and weight loss; clinical signs also result from cytopenias

Common Histologic Type(s): Not clinical relevant to distinguish because of poor prognosis, but terminology includes acute myeloid (granulocytic), myelocytic, promyelocytic, monocytic, monoblastic, myelomonocytic, megakaryocytic, and erythroleukemic; myelomonocytic is most common

Epidemiology and Natural Behavior: Females, large breeds, all ages; median age is 6 years; rapidly progressive; pancytopenia due to myelophthisis

Prognostic Factors : None identified

Treatment Considerations:

Supportive Treatment: Antibiotics and transfusions of blood and blood products

Chemotherapy: No real efficacy of chemotherapy in this disease, aggressive chemotherapy often causes marrow ablation and death

Anal Sac Adenocarcinoma

Common Clinical Presentation : Dyschezia, perianal mass, and polyuria and polydipsia due to hypercalcemia

Common Histologic Type(s): Adenocarcinoma

Epidemiology and Natural Behavior: Old, female dogs; production of PTH-like hormone causes hypercalcemia; metastasis to regional lymph nodes is common

Prognostic Factors : Dogs with hypercalcemia or with detectable metastases have shorter survival times

Treatment Considerations :

Surgery: May require local excision of tumor and sublumbar lymph nodes; surgery usually resolves hypercalcemia

Radiation Therapy: Applied to local tumor site and sublumbar nodes to prevent tumor regrowth; may resolve hypercalcemia

Chemotherapy: May be useful as an adjunct to surgery or radiation therapy; consider Cisplatin, Adriamycin or Mitoxantrone

Brain Tumors in Dogs

Common Clinical Signs: Seizures and temperament changes

Common Histologic Types: Meningioma

Biological Behavior: Mixed breeds and boxers; old dogs (10 years of age and older); slight male predilection; locally invasive, rare metastases

Prognostic Findings: Worse prognosis with severe neurologic dysfunction, abnormal cerebrospinal fluid, or multiple tumors

Treatment Considerations:

Palliation: Corticosteroids and anticonvulsants

Surgery: May be beneficial for meningiomas

Radiation Therapy: Treatment of choice for gliomas; useful alone or as an adjunct to surgery for meningiomas

Chemotherapy: Hindered by blood-brain barrier; possible role for carmustine and lomustine

Cardiac Hemangiosarcoma in Dogs

Common Clinical Signs: Collapse and cardiac tamponade; hindlimb paresis; and right atrial mass

Common Histologic Types: Hemangiosarcoma

Biological Behavior: Average age is 10 years; German shepherds predisposed; metastasis may be widespread, common to lungs

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Palliative in dogs with resectable lesions

Chemotherapy: Consider Adriamycin-based protocols (see Protocol 1)

Chronic Lymphocytic Leukemia in Dogs

Common Clinical Presentation : Nonspecific; often asymptomatic

Common Histologic Type(s): Mature lymphocytosis; differentiate from reactive lymphocytosis and well-differentiated lymphom

Epidemiology and Natural Behavior : Old dogs; often slow to progress

Prognostic Factors: None identified

Treatment Considerations:

Supportive Treatment: Repeated monitoring by blood counts may be all that is required for asymptomatic animals.

Chemotherapy: The combined use of Prednisone and an alkylating agent (Cytoxan, Melphalan or Leukeran) provides long-term remissions in symptomatic dogs

Cutaneous and Extramedullary Plasmacytomas in Dogs

Common Clinical Presentation: Solitary cutaneous mass in trunk or limbs; may affect oral cavity, ears, and head; less commonly, may occur in multiple or other sites, such as diffuse GI tumors

Common Histologic Type(s): Mature plasma cells

Epidemiology and Natural Behavior : Old dogs; cutaneous tumors are usually benign; plasmacytoma of other sites (e.g., GI) may metastasize

Prognostic Factors: None identified

Treatment Considerations:

Surgery: Surgery with wide surgical margins is curative in most cases of cutaneous plasmacytoma

Radiation Therapy: Radiation-sensitive tumor

Chemotherapy: Melphalan, prednisone, and doxorubicin have all caused tumor responses,

often for a long duration in dogs with extramedullary plasmacytoma

Cutaneous Hemangiosarcoma in Dogs

Common Clinical Signs: Raised, red lesion often in skin that is lightly pigmented

Common Histologic Types: Hemangiosarcoma

Biological Behavior: Average age is 10 years; whippets and other dogs with glabrous skin are predisposed; metastasis is uncommon

Prognostic Findings: Histopathologic evidence of solar elastosis adjacent to tumor is good prognostic sign

Treatment Considerations:

Surgery: Is curative for dermal origin tumors; approximately 30% of subcutaneous origin tumors metastasize

Radiation Therapy: Radiation-sensitive tumor; excellent local control for incompletely excised tumors

Chemotherapy: Role undecided due to low metastatic rate and resultant lack of need for adjuvant therapy

Cutaneous Melanoma in Dogs

Common Clinical Signs: Darkly pigmented epidermal lesion, usually raised but not ulcerated

Common Histologic Types: Most are well differentiated (benign); subungual tumors are more aggressive

Biological Behavior: Adult to aged dogs

Prognostic Findings: Subungual melanoma, 50% metastasize; other cutaneous sites, metastasis is rare

Treatment Considerations:

Surgery: Surgical excision curative for most cutaneous lesions

Radiation Therapy: Radiation-sensitive tumor; >85% local control rates observed for 2 years or longer

Chemotherapy: Cisplatin or carboplatin chemotherapy for metastatic lesions (or possibly as an adjunct to surgery in subungual melanoma);

Cutaneous Squamous Cell Carcinoma in Dogs

Common Clinical Signs: Ulcerated cutaneous lesions, most often on limbs (digits); lesions may be induced by sunlight on trunk

Common Histologic Types: Most cutaneous squamous cell carcinomas are well differentiated and rarely metastasize

Biological Behavior: Large, black-breed dogs prone to subungual tumor, which may metastasize; light-skinned dogs prone to actinically-induced tumors

Prognostic Findings: Nasal-plane tumors more aggressive; subungual and skin tumors may metastasize; lymphatic invasion for subungual lesion does not influence prognosis for survival

Treatment Considerations:

Early Lesions: Surgical excision, retinoids, topical 5-fluorouracil or carmustine ointments, and cryotherapy if lesions are < 1 cm
Invasive Lesions: Surgery, with or without radiation therapy and intralesional chemotherapy
Metastatic Lesions: Cisplatin or mitoxantrone chemotherapy

Erythrocytosis in Dogs

Common Clinical Signs: Polyuria, polydipsia, bleeding, seizures, and hyperemic mucous membranes

Common Histologic Types: Mature erythrocytosis; rule out relative and secondary polycythemia

Biological Behavior: Middle-aged animals; no

breed predilection; bleeding and seizures due to hyperviscosity; elevated red cell mass without increase in erythropoietin

Prognostic Findings: None identified

Treatment Considerations:
Phlebotomy: Periodic removal eventually induces iron deficiency and microcytic cells that may assist in palliation

Chemotherapy: Hydroxyurea has shown efficacy giving long remission durations

Pancreatic Tumors (Exocrine) in Dogs

Common Clinical Signs: Nonspecific anorexia and weight loss

Common Histologic Types: Exocrine pancreatic carcinoma

Biological Behavior: Old dogs (mean age is 9 years); cocker spaniels may be predisposed; high metastatic rate

Prognostic Findings: None identified

Treatment Considerations:
Surgery: May not be beneficial due to high metastatic rate

Chemotherapy: Anecdotal reports of Gemzar efficacy in dogs

Hyperadrenocorticism in Dogs

Common Clinical Signs: Hypercortisolism, polydipsia, polyuria, and cutaneous changes; nervous system dysfunction with large pituitary tumors

Common Histologic Types: Pituitary adenomas of par distalis in 80% of dogs; less commonly, adrenal gland tumors (usually carcinoma)

Biological Behavior: Middle-aged to old dogs; poodles, dachshunds, and boxers at higher risk; no gender predilection; metastasis rare for pituitary tumors but common for adrenal tumors

Prognostic Findings: None identified

Treatment Considerations:
Surgery: Treatment of choice for adrenal tumors

Medical Management: For pituitary tumors, mitotane and ketoconazole offer good long-term palliation by their effects of adrenal cortical destruction and interference with steroid synthesis, respectively; L-deprenyl may also be a useful agent; mitotane (o,p'-DDD) may be a useful agent at high doses for adrenal tumors

Radiation Therapy: Provides good palliation for neurologic dysfunction caused by large pituitary tumors and gives moderate control of cortisol levels

Insulinoma in Dogs

Common Clinical Presentation: Hypoglycemia and hyperinsulinemia; tachycardia and neurologic signs may be intermittent; peripheral polyneuropathy may cause tetraparesis

Common Histologic Type(s): Carcinoma

Epidemiology and Natural Behavior: Old dogs with no gender predisposition; large-breed dogs more commonly affected; most tumors are highly metastatic

Prognostic Factors: Dogs with tumors confined to pancreas have a longer symptom free period and survival after surgery; dogs that have only lymph node metastasis live longer than dogs with distant metastasis

Treatment Considerations:
Surgery: Treatment of choice for localized tumors

Medical Management: Prednisone, diazoxide, sandostatin, octreotide, and propranolol may control hypoglycemia
Chemotherapy: Streptozotocin and alloxan may

be effective; however, both are extremely nephrotoxic and require diuresis

Intestinal Tumors in Dogs

Common Clinical Signs: Duodenum/Jejunum: Vomiting, melena Jejunum/Ileum: Weight loss and diarrhea Colon/Rectum: Tenemus and Hematochezia

Common Histologic Types: Adenocarcinoma; less commonly, leiomyosarcoma and lymphoma; leiomyosarcoma common in the cecum

Biological Behavior: Old, male dogs; most tumors are adenocarcinoma; adenocarcinoma more likely to metastasize than leiomyosarcoma, usually to regional lymph nodes

Prognostic Findings: Colorectal: Dogs with annular lesions have poor survival; other types of lesions have a better prognosis

Treatment Considerations:

Surgery: Little information for adenocarcinoma; average survival dogs with colorectal adenocarcinoma is 15 months after surgery; median survival is > 1 year for leiomyosarcoma

Radiation Therapy: Rectal adenocarcinoma may be controlled by high-dose fractions; median control is >6 months

Cryotherapy: Small, minimally invasive tumors of the rectum and distal colon

Chemotherapy: Consider adjunct to surgery or radiation therapy

Liver Tumors in Dogs

Common Clinical Signs: Nonspecific lethargy and weight loss; dogs may be asymptomatic and may have a palpable mass

Common Histologic Types: Primary hepatocellular carcinoma

Biological Behavior: Old dogs; large solitary lesions have low metastatic rate, but the majority have multiple nodular or diffuse involvement

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Treatment of choice; dogs with solitary hepatocellular carcinoma, regardless of size, have a good prognosis after resection (median survival exceeds 1 year)

Chemotherapy: Palliative use of alkylating agents (Cytoxan and Leukeran) have been beneficial in dogs with diffuse or nodular disease

Lower Urinary Tract Tumors in Dogs

Common Clinical Signs: Mimic Infection - Hematuria, stranguria, and pollackiuria; often have secondary infections

Common Histologic Types: Transitional cell carcinoma

Biological Behavior: Old dogs, usually females; insecticidal dips, and obesity may be associated with development of bladder tumors

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Palliative only; most tumors involve trigone region of the bladder

Radiation Therapy: Excellent local control, however fibrosis of bladder may occur as late effect

Chemotherapy: Palliative at best, should be consider adjuvant to surgery or radiation; best results with seen with Mitoxantrone combined with Piroxicam (Protocol 4) followed by Carboplatin or Piroxicam

Lung Tumors in Dogs

Common Clinical Signs: Persistent cough, dyspnea, hemoptysis, lameness in cats (metastasis

to digits), hypertrophic osteopathy (in dogs), anorexia, lethargy, and malaise

Common Histologic Types: Adenocarcinoma (bronchogenic) most common

Biological Behavior: Disease of older aged animals; tumors are likely to cause pleural effusion and respiratory stridor; metastases are common early in the course of the disease

Prognostic Findings: Normal appearing hilar regional lymph nodes are associated with significantly longer survival time following surgery than if nodes are enlarged; effusion, increasing size and presence of metastases are also negative prognostic signs

Treatment Considerations:

Surgery: Lung lobectomy is the treatment of choice in dogs and cats without effusive disease; median survival exceeds 1 year

Chemotherapy: Unproven results, consider Protocols 1-3, or 10 adjuvant to surgery due to the high metastatic potential for lung tumors

Lymphoma in Dogs

Common Clinical Signs: Generalized peripheral lymphadenopathy

Common Histologic Types: Diffuse large cell, immunoblastic, and small lymphocytic

Biological Behavior: All breeds, middle-aged, systemic disease

Prognostic Findings: Clinical Stage: Advancing stage and dogs with clinical signs are associated with a worse prognosis.

Hypercalcemia: Worse when associated with an anterior mediastinal mass.
Sex: Female dogs better than male dogs.
Body Size: Small dogs better than large dogs.
Pretreatment Corticosteroids: Worse (controversial findings).
High Grade: Higher response rate and longer duration of remission.

Treatment Considerations:

Surgery: Rarely considered unless confined to a single node

Radiation Therapy: Unproven efficacy; considered in the palliative care of multidrug resistant lymphoma (4-6 months additional remission)

Chemotherapy:
Single Agent: Prednisone, cyclophosphamide, vincristine - 50% CR for median 1-6 months.
Single Agent: Doxorubicin - 60%-75% CR for median 6-8 months.
Combinations: Various usages of multiple drugs - 70%-80% CR for median 9-18 months

Mammary Tumors in Dogs

Common Clinical Signs: Presence of a mass in the mammary chain

Common Histologic Types: Approximately 50% are benign (e.g., fibroadenomas, simple adenomas, and benign mixed mammary tumors); approximately 50% are malignant (e.g., solid carcinomas and tubular or papillary adenocarcinomas)

Biological Behavior: Most common neoplasm in females; average age is 10-11 years; poodles, terriers, cocker spaniels, and German shepherds are overrepresented; early ovariohysterectomy protective; 50% of tumors are multiple; lungs and lymph nodes are most common sites of metastasis Prognostic Findings:German shepherds have a poor prognosis; poor prognosis associated with increasing tumor size, ulceration, degree of invasion, increasing degree of malignancy, lymph node involvement, and lack of hormone receptors

Treatment Considerations:

Surgery: Regional resection of tumor is as effective as mastectomy for localized tumor(s); removal of lymph node may be of prognostic

value; ovariohysterectomy may not be of value for preventing recurrence

Radiation Therapy: Unproved efficacy; may be considered in the palliation of inflammatory carcinomas

Chemotherapy: Doxorubicin or mitoxantrone based protocols may be effective in some cases (see Protocols

Mast Cell Tumors in Dogs

Common Clinical Signs: Raised or ulcerated intracutaneous mass; may be hairless or haired; may be single or multiple. Mast cell tumors can look and feel like anything

Common Histologic Types: Histologic grade influences surgical prognosis. Moderately differentiated (Grade II) tumors are most common

Biological Behavior: Boxers, Boston terriers, and golden retrievers predisposed, but can occur in any breed, at any age; metastasis is similar to other hematopoietic tumors; to regional lymph nodes as well as liver, spleen and bone marrow

Prognostic Findings: Tumors on limbs have better prognosis than trunk (especially perineum); slow growth and long duration of presence may be favorable; most important prognostic factor is histologic grade

Recurrence rate 6 months after incomplete-excision surgery:

25% for well-differentiated tumors
44% for moderately-differentiated tumors
76% for poorly-differentiated tumors

Treatment Considerations:

Well-differentiated to Moderately-differentiated tumors: Wide surgical excision; adjunctive radiation therapy (88% achieve 5-year control for moderately differentiated tumors); although efficacy is uncertain, recent use of CCNU and/or Velban have shown promise.

Poorly-differentiated tumors: Surgery, with or without radiation therapy, is palliative; H2 blockers, prednisone, and vincristine chemotherapy may be helpful (see Protocol 8)

Mesothelioma in Dogs

Common Clinical Signs: Effusion of body cavities causing abdominal discomfort, tachypnea, and respiratory distress; in decreasing order of incidence: affects pleural, peritoneal, or pericardial cavities

Common Histologic Types: Epithelial-type mesothelioma

Biological Behavior: Old dogs; exposure to asbestos and pesticide powders may be associated with development of mesothelioma in dogs

Prognostic Findings: None identified

Treatment Considerations:

Chemotherapy: Intracavitary cisplatin may provide palliation; responses to intravenous Doxorubicin and Mitoxantrone have been noted

Multiple Myeloma in Dogs

Treatment Considerations:

Surgery: Rarely considered; used to palliate neurologic signs (paralysis) due to vertebral disease

Radiation Therapy: Radiation Therapy: Radiation-sensitive tumor; excellent local palliation of signs and complete remissions reported; guarded prognosis due to systemic nature of disease

Chemotherapy:

Prednisone:

Palliative only; median survival is 220 days

Melphalan and Prednisone:

Complete remission in 40% and partial remission in 50% of dogs for a median survival of 540 days

Other Agents: Cyclophosphamide or chlorambucil may be effective

Consider chemotherapy adjunct to radiation therapy

Treatment Considerations:
Surgery: Contraindicated

Radiation Therapy: Treatment of choice; survival time for nonhematopoietic malignancies is 20 to 27 months; median survival time for cats with nasal lymphoma approaches 16 months

Chemotherapy: Recommended for nasal lymphoma due to systemic disease

Nasal Tumors in Dogs

Common Clinical Signs: Unilateral epistaxis, facial deformity, and epiphora

Common Histologic Types: Adenocarcinoma

Biological Behavior: Most common in old dogs; no breed or sex predilection; tumor is locally invasive and rarely metastasizes to distant sites until late in the course of the disease

Prognostic Findings: Brain involvement is a poor prognostic sign

Treatment Considerations:
Surgery: Contraindicated unless it is combined with radiation therapy

Radiation Therapy: With or without surgery, is the treatment of choice; median survival rates vary from 8 to 23 months

Chemotherapy: Cisplatin is reported to be effective in palliating clinical signs; Mitoxantrone is used concurrent with radiation therapy to improve radiation efficacy (survival times exceeding 2 years)

Ally's story:
http://www.treshanley.com/CIC/ally.html

Nonosteosarcoma Bone Tumors in Dogs

Treatment Considerations:

Surgery: Palliative; may be curative in some dogs, although metastases may arise even months to years after surgery

Radiation Therapy: May improve tumor control; palliative for bone pain

Chemotherapy: Unproven efficacy but consider protocols similar for Osteosarcoma to prevent or delay complications arising from metastatic disease

Osteosarcomas have high metastatic rates

Ocular Tumors in Dogs

Common Clinical Signs: Glaucoma, uveitis, hyphema, or visible mass

Common Histologic Types: Melanoma; less commonly, epithelial tumors of the ciliary body

Biological Behavior: Melanomas and epithelial tumors have low potential for metastasis; old dogs are affected

Prognostic Findings: High mitotic index may indicate potential for metastasis in melanoma

Treatment Considerations:
Surgery: Enucleation is usually curative, even after failure of local excision; other treatment modalities are generally not required

Chemotherapy: Unproved efficacy, possibly consider Piroxicam or Tamoxifen as palliative therapy

Oral Tumors in Dogs

Common Clinical Signs:Oral mass, bleeding from the mouth, and dysphagia

Common Histologic Types: Benign: Fibromatous epulis; acanthomatous epulis (may invade bone)

Biological Behavior: Malignant: Melanoma, Squamous cell carcinoma, and Fibrosarcoma

Prognostic Findings:
Melanoma - High metastatic rate; old dogs
Squamous Cell Carcinoma - Moderately metastatic; lingual and tonsillar types are highly metastatic; old dogs
Fibrosarcoma - Low metastatic rate, young dogs
Epulides - Do not metastasize; all ages

All Tumor Types: Small tumors and rostral location have a better prognosis

Melanoma: Low mitotic index is associated with a better prognosis

Squamous Cell Carcinoma: Dogs with maxillary tumors and young dogs have a better prognosis

Treatment Considerations:
Surgery: Mandibulectomy or maxillectomy for local control of malignant tumors

Radiation Therapy: Curative for acanthomatous epulis; coarse fractionation may be useful for melanoma; adjunctive for squamous cell carcinoma and fibrosarcoma after surgery gives good control

Chemotherapy: Platinum compounds best for melanoma, 50% 1 year survival times reported; chemotherapy not usually required for other tumor types; see Protocols 2, 4 & 5

Biological Response Modifiers: Piroxicam and Tamoxifen have anecdotal efficacy for dogs with melanoma and squamous cell carcinoma

Osteosarcoma of the Appendicular Skeleton in Dogs

Common Clinical Signs: Lameness and pain at metaphyseal sites, particularly distal radius, proximal humerus, proximal tibia, and distal femur; lytic and productive bone lesion on radiographs

Common Histologic Types: Osteoblastic Osteosarcoma is most common; other diagnoses are possible - chondroblastic, telangietic, and fibroblastic

Biological Behavior: Large to giant breeds; no sex predilection; usually middle-aged to old dogs; metastasis occurs early but may not be clinically evident

Prognostic Findings: Survival is poor; prognosis is not correlated with gender, tumor site, or whether a presurgical biopsy is performed

Treatment Considerations:
Surgery: With amputation alone, median survival is 162 days; 11% of dogs are alive at 1 year; limb sparing provides good limb function for distal radius tumors

Radiation Therapy: Radiation sensitive tumor but curative intent protocols rarely considered due to poor prognosis; palliative use for pain control as an alternative to amputation is considered good, median duration of pain control is 8 months

Chemotherapy: Regardless of limb removal, various chemotherapy protocols have shown efficacy in prolonging survival time:
Cisplatin or Carboplatin - 40% to 60% of dogs alive at 1 year
Doxorubicin - 50% of dogs alive at 1 year
Combination - 50% of dogs alive at 18 months

Osteosarcoma of the Axial Skeleton in Dogs

Common Clinical Signs: Tumors of the appendicular skeleton are four times more common than axial tumors

Common Histologic Types: Multilobular Osteochondroma and Osteosarcoma

Biological Behavior: Old dogs (except rib tumors, which often affect young dogs); no breed predilection; more females may be affected; highly metastatic, but local recurrence is more of a

problem; mandibular osteosarcoma may have lower metastatic rate

Prognostic Findings: None identified

Treatment Considerations:
Surgery: Difficult due to location of tumors; mandible and rib tumors can be resected

Radiation Therapy: May be useful adjunct to surgery to reduce local recurrence or for palliation of pain

Chemotherapy: Recommended for osteosarcoma of all sites

Chemotherapy: Unproven

Ovarian Tumors in Dogs

Common Clinical Signs: Abdominal mass or swelling; unexplained or abnormal estrus or bleeding

Common Histologic Types: Adenomas and adenocarcinomas

Biological Behavior: Old dogs (median age is 10 years); teratomas occur in young dogs

Prognostic Findings: None identified

Treatment Considerations:
Surgery: Surgical excision curative for most tumors

Chemotherapy: Consider Protocols 1-4 adjuvant to surgical excision if carcinomatosis observed

Peripheral Nerve Sheath Tumors

Common Clinical Signs: Slowly progressive lameness

Common Histologic Types:
Dogs: Neurofibrosarcoma

Biological Behavior:
Dogs: Large-breed dogs; middle-aged dogs (average age is 7 years); local disease, rare metastasis

Prognostic Findings: None identified

Treatment Considerations:
Surgery: Surgical resection of tumor for small masses; amputation and resection for large masses or if severe neurologic deficits are present; complete excision is difficult, recurrences are common

Radiation Therapy: Used for incompletely excised tumors, disease free times can exceed 2 years

Chemotherapy: Most effective for lymphoma; not necessary for soft tissue variants

Renal Tumors in Dogs

Common Clinical Signs: Often no clinical signs; hematuria with transitional cell carcinoma

Common Histologic Types: Carcinomas and adenocarcinomas

Biological Behavior: Old dogs, usually males; nephroblastoma in young dogs; German shepherds may have cystadenocarcinomas and nodular dermatofibrosis on an inherited basis

Prognostic Findings: None identified

Treatment Considerations:
Surgery: High metastatic rate for carcinomas makes cure unlikely; early removal of nephroblastoma may be curative

Chemotherapy: Only reported for nephroblastoma; vincristine, doxorubicin, and actinomycin D may be palliative

Retrobulbar Tumors in Dogs

Common Clinical Presentation: Exophthalmos, nicitans protrusion, and deviation of globe

Common Histologic Type(s): Multiple types;

osteosarcoma, fibrosarcoma, mast cell tumors, and lymphoma are most common

Epidemiology and Natural Behavior: Most tumors are locally aggressive; metastatic rate varies with tumor type

Prognostic Factors: None identified

Treatment Considerations:
Surgery: Orbitectomy may be curative for small tumors

Radiation Therapy: Should be useful as an adjunct to surgery for all tumor types but is still under investigation

Chemotherapy: May be useful for lymphoma; consider Protocols 1-4 as adjunct to local modalities for treatment of osteosarcoma and osteochondrosarcoma

Salivary Gland Tumors in Dogs

Common Clinical Presentation: Cervical mass; anorexia or dysphagia is possible

Common Histologic Type(s): Adenocarcinoma

Epidemiology and Natural Behavior: May be diffuse oral tumor rather than a mass; metastasis may be more common in cats than dogs; old animals affected (median age is 10 years); poodles and Siamese cats are predisposed

Prognostic Factors: None identified:

Surgery: High rate of local recurrence in dogs

Radiation Therapy: When used as an adjunct to surgery, radiation therapy seems to improve local control in dogs; presumably the same in cats

Chemotherapy: Unproven efficacy

Soft Tissue Sarcoma in Dogs

Common Clinical Presentation : Subcutaneous firm and irregular mass appears (but is not) encapsulated

Common Histologic Type(s): Fibroma, fibrosarcoma, hemangiopericytoma, neurofibroma, neurofibrosarcoma, schwannoma, rhabdomyoma, rhabdomyosarcoma, leiomyoma, leiomyosarcoma, and malignant fibrous histiocytoma

Epidemiology and Natural Behavior: Young cats; may be related to FeSV and FeLV infection; possible correlation with vaccination site in cats; locally invasive with a low metastatic rate

Prognostic Factors: Wide surgical excision at first surgery; metastasis is uncommon

Treatment Options:
Surgery: Rarely results in cure

Radiation Therapy: Adjuvant external beam radiation therapy

Chemotherapy: Doxorubicin-based protocols and intralesional methods are being investigated.

Spinal Tumors in Dogs

Common Clinical Presentation : Pain; slow onset of ataxia and paresis

Common Histologic Type(s): Extradural tumors; vertebral body

Epidemiology and Natural Behavior: Large-breed dogs, young to middle-aged; locally invasive

Prognostic Factors: None identified

Treatment Considerations:
Surgery: Treatment of choice for extradural and intradural-extramedullary tumors; intramedullary tumors are not amenable to surgical excision

Radiation Therapy: May be a useful adjunct to incomplete surgery

Chemotherapy: Rarely considered unless tumor is of lymphoid origin

Splenic Hemangiosarcoma in Dogs

Common Clinical Presentation: Palpable abdominal mass; hemoperitoneum; anemia; shock; and possibly collapse

Common Histologic Type(s): Hemangiosarcoma

Epidemiology and Natural Behavior: Average age is 10 years; German shepherds predisposed; metastasis may be confined to abdominal cavity if no concurrent right atrial lesion exists

Prognostic Factors: None identified

Treatment Considerations:

Surgery: Palliative without gross metastases, but survival is short

Radiation Therapy: Considered palliative for some lesions

Chemotherapy: Prolongs survival; most protocols result in a median survival time of 12 to 15 months; consider Protocols 1-4, 7

Splenic Tumors in Dogs

Common Clinical Presentation: Abdominal swelling and weakness; palpable abdominal mass

Common Histologic Type(s): Leiomyosarcoma, osteosarcoma, and fibrosarcoma

Epidemiology and Natural Behavior: Average age is 11 years; no breed or gender predilection; metastasis commonly occurs to abdominal sites

Prognostic Factors : None identified

Common Clinical Signs: Abdominal swelling and weakness; palpable abdominal mass

Common Histologic Types: Leiomyosarcoma, osteosarcoma, and fibrosarcoma

Biological Behavior: Average age is 11 years; no breed or gender predilection; metastasis commonly occurs to abdominal sites

Prognostic Findings: Ruptured viscera, hemoperitoneum, coagulopathy, signs attributable to anemia are poor prognostic signs

Treatment Considerations:

Surgery: Palliative without gross metastases, but survival is short

Radiation Therapy: Considered palliative for some lesions

Chemotherapy: Prolongs survival; most protocols result in a median survival time of 12 to 15 months; consider Protocols 1-4, 7

Squamous Cell Carcinoma

Surgery: Treatment of choice and margins of at least 2cm are recommended.

Radiation Therapy: Recommended in combination with surgery or chemotherapy.

Chemotherapy: Intralesional implants with 5-fluorouracil, oral cisplatin have variable success.

Other: Retinoids and Photodynamic Therapy.

Stomach Tumors in Dogs

Common Clinical Signs: Chronic vomiting, weight loss, and inappetence

Common Histologic Types: Adenocarcinoma; less commonly, leiomyomas; most common in lower two thirds of stomach

Biological Behavior: Old, male dogs; tumors cause ulceration and commonly metastasize to perigastric lymph nodes or viscera

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Tumors are usually diffuse and have metastasized at the time of diagnosis; therefore, aggressive surgery is rarely successful; recurrence is common

Radiation Therapy: Unproven

Chemotherapy: Unproven

Synovial Cell Sarcoma:

Common Clinical Signs: Lameness and palpable mass

Common Histologic Types: Fibroblastic cell type

Biological Behavior: Middle-aged dogs; medium to large breeds; predominately male dogs; predilection for the stifle

Prognostic Findings: Mitotic index has prognostic value

Treatment Considerations:

Surgery: Amputation, better than 75% chance of 3-year survival

Radiation Therapy: Anecdotal responses reported in soft tissue tumors; provides pain palliation in those with substantial bony involvement

Chemotherapy: Inadequately studied; cisplatin or combination of doxorubicin and cyclophosphamide may be helpful; consider Protocols 1-4, 10 adjunctive to surgery or radiation therapy

Testicular Tumors in Dogs

Common Clinical Signs: Palpable mass in normal or atrophic testis; many are not palpable; feminization changes with some Sertoli cell tumors and seminomas

Common Histologic Types: Seminomas, Sertoli cell tumors, and interstitial cell tumors

Biological Behavior: Seminomas and Sertoli cell tumors have a high incidence in retained testes; old dogs; no breed predilection

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Usually curative as metastatic rate is low

Radiation Therapy: May achieve long-term control for metastatic seminoma to sublumbar lymph nodes

Chemotherapy: No reports of chemotherapy for metastatic tumors

Thymoma in Dogs

Common Clinical Signs: Cough; less commonly, dyspnea and lethargy; may have aspiration pneumonia secondary to myasthenia gravis and megaesophagus

Common Histologic Types: Epithelial malignant component associated with mature lymphocytes and mast cells

Biological Behavior: Old dogs; females possibly predisposed; usually large, invasive, slow-growing tumors with low metastatic rate

Paraneoplastic Syndromes: Myasthenia gravis is most common; polymyositis, hypercalcemia, and second malignancies may occur

Prognostic Findings: Dogs with megaesophagus have a very poor prognosis

Treatment Considerations:

Surgery: May be curative for small or encapsulated tumors; dogs with megaesophagus need to be monitored for aspiration pneumonia; most thymomas are unresectable

Radiation Therapy: Long term remissions (> 2 years) in nonsurgical patients

Thyroid Tumors in Dogs

Common Clinical Signs: Mass in ventral neck; rarely signs of hyperthyroidism

Common Histologic Types: Adenocarcinoma

Biological Behavior: Old dogs; no gender

predilection; beagles, golden retrievers, and boxers predisposed; local invasion is common; moderate metastatic rate

Prognostic Findings: Dogs with invasive tumors ("fixed" to underlying tissues) or large tumors have worse survival rates; not correlated with histologic type, age, breed, or gender

Treatment Considerations:

Surgery: Curative for adenomas; may provide long-term control for small, non-invasive carcinomas, but these have potential to metastasize

Radiation Therapy: External beam radiation may improve local control or reduce size of mass before surgery; radioactive iodine (131I) may cause regression in active hormonal tumors (which are rarely seen in dogs)

Chemotherapy: Significant control of metastatic lesions observed with platinum-based protocols; consider Protocols 1-4

Hormonal Therapy: Anecdotal reports of long-term palliation of metastatic lesions (>1 year) seen with thyroxine supplementation

Transmissible Venereal Tumor in Dogs

Common Clinical Signs: Bleeding mass on external genitalia

Common Histologic Types: Transmissible venereal tumor

Biological Behavior: Spread by coitus and canine social behavior; females more susceptible than males; spontaneous regression is most cases after months, but not in immunosuppressed animals; rare metastasis

Prognostic Findings: None identified

Treatment Considerations:

Surgery: Curative if wide excision and localized tumor

Radiation Therapy: Low doses (10 Gy); may be curative if localized

Chemotherapy: Weekly Vincristine for 5-6 weeks may provide cure in 90% of dogs

Vaginal and Uterine Tumors in Dogs & Cats

Common Clinical Signs: Signs due to pelvic or urethral obstruction

Common Histologic Types: Leiomyoma and fibroma

Biological Behavior: Rare tumors, usually benign; often associated with ovarian cysts and endometrial hyperplasia

Prognostic Findings: None identified

Treatment Considerations:

Surgery: May be curative for benign lesions

Radiation Therapy: Radiation-sensitive tumor; excellent responses observed

Chemotherapy Protocols

Weeks	Protocol 1	Protocol 2	Protocol 3	Protocol 4	Protocol 5	Protocol 6	Protocol 7	Protocol 8	Protocol 9	Protocol 10
1	A	A	CB	M	CB	V,E	V V	BL		V,D,P
2				CB		C	C	V	BL	C,D,P
3	A CB				CB		A V		BL	C,D,P
4			CB	M	CB	V	V		BL	V,D,P
5	A				CB	C	V	Go to 10	BL	C,D,P
6	A			CB			C	G	o to 10	C,D,P
7	A		CB	M	Go to 10	V,E	A			V,D,P
8	CB				C			C,D,P		
9	A						V			C,D,P
10			CB	M		V				V,D,P
11	A				CC		C		C,D,P	
12	Go to 10							C		,D,P
13	CB		CB	M	V	,E	V		V	,D,P
14						C				C,D,P
15							MT			C,D,P
16		Go to 10	Go to 10	Go to 10		V				V,D, P
17						C	V			C,D,P
18						V,E	C			V,D,P
19						C				C,D,P
20							V			C,D,P
21										C,D,P
22						V				V,D,P
23						C	MT			C,D,P
24										C,D,P
25					V,	E	V		V,	D, P

A = Adriamycin, 30 mg/m2 or 1 mg/kg
D = Doxycycline, 50 mg/10 kg, daily
MT = Methotrexate, 0.5 mg/m2

B = Bleomycin, 2 mg/m2
E = Elspar, 10,000 IU/m2
P = Piroxicam, 0.3 mg/kg, daily (with an antacid)

C = Cytoxan, 200-300 mg/m2 divided over 4 days (50-100 mg/m2 in Protocol 10).
L = Leukeran, 4 mg/m2
V = Vincristine, 0.5 mg/m2

CB = Carboplatin, 200 (cat) or 300 (dog)/m2
M = Mitoxantrone, 5 mg/m2

For all protocols, consider concurrent irradiation

Protocol 1: Osteosarcoma, Hemangiosarcoma, Soft Tissue Carcinomas & Adenocarcinomas.

Protocol 2: Osteosarcoma, Bladder Tumors.

Protocol 3: Osteosarcoma, Thyroid Carcinoma, & Lung Tumors.

Protocol 4: Bladder Tumors, Feline Injection-Site Associated Sarcomas.

Protocol 5: Oral and Subungal Melanomas (Carboplatin is 90 mg/m2 IV weekly). Tamoxifen may also be indicated.

Protocol 6: Lymphoma (continue as scheduled for 18 months; consider adding Doxycyline daily).

Protocol 7: Lymphoma (continue as scheduled for 18 months). Soft Tissue Tumors (excluding the use of Elspar). Consider concurrent radiation.

Protocol 8: Mast Cell Tumors, Cutaneous Lymphomas. Consider concurrent radiation. CCNU may also be indicated.

Protocol 9: Tonsillar Squamous Cell Carcinoma.

Protocol 10: Maintenance Protocol for various malignancies (Cytoxan is 100 mg/m2; Leukeran can be substituted).

Supportive Drugs :

Metoclopramide (Reglan), 0.5 mg/kg PO every 8 hours for 5 days

Sulfasalazine (Asulfadine), 33 mg/kg PO every 8 hours for 5 days

Cimetidine (Tagamet), 4 mg/kg PO every 8-12 hours

Mammary Cancer

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Mammary tumors are the most common ***tumors*** in female dogs who have not been **spayed**. Mammary tumors can be small, simple nodules or large, aggressive, ***metastatic*** growths. With early detection and prompt treatment, even some of the more serious tumors can be successfully treated. Cats also suffer from mammary tumors and they have their own unique set of problems that are discussed in a separate article.

Which dogs are at risk for developing mammary tumors?

Mammary tumors are more common in unspayed, middle-aged female dogs (those between 5 and 10 years of age), although they can, on rare occasions, be found in dogs as young as 2 years. These tumors are rare in dogs that were spayed under 2 years of age. Occasionally, mammary tumors will develop in male dogs and these are usually very aggressive and have a poor prognosis.

Spaying greatly reduces the chances of a female dog developing this condition. In those females spayed prior to their first heat cycle, breast cancer is very, very rare. Those that are spayed after their first heat, but before their fourth heat or before 2.5 years of age will have a somewhat decreased incidence of breast cancer than those who are never spayed. Those spayed after 2.5 years of age have the same incidence of disease as those who were never spayed. It is believed that the elimination or reduction of certain hormonal factors causes the lowering of incidence of the disease in dogs that have been spayed. These factors would probably be ***estrogen***, ***progesterone***, a similar hormone or possibly a combination of two or more of these.

The risk of breast cancer is virtually eliminated in dogs that are spayed before their first heat.

What are the types of mammary tumors in dogs?

There are multiple types of mammary tumors in dogs. Approximately one-half of all mammary tumors in dogs are ***benign***, and half are ***malignant***. All mammary tumors should be identified through a biopsy and histopathology (microscopic examination of the tissue) to help in the treatment of that particular type of tumor.

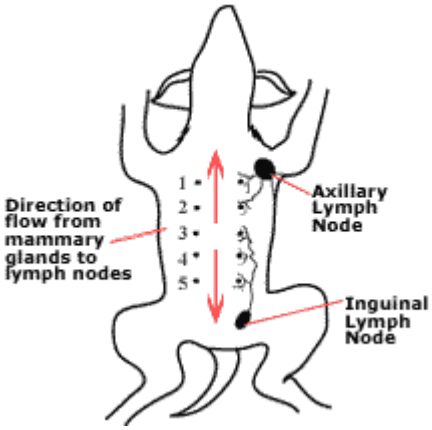
The most common benign form of canine mammary tumors is actually a mixture of several different types of cells. For a single tumor to possess more than one kind of cancerous cell is actually rare in many species. This combination cancer in the dog is called a 'benign mixed mammary tumor' and contains glandular and connective tissue. Other benign tumors include complex adenomas, fibroadenomas, duct papillomas, and simple adenomas.

The malignant mammary tumors include: tubular adenocarcinomas, papillary adenocarcinomas, papillary cystic adenocarcinomas, solid carcinomas, anaplastic carcinomas, osteosarcomas, fibrosarcomas, and malignant mixed tumors.

What are the symptoms of mammary tumors?

Mammary tumors present as a solid mass or as multiple swellings. When tumors do arise in the mammary tissue, they are usually easy to detect by gently ***palpating*** the mammary glands. When tumors first appear they will feel like small pieces of pea gravel just under the skin. They are very hard and are difficult to move around under the skin. They can grow rapidly in a short period of time, doubling their size every month or so.

The dog normally has five mammary glands, each with its own nipple, on both the right and left side of its lower abdomen. Although breast cancer can and does occur in all of the glands, it usually occurs most frequently in the 4th and 5th. In half of the cases, more than one growth is observed. Benign growths are often smooth, small and slow growing. Signs of malignant tumors include rapid growth, irregular shape, firm attachment to the skin or underlying tissue, bleeding, and ***ulceration***. Occasionally tumors that have been small for a long period of time may suddenly grow quickly and aggressively, but this is the exception not the rule.



It is very difficult to determine the type of tumor based on physical inspection. A ***biopsy*** or tumor removal and analysis are almost always needed to determine if the tumor is benign or malignant, and to identify what type it is. Tumors, which are more aggressive may metastasize and spread to the surrounding ***lymph nodes*** or to the lungs. A chest x-ray and physical inspection of the lymph nodes will often help in confirming this.

Mammary cancer spreads to the rest of the body through the release of individual cancer cells from the various tumors into the lymphatics. The lymphatic system includes special vessels and ***lymph nodes***. There are regional lymph nodes on both the right and left sides of the body under the front and rear legs. They are called the ***'axillary'*** and 'inguinal' lymph nodes, respectively. Mammary glands 1, 2, and 3 drain and spread their tumor cells forward to axillary lymph nodes, while cells from 3, 4, and 5 spread to the inguinal ones. New tumors form at these sites and then release more cells that go to other organs such as the lungs, liver, or kidneys.

What is the treatment?

Surgical Removal: Upon finding any mass within the breast of a dog, surgical removal is recommended unless the patient is very old. If a surgery is done early in the course of this disease, the cancer can be totally eliminated in over 50% of the cases having a malignant form of cancer. The area excised depends on the judgment and preference of the practitioner. Some will only remove the mass itself. Others, taking into consideration how the cancer spreads, will remove the mass and the rest of the mammary tissue and lymph nodes that drain with the gland. For example, if a growth were detected in the number 2 gland on the left side, we would therefore remove glands, 1, 2, and 3 and the axillary lymph node on that side. If it were found in the number 4 gland on the right side, then glands 3, 4, 5, and the inguinal lymph node on that side would be completely removed. With some tumor types, especially sarcomas, complete removal is very difficult and many of these cases will have tumor regrowth at the site of the previously removed tumor.

Owners may confuse a surgical removal of a mammary gland in the dog with a radical mastectomy in humans, with all of the associated problems. In humans, this type of surgery would affect the underlying muscle tissue which complicates the recovery. In the dog, however, all of the breast tissue and the related lymphatics are outside of the muscle layer, so we only need to cut through the skin and the mammary tissue. This makes the surgery much easier and recovery much faster. A radical mastectomy in a dog means all the breasts, the skin covering them, and the four lymph nodes are all removed at the same time. Although this is truly major surgery, suture removal usually occurs in 10 to 14 days with normal activity resuming at that point.

Many veterinarians will spay a dog having a mastectomy (unless she is very old). The value of this in decreasing the recurrence of tumors is still controversial.

Chemotherapy and Radiation Therapy: Chemotherapy has not been a very successful nor widely used treatment for mammary tumors in dogs. However, with the constantly changing and improving drugs available, a veterinary oncologist should be consulted to find out if there is an effective drug available for your dog's particular type of mammary cancer. The effectiveness of radiation therapy has not been thoroughly researched. Some anti-hormonal drug regimens are being tested in dogs. At this point in time, surgical removal of the tumors is the treatment of choice.

How can I prevent mammary cancer in my dog?

There are few cancers that are as easily prevented as mammary cancer in dogs. There is a direct and well-documented link between the early spaying of female dogs and the reduction in the incidence in mammary cancer. Dogs spayed before coming into their first heat have an extremely small chance of ever developing mammary cancer. Dogs spayed after their first heat but before 2.5 years are at more risk, but less risk than that of dogs who were never spayed, or spayed later in life. We all know the huge benefits of spaying females at an early age, but every day, veterinarians still deal with this easily preventable disease. Early spaying is still one of the best things pet owners can do to improve the health and ensure a long life for their dogs.

Conclusion

Mammary cancer is a very common cancer and can often be successfully treated, if caught early. If all non-breeding dogs and cats were spayed before their first heat this disease could be almost completely eliminated. If you find a growth or lump in the mammary tissue of your dog, you should inform your veterinarian immediately and not take a "wait and see" attitude.

References

Bonagura, J. Current Veterinary Therapy 12. W.B. Saunders Co. Philadelphia, PA; 1995.

Ettinger, S. Textbook of Veterinary Internal Medicine. W.B. Saunders Co. Philadelphia, PA; 1989.

Causes of Solid-Appearing Lumps & Bumps on the Skin

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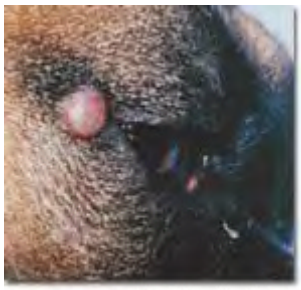


Photo courtesy TFH Publications

Dogs and cats can develop small bumps (papules) or larger lumps (nodules) on their skin. The term 'tumor' means an abnormal growth or swelling, and is often used to designate cancer. Often, the word 'lump' also brings the word 'cancer' to mind. There are, however, many other causes of lumps and bumps. The following table includes most of the conditions which result in solid lumps and bumps. The list is rather extensive, so you can understand why a quick diagnosis may be difficult to make and various diagnostic tests, such as biopsies, may need to be performed. The most common causes of solid lumps and bumps are color-coded gray in the table (some may be more common in certain geographical areas).

Condition	Description	Symptoms	Diagnosis	Treatment
Abscesses	Accumulation of pus; may or may not be caused by an infection; in cats, often due to bite wounds	These may appear as firm or fluid-filled *nodules* of varying shapes and sizes; if due to infection, the animal may have fever, loss of appetite, and depression; may open and drain	History, physical exam, needle aspirate	Surgically open, drain and flush; if infected, administer appropriate antibiotics
Acral lick dermatitis (neurodermatitis)	Self-licking in dogs results in self-trauma; possible causes include anxiety, boredom, stress (e.g., new member in household); licking can develop into an obsessive behavior	Red, hairless, well-circumscribed, sometimes raised lesion usually on leg; if chronic, will drain	Exclude other causes; history important	Relieve underlying cause e.g., anxiety; restrict licking, e.g., Elizabethan collar; behavior modifying medication may be necessary
Allergic and irritant contact dermatitis	An allergic reaction following exposure to antibiotics applied to the skin; metals such as nickel; materials such as rubber, wool, and plastic; and chemicals such as dyes and carpet deodorizers; or inflammation caused by irritating substances such as poison ivy. Generally requires multiple exposures.	Red skin and small bumps or blisters on the areas of skin that are sparsely haired and directly exposed to the offending substance; itching; hair loss in chronic conditions	Patch test, exclusion trials	Restrict exposure to the allergen or contact irritant in the dog's environment; steroids, antihistamines
Apocrine sweat gland cyst	Common	Single, round, smooth *nodules* with no hair; may appear bluish; usually filled with a watery liquid; most common on head, neck, and limbs	Physical exam; biopsy	Surgical removal is optional
Basal cell tumors	*Cancerous*, slow-growing *tumor* which rarely metastasizes; seen in older dogs	Single, sometimes fluid-filled *nodules*, which may ulcerate; usually on the head, neck, and chest; may be *hyperpigmented*	Biopsy	Surgical removal

Bee, wasp, hornet stings	Skin reactions can vary dramatically in severity	Immediately after the bite, see swelling, redness, pain, possibly itching; subsequently may develop extensive *ulcers* with draining; may develop hives or anaphylaxis	History, physical exam	Antihistamines, steroids; wet dressings, if ulcerated; protect the area from self-inflicted trauma
Benign tumors	*See specific type, e.g., Fibromas, Lipomas, Histiocytomas, Basal cell tumor*			
Calcinosis cutis	*Mineralization* of the skin usually due to an excess of corticosteroids; also rarely occurs in kidney failure, or in granulomas and *tumors*	Hard *nodules* and *papules* usually on the back, groin, or *axilla* ulcerate, drain, and develop *crusts*; severe itching; may become infected; often see other signs of Cushing's disease	Skin scrapings, biopsy, history, and other clinical signs, adrenal gland function tests	If due to glandular tumors, selegiline, o,p-DDD (Mitotane), or surgical removal of tumor; if due to high steroid doses, withdraw use of steroids slowly
Callus	Results from chronic pressure, especially in large breed dogs	Thickened, hairless raised areas over bony pressure points such as elbows; may become secondarily infected	History, clinical signs	Provide softer bedding and padding around affected area
Canine acne	Deep inflammation of hair *follicles*; exact cause unknown; usually in young dogs; may see secondary bacterial infection	*Papules*, and sometimes draining lesions on chin and lips	Skin biopsy	Mild: Benzoyl peroxide; Severe: Also treat with antibiotics
Chiggers (harvest mites)	Seasonal disease caused by larvae of the chigger	Itching, bumps usually on feet, abdomen (belly), folds at base of ears	Visualization of mite larvae or microscopic examination of skin scraping	Pyrethrin, Permethrin (Do NOT use permethrin on cats.)
Coccidioidomycosis	Caused by the fungus *Coccidioides immitis* found in the soil in the Southwestern U.S.	Draining *nodules* over infected bones; usually see *respiratory* signs, fever, weight loss	Microscopic examination of drainage; blood tests	Ketoconazole, itraconazole
Cryptococcosis	Fungal infection often transmitted through bird droppings; more common in dogs with suppressed immune systems	*Nodules* often over the nose, which may ulcerate; many other signs depending on what other body systems are infected	Microscopic exam of discharge, blood tests, culture, biopsy; look for underlying cause of immunosuppression	Itraconazole
Cutaneous horn	*Benign* growths of hard tissue, which look like small horns; cause unknown, though may be associated with some underlying disease such as *cancers* or follicular *cysts*	½ to 2 inch hard horn-like growths; may be single or multiple; in cats, may occur on foot pads	Clinical appearance; look for underlying cause	Surgical removal
Cuterebra	Caused by the 1-1½ inch larva of the *Cuterebra* fly; usually seen in late summer	*Nodule* forms around the larva; usually found on the head and neck; nodule has a small opening through which the larva breathes and will eventually escape	Clinical signs; opening the nodule and finding the larva	Surgically open the nodule and remove the larva; do NOT squeeze the nodule or break up the larva or a severe allergic reaction may occur

Dracunculiasis	*Nodule* formed around the parasitic worm *Dracunculus insignis* (Guinea worm)	Single or multiple nodules on limbs, head, and belly; nodules may drain	Clinical signs; opening nodule and finding the female worm (1-4 feet in length!)	Surgical removal
Drug or injection reaction	Rare skin reaction to a drug which is inhaled, given orally, or applied *topically*; more common with penicillins, sulfonamides, and cephalosporins; usually occurs within 2 weeks of giving the drug	Can vary widely and may include itching, hair loss, redness, swelling, *papules*, *crusts*, *ulcers*, and draining wounds	History of being treated with a drug, symptoms, biopsy	Discontinue offending drug; treat symptomatically
Epidermal inclusion cysts (infundibular cysts)	Result from body's reaction to certain skin cells	Very small, up to 2 inch diameter *nodules*, which often contain thick sebaceous material	Needle aspirate, histopathology on removed nodule	Surgical removal may be performed, although new nodules will often form elsewhere; do NOT squeeze these *cysts*, since a more severe skin reaction will occur
Epitheliotrophic lymphoma (mycosis fungoides)	Rare *cancer* of *T lymphocytes* seen in older dogs	Can take multiple forms: redness with itching and *scale*; *ulcers* and loss of pigment; one or more nodules; oral ulcers	Needle or other biopsy	Poor response to treatments, which include chemotherapy, surgical removal, retinoids, fatty acids
Fibroma	Uncommon *benign* tumor	Single *nodule* with a pedicle, usually on legs, groin, or sides	Biopsy	Surgical removal is optional
Fibrosarcoma	Rapidly growing, invasive *tumor*; may occur at the site of a vaccination or injection	Irregular-shaped, firm *nodule*; may ulcerate	Biopsy	Surgical removal, however, since tumor is invasive need to remove large area around tumor, sometimes including large masses of muscle and bone; if tumor is on a leg, amputation of the leg is commonly recommended; surgery may be combined with chemotherapy and radiation
Flea allergy dermatitis (flea bite hypersensitivity)	Severe reaction by the dog to the saliva of the flea	Intense itching, redness, hair loss *papules*, *crusts*, and *scales*; sometimes development of infection or hot spots	Presence of fleas; reaction to intradermal testing	Flea control in the environment and on the dog; steroids and antihistamines for the itching
Follicular cyst	Most common *cyst*; may be called 'sebaceous cysts' by some veterinarians	Single round *nodules* on or underneath the skin; may appear bluish; may contain a thick, yellowish to gray material; usually found on the head, neck, and trunk	Biopsy	Surgical removal optional; do NOT squeeze these cysts, since a severe skin reaction will occur
Granulomas	May be due to infections; the body's reaction to foreign material such as plant material (e.g., foxtail) and suture material; other constant irritation; or unknown causes	Solid firm *nodules* of varying sizes; those due to foreign bodies often have draining tracts; may develop hair loss, *ulcers*, and *secondary infections*	History, clinical signs, biopsy, surgical exploratory	Surgical removal of the foreign body (in the case of plant material, tracts may be extensive and require major surgery); antibiotics, if infected; treat any other underlying cause

Hemangiosarcoma	*Malignant*, invasive *tumor* more common on sun-damaged skin	Blue to reddish black *nodule*; usually on chest or abdomen; often ulcerate	Biopsy	Surgical removal; need to remove large area around the tumor; if tumor is on a leg, amputation of the leg is commonly recommended
Hematoma	Localized collection of blood that has leaked out of blood vessels; often occurs in dogs with ear infections and pendulous ears	These may appear as firm or fluid-filled *nodules* of varying shapes and sizes	Needle aspirate	Depending on location and size, may resolve on their own, or need drainage (e.g., on ear flap)
Histiocytoma	*Benign* tumor of younger dogs	Solitary raised, red *nodules* with a strawberry-like appearance; usually on the legs, head, and ears	Needle aspirate, biopsy	Generally resolve on their own; can be surgically removed
Histiocytosis	There are several kinds of histiocytosis: *Malignant*, which is a *cancer* that affects the skin and internal organs; Systemic, which is a rare disease which affects skin and internal organs; *Cutaneous*, which is a *benign* disease affecting the skin	All cause *nodules* with hair loss; malignant and systemic also have *ulcers*	Biopsy, *fine needle aspirate*;	Malignant: None effective, may need to consider euthanasia; Systemic: Poor response to chemotherapy; Cutaneous: Corticosteroids, relapse is common, especially in Shar-Peis
Histoplasmosis	Fungal infection, which can rarely cause skin lesions	Ulcerated and draining *nodules*; most commonly see respiratory and gastrointestinal symptoms	Needle aspirate or biopsy	Ketoconazole, itraconazole
Hookworms	Infection with the larvae (immature forms) of hookworms	Red bumps, usually on feet, rough foot pads, abnormal nail growth, itching	Physical exam, history of poor sanitation	Treat for intestinal infection; move dog to different environment
Infundibular keratinizing acanthoma	Rare *benign* nodules more common in young Norwegian Elkhounds	One or more small to 1½ inch *nodules*, with small opening through which thick material can be expressed	Biopsy	Surgical removal; retinoids, if multiple lesions
Kerion	Complication of ringworm infection	*Nodule* with hair loss and multiple draining tracts; may not see other signs of ringworm	Culture, biopsy	Clip area and apply *topical* treatment and shampoos; may require systemic treatment with ketoconazole or itraconazole
Leishmaniasis	Caused by a parasite of blood cells; can be transmitted to people who develop a very severe disease	Hair loss, scaling, *ulcers* on nose and ears, sometimes *nodules*; many other nonskin-related signs	Identify the organism in blood or biopsy; blood tests	Because it causes severe disease in people, and treatment of dogs is not curative, euthanasia may be performed
Lichenoid dermatosis	Often a response to other underlying disease such as fleas or bacterial infections	Small flat *nodules* with thick surfaces	Biopsy, look for underlying disease	Treat underlying cause; this reaction usually resolves on its own
Lipoma	Uncommon *benign* fatty tumor	Usually single, soft, domed *nodule*; can become very large	Fine needle biopsy	Surgical removal, if large or interferes with movement

Lymphoma	Common cancer in dogs; can involve the skin	Itching, *ulcers*, nodules, redness	Biopsy	Surgery, chemotherapy, radiation; lymphoma of the skin does not usually respond to treatment as well as other lymphomas
Mammary cancer	Most common in unspayed females; in dogs, 50% are *malignant*	Single or multiple *nodules* under the skin, of varying sizes, often irregular in shape; may ulcerate and drain	Biopsy	Surgical removal
Mast cell tumor	Common *cancer* which is graded from 1-4: Grade 1 is slow-growing *tumors*, and Grade 4 is rapidly growing *malignant* tumors with metastases	Tumors may be of various sizes, appearances, and numbers	Biopsy to grade the tumors, which determines treatment and prognosis	Depends upon grade; surgical removal, taking large area around tumor; chemotherapy; prednisone; radiation
Melanoma	*Malignant* tumor of older dogs	Usually single dark-colored *nodule*, which often ulcerates	Biopsy	Surgical removal, taking large area around *tumor*
Nevi	Usually *benign* lesions; some types may indicate the presence of an underlying disease	Well-delineated firm *nodules*, often multiple and on the head and neck	Biopsy	Surgical removal, although recurrence is common; depending upon the type, look for underlying disease
Nocardia	Bacterial infection usually acquired from a puncture wound	Usually see respiratory signs; skin lesions include draining *nodules*	Bacterial culture, microscopic examination of drainage	Poor prognosis; antibiotics
Panniculitis	May be caused by trauma, foreign bodies, infections, autoimmune diseases or unknown causes	Deep-seated *nodules*, often ulcerated and draining; usually on the body vs. the head or limbs; may see loss of appetite, depression	Microscopic exam of drainage; biopsy; tests to rule out other causes	Surgical removal; if multiple lesions, prednisone and Vitamin E; may need long-term treatment
Pelodera dermatitis	Accidental infection with larvae from a non-parasitic worm that lives in straw and other organic material	Affects areas of skin touching ground; intense itching, redness, hair loss, *papules*, *crusts*, and *scales*	Skin scraping and microscopic examination	Remove bedding; mild antibacterial shampoo; steroids if necessary, to control itching
Phaeohyphomycosis	Caused by wound contamination with a fungus	A single *nodule* on the legs or multiple ulcerated and draining nodules over the body	Microscopic examination of drainage, culture, biopsy	Surgical removal, though often recurs; possible antifungal medications
Pyoderma-deep (bacterial infections of skin and underlying tissue)	Often secondary to another skin disease such as self-inflicted trauma, wounds, acral lick granulomas, allergies, seborrhea	Ulcerated *pustules* or nodules, draining tracts, *crusts*, and thickened skin	Skin scrapings, biopsy, culture	Clip and cleanse area; antibiotics, prevent self-trauma (licking, scratching), NO Steroids
Pythiosis	Caused by an aquatic mold	Ulcerated draining nodules on the legs, head, and base of tail, which may itch; often see other signs of illness due to infection of the gastrointestinal tract	Microscopic examination of drainage; biopsy	Often fatal; surgical removal
Ringworm	Infection with several types of fungus	Hair loss, *scaliness*, *crusty* areas, *pustules*, and *vesicles*, some itching; can develop a draining *nodule* called a 'kerion'	Culture	Miconazole, lime sulfur dips; oral griseofulvin or itraconazole

Sarcoptic mange	**Infection with the *Sarcoptes* mite**	**Intense itching and self-trauma, hair loss, *papules*, *crusts*, and *scales***	**Skin scraping and microscopic examination - the mite is often very difficult to find**	**Amitraz (Mitaban) dips (off-label use*); ivermectin (off-label use*)**
Schnauzer comedo syndrome	**Uncommon; only seen in Miniature Schnauzers**	**Comedones (black heads) on back, mild itching; may see *secondary infection*, thinning of hair; small crusts may develop**	**Clinical signs, breed, skin biopsy**	**Long-term antiseborrheic shampoos; sometimes antibiotics and retinoids**
Sebaceous gland cyst	**Extremely rare**	**Firm *nodules*, usually less than ½ inch in diameter**	**Biopsy**	**Surgical removal**
Sebaceous gland tumors	**Common; rarely spread or recur; several types**	***Nodules*, which may ulcerate; usually on the head and legs**	**Biopsy**	**Surgical removal, if invasive; if a *benign* lesion, removal is optional**
Skin cancer	***See specific type, e.g., Fibrosarcoma, Melanoma, Squamous cell carcinoma, Mast cell tumor, Lymphoma***			
Spider bites/eosinophilic folliculitis	**Bites from some spiders and caterpillars contain strong toxins; usually appear on the nose of dogs and paws of cats**	**Immediately after the bite, swelling, redness, pain; subsequently may develop extensive *ulcers* with draining**	**History, biopsy**	**Corticosteroids, wet dressings, protect the area from self-inflicted trauma; may develop permanent loss of hair and scarring**
Sporotrichosis	**Caused by the fungus *Sporothrix schenckii*, which generaly enters through a puncture wound**	**Raised *nodules* with multiple draining tracts; cats may develop fever, depression, and loss of appetite**	**Microscopic exam of drainage; culture; fluorescent antibody test**	**Potassium iodide, ketoconazole, itraconazole**
Squamous cell carcinoma	**Common *malignant* tumor; may occur more commonly in sun-damaged or chronically irritated skin**	**Two forms: Cauliflower-like lesions, often ulcerated more common on lips and nose; Crusted *ulcers* on limbs or body**	**Biopsy**	**Surgical removal, radiation, *hyperthermia***
Superficial necrolytic dermatitis of Miniature Schnauzers	**Skin reaction to shampoos (usually insecticidal or medicated)**	***Papules*, *pustules*, and *ulcers* with drainage; develop 2-3 days after exposure to the shampoo; may also see fever and depression**	**Breed, history of exposure, clinical signs**	**Treat symptomatically**
Tail dock neuroma	**Nerve regrowth after tail docking causes symptoms**	***Nodule* at site of docking, itching with self-mutilation, hair loss, and *hyperpigmentation***	**History and symptoms**	**Surgical removal**
Tail gland hyperplasia	**Dogs have a *sebaceous gland* on the top of the tail near its base; in this disorder, the gland enlarges; seen in unneutered dogs and secondary to other diseases such as hypothyroidism**	**Oily area, hair loss, *crusts*, and *hyperpigmentation* on area over gland**	**Clinical signs; look for underlying cause**	**Castration may help; treat underlying cause; surgical removal**
Tick bites	**Ticks cause a local inflammation in the skin, even when the entire tick is removed**	***Nodule* and redness at site of the bite; may itch and develop *crusts*; may last several months**	**History**	**Remove the tick; use a tick preventative; allow nodule to resolve on its own**

Urticaria (hives)	**Reaction, often allergic, to insect bite, drug, vaccine, sunlight, etc.**	**Multiple swellings, with hair standing up over swellings; itching may occur**	**History, physical exam**	**Often resolves on its own; in the case of allergic reactions, antihistamines, epinephrine, or corticosteroids depending upon severity**
Warts (cutaneous papilloma)	***Benign*** **growths caused by a virus; usually seen in puppies**	**Light-colored growths with a cauliflower appearance; usually on the lips, tongue, inside of the mouth, and eyelids**	**Clinical appearance, biopsy**	**Usually none - they resolve by themselves; if severe, removal by cryosurgery**
Zygomycosis	**Uncommon fungal disease**	**Draining** ***nodules***; **may also see pneumonia, vomiting, or jaundice depending upon the body organs involved**	**Microscopic examination of the drainage; biopsy**	**Often fatal; surgical removal of nodules followed by amphotericin B, benzimidazoles, or potassium iodide**

References

Birchard, SJ; Sherding RG (eds.) Saunders Manual of Small Animal Practice. W.B. Saunders Co. Philadelphia, PA; 1994.

Greene, CE (ed). Infectious Diseases of the Dog and Cat. W.B. Saunders Co. Philadelphia, PA; 1998.

Griffin, C.; Kwochka, K.; Macdonald, J. Current Veterinary Dermatology. Mosby Publications. Linn, MO; 1993.

McKeever, PJ; Harvey, RG. Skin Diseases of the Dog and Cat. Iowa State University Press. Ames, Iowa; 1998.

Paterson, S. Skin Diseases of the Cat. Blackwell Science Ltd. London, England; 2000.

Paterson, S. Skin Diseases of the Dog. Blackwell Science Ltd. London, England; 1998.

Scott, D.; Miller, W.; Griffin, C. Muller and Kirk's Small Animal Dermatology. W.B. Saunders Co. Philadelphia, PA; 1995.

Limb Sparing and Osteosarcoma

By Dr. Steven Withrow

Canine osteosarcoma (OSA) is a common malignancy of dogs with over 10,000 new dogs affected each year. It is by far the most common primary bone cancer. It generally occurs in large breed (> 20 kg), middle-aged dogs with a slight predilection for males over females. Seventy-five percent affect the limbs with 60% in the front leg and 40% in the back leg. Metaphyseal sites are most common with only rare involvement of the bones of the elbow. Histologic varieties occur (osteoblastic, chondroblastic, fibroblastic, and telangiectatic) but no proof exists that these variants have a different biologic behavior or response to therapy. Radiographic features are generally of a mixed pattern (lytic and blastic change). Many tumors can be "diagnosed" on signalment, history, and radiographs but a needle core biopsy (Jamshidi) is generally recom-mended. If limb sparing is contemplated, the biopsy technique and position should be carefully planned.

The pretreatment evaluation should generally include a CBC, urinalysis, biochemical profile (paying particular emphasis to the serum alkaline phosphatase, which has negative prognostic implications), thoracic radiographs, and bone survey or nuclear bone scan. As many as 10-15% of patients will have multiple lesions demonstrable at presentation and these patients carry a very poor prog-nosis. Metastasis is generally hematogenous to lung or other bones while lymph node metastasis is rare. Once a diagnosis is confirmed, numerous options exist for therapy. Two major areas of concern must be addressed: leg and life.

Leg

Without treatment, most dogs will be euthanized within one to two months for intrac-table pain. Minimal local treatment would include nonsteroidal anti-inflammatories and/or palliative radiation. Amputation is an easy, inexpensive, and effective method of permanent local disease control. Virtually any size dog can undergo an amputation with good quality of life postoperatively.

Limb sparing is designed to produce a pain-free and functional extremity without jeopard-izing survival. In a series of almost 400 limb sparings performed at CSU, the following conclu-sions can be drawn:

Front leg sites (radius, ulna, and occasionally diaphyseal sites in any bone) are better salvage candidates than most metaphyseal sites.

Preoperative treatment that produces significant local tumor death will facilitate the surgical resection and decrease local recurrences. The "best" preoperative treatment ap-pears to be cisplatin to act as a radiation sensitizer and a moderate dose of radiation (30 Gy in 10 frac-tions). The optimal dose, route of delivery, and timing of cisplatin relative to the radiation is still unclear. This adds significantly to the cost of treatment and is not in common usage.

The tumor is excised and replaced with a cortical allograft. Plate fixation usually results in fusion of the radiocarpal or adjacent joint. Occasionally, osteoarticular or composite (bone and prosthesis) grafts are utilized. Partial ulnectomy does not require an allograft or internal fixation.

Complications include infection (~30%), local recurrence (10-20%), and mechanical instability (< 5%). Most of these complications can be controlled or corrected (except local recurrence) with re-opera-tion or antibiotics (oral and/or local antibiotic beads). The "overall" success rate with limb sparing is approximately 80% for a pain free and functional leg.

Graft instability and infection have been decreased by the use of antibiotic im-preg-nated cement in the marrow space of the allograft.

A new biodegradable form of local chemotherapy using a polymer sponge and cisplatin has allowed immediate limb salvage and a less than 20% local recurrence rate.

Limb salvage is difficult, costly, and not as predictable as amputation but offers an alter-native

to amputation for selected patients.

A palliative form of limb salvage is course fractions of radiation (800 rads) given two or three times to the local or metastatic site. Pain relief is often good but long-term control (> 6 months) is rare. Feldene (nonsteroidal anti-inflammatory agent) may allow transient pain relief.

Newer techniques under investigation include intraoperative irradiation of the exposed bone (70 Gy) and reimplantation as well as full course fractionated radiation with cisplatin chemosensitization.

Life

With local disease control alone (amputation or limb sparing), the one-year survival is less than 10% and most patients die of pulmonary metastasis. The most intensely studied chemo-therapies for OSA are doxorubicin, cisplatin, and carboplatin. Most chemotherapy regimens (doxorubicin alone or doxorubicin and one of the platinum drugs) result in an approximate 50% one-year survival, 30% two-year survival, and 15% long-term systemic control rate. The optimal adjuvant chemotherapy protocol is unclear at this time.

Metastasis, especially to lung, is not hopeless; pulmonary metastasectomy in carefully selected patients can result in long-term remission or cure. These treatments are expensive and for a M2 dog (~ 30 kg), the cost of each drug treatment with cisplatin is approximately $400, carbo-platin is approximately $1,000, and doxorubicin is approximately $200. Limb salvage alone is approximately $4,000-$5,000 U.S.

Canine OSA offers a readily available and biologically predictable model for study to ben-efit both dogs and man. Studies on normal dogs as well as dogs with osteosarcoma have led to many innovations and advances in the use of allografts and the treatment of malignant bone tumors in humans.

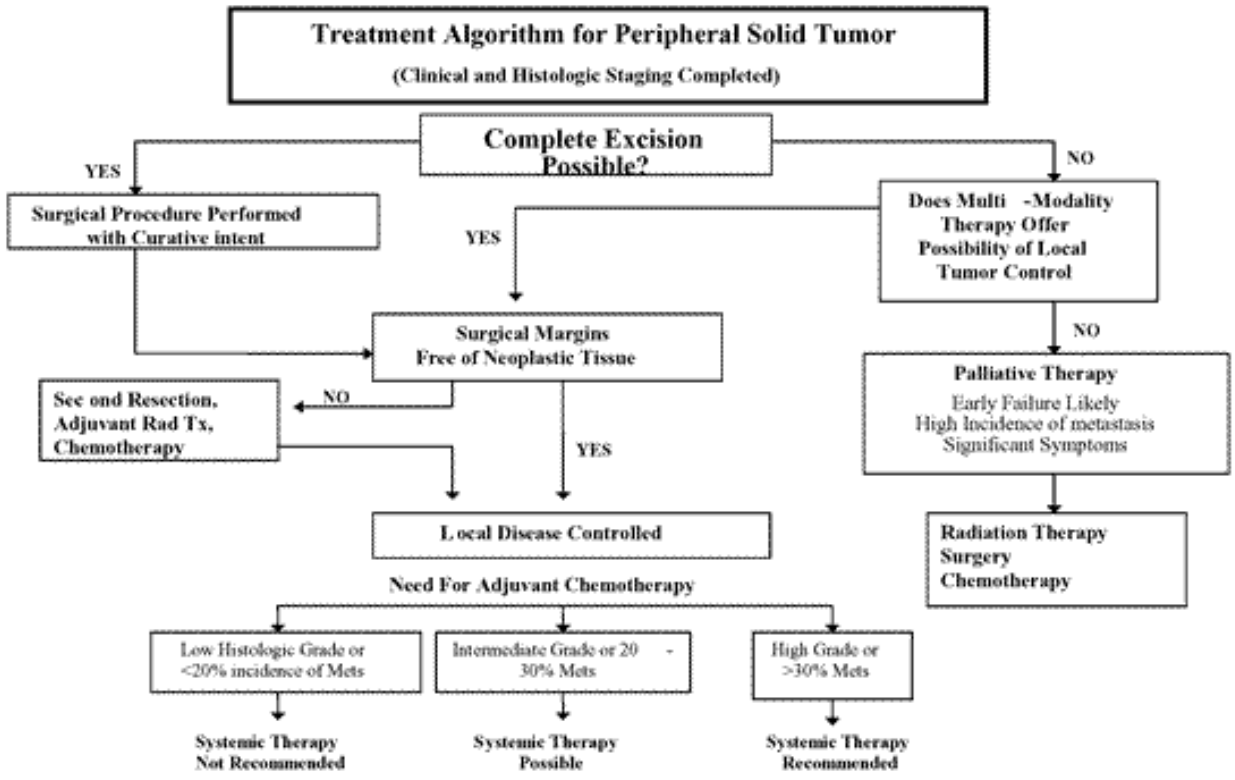
Selected References

1. Straw RC, Withrow SJ, Richter SL, et al. Amputation and cisplatin for treatment of canine os-teosar-coma. J Vet Int Med 5 (No 4), 1991.
2. Carberry CA, Harvey HJ. Owner satisfaction with limb amputation in dogs and cats. J Am Anim Hosp Assoc 1987;23:227-232.
3. Mauldin GN, Matus RE, Withrow SJ, Patnaik AK. Canine osteosarcoma: Treatment by am-puta-tion versus amputation and adjuvant chemotherapy using doxorubicin and cisplat-in. J Vet Int Med 1988;2:177-180.
4. Powers BE, LaRue SM, Withrow SJ, et al. Jamshidi needle biopsy for diagnosis of bone lesions in small animals. J Am Vet Med Assoc 1988;193:205-210.
5. Withrow SJ, Powers BE, Straw RC, et al. Comparative aspects of osteosarcoma. Clin Orthop Rel Res 1991;270:159-168.
6. Straw RC, Powers BE, Withrow SJ, et al. The effect of intramedullary polymethyl-methacrylate on healing of intercalary cortical allografts in a canine model. J Orthop Res 1992;10:434-439.
7. Withrow SJ, Thrall DE, Straw RC, et al. Intra-arterial cisplatin with or without radiation in limb sparing for canine osteosarcoma. Cancer 1993;71:2484-2490.
8. O'Brien MG, Straw RC, Withrow SJ, et al. Resection of pulmonary metastases in canine osteosar-coma: 36 cases (1983-1992). Vet Surg 1993;22:105-109.
9. Straw RC, Withrow SJ, Douple EB, et al. Effects of Cis-diamminedichloroplatinum II released from D,L-polylactic acid implanted adjacent to cortical allografts in dog. J Orthop Res 1994;12:871-877.
10. Bergman PJ, MacEwen EG, Kurzman ID, et al. Amputation and carboplatin for treatment of dogs with osteosarcoma: 48 cases (1991 to 1993). J Vet Int Med 1996;10:76-81.
11. Withrow SJ, Straw RC, Brekke JH, et al. Slow release adjuvant cisplatin for treatment of metastatic canine osteosarcoma. Eur J Exp Musculoskel Res 1995;4:105-110.
12. Straw RC, Withrow SJ. Limb-sparing surgery versus amputation for dogs with bone tumors. Vet Clin North Am: Small Anim Pract 1996;26:135-143.
13. Withrow SJ. Surgery for skeletal sarcomas. Clin Tech Small Anim Pract 1998;13:53-58.
14. Ehrhart N, Dernell WS, Hoffmann WE, et al. Prognostic importance of alkaline phosphatase activity in serum from dogs with appendicular osteosarcoma: 75 cases (1990-1996). J Am Vet Med Assoc 1998;213:1002-1006.

Palliative care in Companion Animal Oncology

By Rodney Page

The world health organization defines palliative care as "The active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological social and spiritual problems, is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families." The goals of veterinary oncology and palliative care have always been well aligned since quality of life has been the overriding concern for animals undergoing cancer treatment. Approximately half of all animals with cancer will die because of the disease and most will require symptom or pain control. The need for palliative care in veterinary oncology is already great, but will likely continue to increase as the field better defines the indications for curative and palliative therapy and recognizes that some aspects of palliative care can be integrated into curative therapies in order to create a continuum of cancer management. For purposes of discussion, the definition of curative therapy will be median control of the primary and any metastatic disease for at least one year with conventional therapy for a given tumor type. Patients with tumors that cannot be controlled for this arbitrary endpoint may be considered eligible for palliative treatment. However, the need for palliative intervention and the type of intervention used is of great debate. The ease of prescribing palliative treatments may restrict future therapies or hinder progress toward a curative treatment. The concept of palliative care in both human and veterinary oncology is in need of rigorous study. The figure below illustrates a treatment decision algorithm based on the concept of curative vs. palliative primary control.



Primary Palliative Therapy:

Primary therapy for palliative purposes is accomplished in order to control a variety of symptoms. Symptoms associated with advanced cancers includes physical disruption of vegetative functions such as dysphasia, tenesmus, dysuria and dyspnea, and symptoms associated with metabolic or paraneoplastic sequelae to cancer such as anemia, cachexia, hypoglycemia, or hypercalcemia. All of these may induce discomfort, anxiety or pain in addition to organic abnormalities. If symptoms are associated with physical presence of a mass, it is generally assumed that reduction of the mass will improve both organic symptoms and pain associated with mass. Primary therapy for palliation includes surgery, chemotherapy, and radiotherapy. The goals of primary therapy in a palliative setting are different than in a curative setting. Palliative surgical debulking is not intended to include large normal tissue margins. Palliative radiation therapy is a combination of doses associated with little acute normal tissue effects. Palliative chemotherapy is administered to attempt reduction or stabilization of nodules to improve quality of life. Supportive medications such as antibiotics, stool softeners, anti-emetics, and others are delivered to ease symptoms either with or without primary therapy. Supportive procedures that may be necessary include transfusions, thoracentesis, cystostomy tubes/valves, nutritional support via feeding tube, etc. Even multimodality therapy (surgery plus chemotherapy or palliative radiation plus chemotherapy) may be appropriate in certain instances. However, certain combinations are problematic, such as palliative radiation and surgery.

Pain Management

Pain can be defined as an unpleasant sensory or emotional experience associated with actual or anticipated tissue damage. Pain is the most feared complication of cancer in humans. Approximately 40% of human patients with cancer suffer from pain and 80% with advanced cancer have pain. Pain control in humans and animals has become a major clinical focus in the last five years. Pain recognition in animals requires close observation. Vocalization is a very late event for animals in response to pain. Physiologic changes in heart rate, respiratory rate, and pupil size (mydriasis) are early signs. Postural signs such as reluctance to lie down and abdominal guarding are also early signs. Restlessness and a change from being interactive to reclusive may be noticeable as well. Pain can be categorized as either acute or chronic. Acute pain may accompany procedures such as surgery or irradiation. Local anesthetics, appropriate use of tranquilizers, and pre-emptive pain management is generally sufficient. Chronic pain requires a more comprehensive approach, often involving a combination of pharmacologic and nonpharmcologic analgesic strategies.

Primary treatment of the tumor can cause a direct reduction in pain even if the tumor does not respond by reduction in volume. The analgesic effectiveness of radiation therapy is well documented in the treatment of bone pain, metastases, and CNS neoplasia. In humans, irradiation of peripheral nerves for perineal pain and hepatic irradiation (2,000-3,000 cGy) for capsular distention is effective and well tolerated. The effect of primary chemotherapy on cancer pain is most often observed when treatment is associated with reduction in tumor size. Surgery can relieve pain and discomfort from problems such as abscessed or ulcerated superficial masses, GI obstruction, CNS compression and unstable boney structures. The benefits of primary therapy should be weighed against the risks, hospitalization, recovery time, and expected duration of benefit.

Use of specific analgesic agents is frequent for patients with cancer-related pain. Glucocorticosteroids have been used generously for animals with cancer in hopes of increasing appetite, mood, and well-being. Specific painful conditions associated with tumors that are known to respond to steroids include: raised intracranial pressure, acute spinal cord compression, metastatic bone pain, neuropathic pain due to

infiltration or compression by tumor, symptomatic lymphedema, and hepatic capsular distention. Non-Opioid analgesics are usually the first line of management in humans. Escalation of the dose to determine analgesic activity to approximately 2X the normal dose is considered the maximum.

Nonsteroidals such as carprofen and piroxicam (0.3 mg/kg pl q 24 hrs) are generally the initial drugs of choice in this category. If insufficient analgesia is achieved with non-opioids, an oral form of opioid is often used and is most often combined with Tylenol (Tylenol 4 with 60 mg codeine dosed at 1-2 mg/kg q6-8h PO, based on the codeine component). In cats, oral butorphanol (0.2-1.0 mg/cat q6-12h PO) may be used as single therapy. Morphine tablets or morphine suppositories may also be used. Transdermal fentanyl administration has been very useful for both pre-emptive pain relief and ongoing pain relief from chronic pain. Companion animals are rarely sustained on long-term opioid narcotics for chronic pain. Many alternatives exist now for administration of pain medication in humans for prolonged periods such as indwelling SQ ports, implants, etc. In some situations, prolonged pain control in dogs or cats may be indicated.

Acupuncture, chiropractic management and physical therapy may be incorporated into pharmacologic management of pain to enhance overall well being.

When is Radiation Therapy Really Indicated?

By Donald Thrall

Radiation Therapy Technique

Considerable knowledge has been gained in the past 10 years about the best way to administer radiation therapy. Guidelines for total dose, the size of dose per fraction, and overall time are now developed. In earlier days of veterinary radiation therapy, it was commonplace to give relatively large fractions (4.5 Gy) three days per week, for a total of 10 fractions (45 Gy total dose). We now know this total dose is too low, and the fraction size is too big. It is also known that prolongation of treatment time is disadvantageous and administration of daily fractions is now commonplace.

Large fraction sizes predispose to serious complications in slowly proliferating normal tissues, such as spinal cord or heart. These complications are life threatening and limit the dose of radiation that may be administered. By using smaller doses per fraction, the probability of these complications in slowly proliferating tissues can be avoided. Use of smaller fraction sizes necessitates prolongation of overall time to administer a sufficiently large total dose. This will increase stress on animal owners and the expense of treatment but shortcuts around this basic fact are not realistic.

Increasing the intensity of dose administration by giving small fractions, but on a daily basis, may increase the frequency of complications in rapidly proliferating tissues, such as skin. Unfortunately, the tumor behaves like a rapidly proliferating tissue and it is not generally possible to give a dose of radiation likely to control the tumor and not have some demonstrable change in proliferating normal tissue. Fortunately, although temporarily discomforting, these reactions in rapidly proliferating tissues heal and do not generally limit the dose of radiation that may be administered to the patient.
Prolongation of treatment time allows tumor proliferation during treatment. This proliferation increases the number of tumor clonogens that must be sterilized by the radiation. The biologic basis for proliferation during protracted treatment schemes being detrimental to radiation response of the tumor is indisputable and unnecessary gaps in treatment or prolongation of treatment should be avoided.

Typical definitive radiation therapy protocols in veterinary medicine involve daily administration of 3.0 Gy fractions for a total dose of 57-60 Gy.

Decision Making

When one considers therapeutic options for a tumor, typically only one modality is chosen. Often this is a bad decision, making permanent local control of the tumor impossible. The first therapy administered should be the optimal therapy, and this may entail combinations of modalities. Clearly, combination therapy will initially be more expensive than one single therapy, but in treating recurrent tumors, considerable additional expense will be incurred. Additionally, recurrent tumors are more refractory to permanent local control and the best chance for curing the tumor is administration of the optimal therapy the first time the tumor is treated.

The tumor factors that should be considered when selecting the initial therapy are: 1) location; 2) volume; 3) grade; and 4) histologic type. Many individuals place the greatest amount of significance on histologic type, but the other three factors often play a bigger role in determining response to therapy.

When using any single modality, killing less than 10% of the tumor cells will result in a partial response where the tumor will be visibly smaller, but still grossly apparent. Killing 99% of the cells will typically result in a complete response where there is no gross evidence of the tumor. However, this amount of cell killing is far from a cure. Assume that a tumor contains 1010 cells (not an unreasonable assumption). If one kills 99% of 1010 cells, there are 108 (100,000,000) cells remaining. Clearly, this tumor is going to recur. A complete response lulls the clinician into thinking that an effective therapy has been administered. Therapy of solid tumors should be aimed at permanent local control, not simply obtaining a complete response. This requires killing 10 to 12 logs of cells, not just two or three.

Efficacy of Radiation Therapy Alone

Very few macroscopic tumors can be controlled with radiation therapy alone. Some examples are: 1) acanthomatous epulides; 2) gingival carcinomas (canine); 3) small grade II mast cell tumors; and 4) transmissible venereal tumors.(4,5,9,10) This small list is the result of tumor volume being the biggest factor contributing to the failure of radiation therapy to control tumors. The detrimental effect of increasing tumor volume occurs at surprisingly small tumor volumes.(5) Thus, for gross tumors where complete surgical excision is not possible, combinations of therapy should be considered as the first-line therapy rather than trying a less aggressive, and ineffective, treatment.

Surgery and Radiation Therapy

The combination of surgery and radiation therapy is one of the most effective cancer treatment options available to veterinarians. Optimal use of this combination requires thoughtful preplanning and communication among all involved parties as well as adherence to good surgical oncologic principles. Surgery can be used either before or after radiation therapy, and there are indications for each sequence. This will not be discussed here, but more information is available.(7)

By judicious combination of surgery and radiation, permanent local control of various solid tumors may be achieved. These include: 1) grade I and II mast cell tumors; 2) canine and feline soft tissue sarcomas; and 3) miscellaneous soft tissue tumors such as thyroid, perianal tumors, ear canal tumors.(3,6) The combination of surgery and radiation may also be beneficial for canine nasal tumors, but the probability for permanent local control is not high.

Chemotherapy and Radiation Therapy

The combination of chemotherapy and radiation therapy is clearly superior to radiation therapy alone for some human tumors. Clinical trials documenting this principle in veterinary medicine have not been performed. Nevertheless, in theory this may be useful in some patients. Problems relate to the uncertainties of scheduling of the two agents, possible chemotherapy dose reductions, and unexpected toxicity.

Some chemotherapeutic agents are actual radiosensitizers, but in reality, one should expect only an additive interaction in vivo. Even with additivity, increased response is a reasonable expectation if chemotherapy kills cells that would not have been killed by radiation. Agents that are used in combination with radiation in veterinary medicine include cisplatin, carboplatin, and doxorubicin.

Chemotherapy has been added to the combination of surgery and radiation therapy in treatment of canine nasal tumors, feline vaccine associated sarcomas, and high-grade canine soft tissue sarcomas. Results documenting the superiority of these combinations are not yet available.

Chemotherapy in combination with radiation is also used in canine melanoma. Canine melanoma cells have been characterized by a large capacity to accumulate and repair sublethal radiation damage. Thus, because of their large repair capacity, similar to slowly proliferating normal tissues as described above, there have been trials using large fractional doses of radiation, sometimes in combination with chemotherapy. These trials have proven that complete response of the primary tumor is possible in many patients.(1,2) Metastasis remains a serious issue.

Palliative Radiation Therapy

Often, patients have tumors where the chance for definitive control is very low regardless of the modality or modalities used. Many of these patients can benefit from palliative radiation therapy. The intent of palliative radiation therapy is alleviation of discomforting clinical signs associated with the tumor, not prolongation of survival. This intent must be made perfectly clear to the pet owner. Palliative irradiation involves administration of fewer fractions (typically 1-5) with larger doses per fraction (4-8 Gy) than employed in definitive irradiation. Palliative irradiation has been used for treatment of bone and soft tissue tumors with some success and in osteosarcoma, factors associated with long remission times have been identified (8). These include length of bone involved and degree of tumor lysis.

Summary

The knowledge of technical aspects of delivering radiation therapeutically, and the biologic aspects of interaction of radiation with tissue, and behavior of the tumor, has increased considerably in the past 10 years. The limitations of any single modality are well understood. There are some tumors that may be controlled with radiation therapy, but many are best treated with a combination of modalities. It is important that the first therapy administered be the absolute best therapy. Radiation has a role in palliation of signs associated with advanced bone and soft tissue tumors.

References

1. Bateman, K.; Catton, P.; Pennock, P.; Kruth, S. 0-7-21 Radiation therapy for the treatment of canine oral melanoma. J Vet Int Med 8:267-272; 1994.
2. Blackwood, L.; Dobson, J. Radiotherapy of oral malignant melanomas in dogs. J Am Vet Med Assoc 209:98-102; 1996.
3. Cronin, K.; Page, R.; Spodnick, G.; Dodge, R.; Hardie, E.; Price, G.; Ruslander, D.; Thrall, D. Radiation therapy and surgery for fibrosarcoma in 33 cats. Vet Radiol and Ultrasound 39:51-56; 1998.
4. Gillette, E.; McChesney, S.; Dewhirst, M.; Scott, R. Response of canine oral carcinomas to heat and radiation. Int J Radiat Oncol Biol Phys 13:1861-1867; 1987.
5. LaDue, T.; Price, G.; Dodge, R.; Page, R.; Thrall, D. Radiation therapy for incompletely resected canine mast cell tumors. Vet Radiol and Ultrasound 39:57-662; 1998.
6. McKnight, J.; Mauldin, G.; McEntee, M.; Meleo, K.; Patnaik, A. Radiation treatment for incompletely resected soft-tissue sarcomas in dogs. J Am Vet Med Assoc 217:205-210; 2000.
7. McLeod, D.; Thrall, D. The combination of surgery and radiation in the treatment of cancer: A review. Vet Surg 18:1-6; 1989.
8. Ramirez III, O.; Dodge, R.; Page, R.; Price, G.; Hauck, M.; LaDue, T.; Nutter, F.; Thrall, D. E. Palliative Radiotherapy of Appendicular Osteosarcoma in 95 Dog. Vet Radiol and Ultrasound 40:517-522; 1999.
9. Thrall, D. Orthovoltage radiotherapy of canine transmissible venereal tumors. Vet Radiol 23:217-219; 1982.
10. Thrall, D. Orthovoltage radiotherapy of acanthomatous epulides in 39 dogs. J am Vet Med Assoc 184:826-829; 1984.

Indications and Toxicities of Selected Antineoplastic Agents

There are five major categories of antineoplastic agents:

Akylating agents: Interfere with the replication and transcription of DNA.
Antimetabolites: Interfere with the synthesis of DNA or RNA.
Antitumor antibiotics: Interfere with the replication and transcription of DNA
Vinca Alkaloids: Are anti-mitotic. The act specifically on the mitotic spindle and Cause a metaphase arrest.
Miscellanous Agents: Interfere with the replication and transcription of DNA.

Combination antineoplastic chemotherapy offers many advantage. For example, drugs used with different target sites or mechanisms of action are used together to enhance destruction of tumor cells. Combinations that include a cycle non-specific drug administered first, followed by a phase-specific drug, may offer the advantage that cells surviving treatment with the first drug are provoked into mitosis and therefore, are more susceptible to the second drug.

AA : Antibiotic Antineoplastics
ALA: Alkylating Agent
AM: Antimetabolites
OAA: Other Alkylating agents
HA: Hormonal Agents
MISC: Antineoplastic agents with unique mechanisms of actions
MI = Mitotic Inhibitors

Drug: **Bleomycin (AA)**

Major Indications: Carcinomas (testicular, squamous cell of head and neck, cervical, penile), lymphoma, seminoma, malignant teratoma
Acute Toxicities: Nausea, vomiting, anorexia, fever, allergic reactions including anaphylaxis
Delayed Toxicities: Pneumonitis, pulmonary fibrosis, mild myelosuppression, alopecia, hyperpigmentation, skin ulceration, stomatitis

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Drug: **Carmustine (ALA)**

Major Indications: CNS neoplasias (astrocytomas and gliomas), GI carcinomas, multiple myeloma
Acute Toxicities: Nausea, vomiting, anorexia
Delayed Toxicities: Moderate myelosuppression, (may be delayed for 4-6 wk, nephrotoxicity, hepatotoxicity, pulmonary toxicity

§

Drug: Chlorambucil (ALA)

Major Indications: Chronic lymphocytic leukemia, lymphoma
Acute Toxicities: Nausea, vomiting, anorexia
Delayed Toxicities: Moderate myelosuppression

§

Drug: Cisplatin (OAA)

Major Indications: Osteosarcoma, carcinomas (transitional cell, testicular, squamous cell of head and neck, ovarian, cervical, bladder, and lung), mesothelioma
Acute Toxicities: Intense nausea, vomiting, anorexia, diarrhea, anaphylaxis
Delayed Toxicities: Extreme nephrotoxicity, renal potassium and calcium wasting, ototoxicity, moderate to severe myelosuppression, peripheral neuropathy, hyperuricemia, hypermagnesemia.

NOTE: Severe, potentially fatal pulmonaryedema may occur in cats.

§

Drug: Cyclophosphamide (AA)

Major Indications: Lymphoma, sarcomas, mammary adenocarcinoma, ymphocytic leukemia
Acute Toxicities: Nausea, vomiting, anorexia
Delayed Toxicities: Severe myelosuppression, alopecia, sterile hemorrhagic cystitis

§

Drug: Cytarabine (AM)

Major Indications: Lymphoma, (including CNS), leukemia
Acute Toxicities: Nausea, vomiting, anorexia, nephrotoxicity, hepattoxicity
Delayed Toxicities: Moderate myelosuppression, alopecia

§

Drug: Dacarbizane (AA)

Major Indications: Lymphoma, (for use in protocols after relapse)
Acute Toxicities: Nausea, vomiting, anorexia, extravasation results in tissue damage; hepatotoxicity
Delayed Toxicities: Moderate myelosuppression, alopecia, hepatotoxicity

§

Drug: Doxurubicin (Adriamycin) (AA)

Major Indications: Lymphoma, acute lymphocytic and granylocytic leukemia, sarcomas, (osteosarcoma, hemangiosarcoma, rhabdomyosarcoma) and carcinomas (mammary, ovarian, small cell lung, thyroid, testicular, prostatic, transitional cell, squamous cell of the head and neck, cervical), plasma cell myeloma, hepatoma, neuroblastoma

Acute Toxicities: Nausea, vomiting, anorexia, hemorrhagic colitis, red urine (not hematuria), transient ECG changes, arrhythmias, nephrotoxicity, urticaria, pruritus, anaphylactoid reactions, severe tissue reaction if extravasated.

Delayed Toxicities: Cumulative, dose-related digitalis-unresponsive congestive heart failure, severe myelosuppression, alopecia, stomatitis, anorexia, GI irritation, cutaneous reactions

§

Drug: 5-Fluorouracil (AM)

Major Indications: GI, lung, liver, and mammary carcinomas (systemic); cutaneous carcinomas (topical)

Acute Toxicities: Systemic: nausea, vomiting, anorexia, GI ulceration, neurotoxicity, hepatotoxicity

Topical: local irritation, pain, hyperpigmentation

NOTE:Topical administration in cats has resulted in fatal neurotoxicity

Delayed Toxicities: Moderate myelosuppression, oral and enteric ulcers, neurotoxicity

§

Drug: L-Asparaginase (Misc.)

Major Indications: Acute lymphocytic and lymphoblastic leukemia and lymphoma

Acute Toxicities Nausea, vomiting, anorexia, abdominal pain, hypersensitivity reactions, anaphylaxis, especially after repeated doses

Delayed Toxicities: Hepatotoxicity, nephrotoxicity, pancreatitis, CNS effects, inhibition of coagulation and immune responsiveness (B and T cells), mild myelosuppression

§

Drug: Melphalan (AA)

Major Indications: Multiple myeloma

Acute Toxicities: Nausea, vomiting, anorexia, (infrequent)

Delayed Toxicities: Moderate myelosuppression, alopecia (infrequent)

Drug: **Methotrexate (AM)**

Major Indications: Lymphoma, Sertoli cell tumor, osteosarcoma, metastic transmissible venereal tumor
Acute Toxicities: Nausea, vomiting, anorexia, ulceration, stomatitis, hepatotoxicity, pulmonary toxicity
Delayed Toxicities: Moderate myelosuppression, alopecia

§

Drug: **Mitoxantrone (AA)**

Major Indications Lymphoma, carcinomas (squamous cell, transitional cell, mammary, thyroid), fibrosarcoma, hemangiopericytoma
Acute Toxicities: Nausea, vomiting, anorexia, diarrhea, depression
Delayed Toxicities: Moderate myelosuppression

§

Drug: **Prednisolone (HA)**

Major Indications: Lymphoma, mast cell tumors, palliative treatment of brain tumors
Acute Toxicities: Sodium retention, GI ulceration, pancreatitis
Delayed Toxicities: Protein catabolism, muscle wasting, delayed wound healing, suppression of hypothalamic-pituitary adrenal axis, immuno-suppression

§

Drug: **Tamoxifen (HA)**

Major Indications: Estrogen-receptor-positive mammary carcinomas
Acute Toxicities: Vomiting, abnormalities in estrous cycle
Delayed Toxicities:

§

Drug: **Vinblastine (MI)**

Major Indications: Lymphoma and leukemias, mastocytoma
Acute Toxicities: Mild nausea, vomiting, anorexia, phlebitis, severe tissue if extravasated
Delayed Toxicities: Severe myelosuppression, neurotoxicity with high doses, stomatitis, paralytic ileus, alopecia, inappropriate secretion of antidiuretic hormone

§

Drug: Vincristine (MI)

Major Indications	Lymphoma, leukemias, CNS tumors, mast cell tumors, mast cell tumors, mammary adenocarcinoma, soft-tissue sarcomas, immune-mediated thrombocytopenia
Acute Toxicities:	Mild nausea, vomiting, anorexia, phlebitis, severe tissue reaction if extravasated
Delayed Toxicities:	Slowly reversible sensorimotor peripheral neuropathy and muscle weakness, constipation, paralytic ileus, alopecia, inappropriate secretion of antidiuretic hormone, mild myelosuppression

The following material, has been excerpted and adapted from The Merck Veterinary Manual, Eighth Edition, 1998. We are indebted to Dr. Susan Aiello for permission to reprint.
http://www.merck.com

Chemotherapy Side Effects

By Sarah E. Sheafor, DVM, Diplomate, ACVIM (Oncology)

There are very few words in the English language with quite as much emotional baggage as the words "cancer " and "chemotherapy". I routinely see clients who start out their conversations with me by saying that while they want to hear what I have to say about their pet's cancer, they feel that giving chemotherapy is cruel and inhumane (or words to that effect). In veterinary oncology, our goal is to maintain a normal quality of life at all times. How can we help all of our patients on therapy to be happy, eating and normal at home?

1. Correct dose. This point seems to be an obvious one in that we should always weigh each patient prior to each treatment, and recalculate the amount of drug based on the scheduled dose, but the issue is actually more complex. For example, the body surface area chart is inaccurate for dogs under 20 pounds if they are being given doxorubicin, carboplatin or melphalan, (and possibly other drugs as well). These drugs need adjustments in the dose (ie, decreasing the dose of doxorubicin to 25mg/m2 from 30mg/m2 in a miniature poodle).

2. Correct dose for the species. Cats, as we all know, are not small dogs. Using dog doses in cats will result in unacceptable toxicity when we administer doxorubicin, carboplatin and vincristine.

3. Prophylactic antibiotics when using myelosuppressive chemotherapy or doxorubicin. When we can predict that many patients will become severely neutropenic (<1200 neutrophils) following administration of a drug or drug combination, administration of a broad spectrum antibiotic can be helpful. CCNU, doxorubicin/dacarbazine, and high dose carboplatin, are all examples of drug therapy where we will see at least one in five dogs become neutropenic 5-10 days after therapy. A study presented at last year's VCS meeting proved that administering sulfa-trimethoprim to all dogs after standard single agent doxorubicin chemotherapy resulted in many fewer dogs developing gastroenteritis as well as fewer dogs developing sepsis.

4. Anti-emetics. Different chemotherapy drugs cause nausea/vomiting or diarrhea in different ways. In order to prescribe an effective anti-emetic, we must first understand the mechanism of toxicity. For example, cisplatin activates the chemoreceptor trigger zone as it is being administerd, so drugs designed to block that pathway of nausea (IV butorphanol, ondansetron, dolasetron) are the most effective and are given prior to the cisplatin administration. In contrast, those few dogs who develop nausea/vomiting or diarrhea after doxorubicin treatment most commonly do so 2-4 days after the chemotherapy is given. The mechanism of the vomiting/diarrhea is that the chemotherapy kills the gut crypt enterocytes, so several days later, the villus tips in the small intestine are denuded (similar to viral enteritis). Carafate and pepcid will not help as the problem is rarely gastric. Peptobismol is often very helpful, as is metoclopramide. If this side effect of doxorubicin occurs in one patient, that same patient will develop the problem with subsequent doses of doxorubicin. Prevention by using glutamine (an essential amino acid for gut enterocytes) and peptobismol beginning prior to the next chemo and continuing for 4 days after that chemo is usually successful.

5. Monitoring for complications/picking the right drug for the patient. We must know the organ toxicities of chemotherapy agents in each species. Doxorubicin, for example, is not a good choice for a dog with congestive heart failure/myocardial disease, but is also a poor choice for a cat with renal failure. Dogs receiving long term CCNU therapy need to be monitored for liver disease (chronic effect of this drug in some dogs). If renal/hepatic function is compromised, drugs that are metabolized or eliminated by these organs will need dose adjustments as their half lives in circulation may be prolonged.

6. Urologic toxicity. Cyclophosphamide and ifosphamide can both cause sterile hemorrhagic cystitis, a painful condition that mimics a severe bladder infection in clinical signs. Cyclophosphamide should not be given to dogs showing signs of lower urinary tract disease. While this side effect is most common with chronic cyclophosphamide administration, it is an occasional acute effect. Co-administration with prednisone is somewhat effective as a preventative. Ifosphamide should never be given without MESNA concurrently to prevent cystitis.

7. Hair loss. Only some chemotherapy drugs can cause hair loss in some veterinary patients. Doxorubicin, liposome-encapsulated doxorubicin, and taxol are the major culprits. Poodles, bichon frises and their mixes are the most susceptible to hair loss, although there are individual dogs where thinning haircoats can be seen (I have seen this problem in the occasional Briard, Golden Retriever, Schnauzers, and Labs). Often when we see hair loss in breeds like labs or golden retrievers, they have underlying pruritic allergic dermatitis, and the places that they rub become bald as the growth rate of their fur has been slowed by the chemotherapy. Chemo alopecia cannot be treated or prevented. Pruritic skin disease (except in the case of liposome-encapsuled doxorubicin) is NOT caused by chemotherapy - there must be an allergic dermatitis, scabies, pyoderma, or other cause. Whisker loss in cats is common with doxorubicin treatment, although hair loss is rare.

8. Knowing breed related problems. Shetland Sheepdogs and giant breed dogs (Deerhounds, Wolfhounds) are more likely to have chemotherapy problems than other breeds of the same size. We routinely adjust doses and use prophylactic medications in dogs like these.

9. Adjusting doses/altering drugs if side effects occur that cannot be prevented. No chemotherapy protocol is set in stone. All protocols can be adjusted to meet individual needs.

By following these simple steps, we all can try to make certain that few dogs or cats have "human-like" chemotherapy experiences.

The Immune System

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The immune system is the surveillance and defense system of the body. It recognizes foreign substances (those not belonging to the body, e.g., ***viruses***, bacteria, pollen) by their molecular features and eliminates them from the body.

Two functional divisions of the immune system (innate and adaptive)

The immune system can be divided into two parts based on how specific their functions are. These two divisions are called the innate immune system and the adaptive immune system.

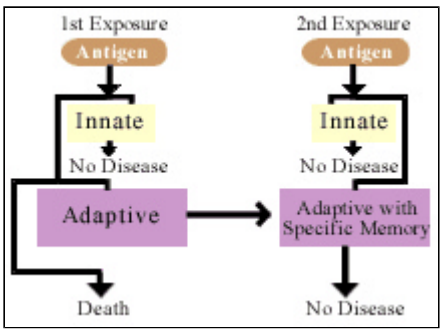
Innate immune system: All organisms, even trees, have what could be considered an innate defense system. For trees it would be their bark, for dogs and cats it would be their skin, and for a bacterium it would be the cellular wall around it.

The innate immune system is the first line of defense. It is nonspecific, meaning it is designed to more or less keep everything out. And it is nonadaptive, meaning its effectiveness is not changed by repeated exposure to a foreign substance. In addition to the skin, stomach acid, mucous in the ***respiratory*** system, and special chemicals in saliva are part of this innate system. There are also certain cells in the body called phagocytes (eaters) and include cells called monocytes and macrophages (literally, 'big eaters'). These cells will basically eat anything foreign that is in sight.

A medieval castle would be a good analogy of the innate immune system. The high castle walls and the moat around the castle are designed to keep almost everything out. They act like the body's skin, mucous, and stomach acid. In the moat, we have alligators, which like the macrophages in the body, will basically eat anything.

Adaptive immune system: In addition to the innate system, dogs, cats, and other animals including humans have an adaptive immune system. The adaptive system defends the body against specific foreign invaders, designing different tactics for different invaders. The parts of the adaptive system communicate with each other and develop a memory of the various invaders they encounter.

In our castle analogy, the adaptive immune system would include archers, spear-throwers, cannoneers, and swordsmen. They each use different tools and defend against those invaders for which they are best designed. They remember previous battles and can improve the speed and efficiency in which they defend the castle.

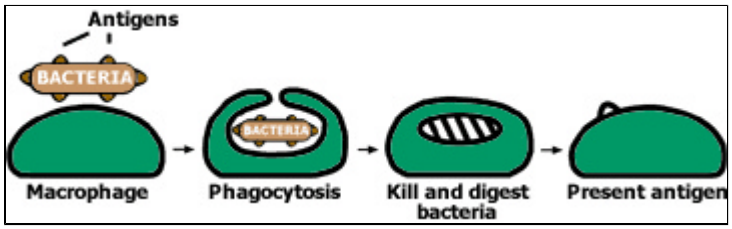


Working together: The innate system is the first line of defense. If the invader is stopped by the innate system, no disease will occur. If, however, the invader cannot be stopped by the innate system, the adaptive system is activated. If the adaptive system is successful, the body will recover. The adaptive system will also retain memory of the invader. So, if a second exposure to the invader occurs, the adaptive system will mount a greater and faster response, usually preventing disease. If neither the innate or adaptive systems are effective, death can occur.

Cells of the immune system

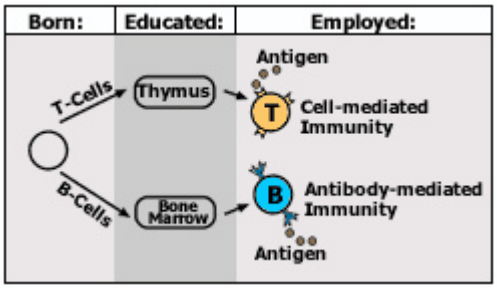
As we learn more about how the immune system works, it will help to have a better understanding of the players. The cells of the immune system all start out in the bone marrow, but mature along different pathways.

Monocytes and macrophages: When mature, monocytes and macrophages leave the bone marrow and spread throughout the body. Monocytes generally stay within the bloodstream. Macrophages enter the ***tissues*** and do their work there.



As part of the innate immune system, the phagocytose (eat), digest, and kill foreign invaders. They can also serve as part of the adaptive system by presenting portions of the invaders (the antigens) to other cells in the adaptive system, alerting them to the presence of the invader.

Granulocytes: There are several different types of granulocytes, which differ in function and in appearance when stained with certain stains in the laboratory. They mature in the bone marrow and then circulate in the blood and also enter tissues. They are also phagocytes, and are part of the innate system.



Lymphocytes: Lymphocytes have a life cycle similar to animals. They are 'born' in the bone marrow. As they mature, they are 'educated.' Some of them go to the thymus gland (different than the thyroid gland) and are educated there. These are called 'T cells' - 'T' for 'thymus.'

The other lymphocytes are educated in a different area. In the chicken, the area is called the 'bursa' and so these are called 'B cells.' In birds, the bursa is a modified piece of intestine. Mammals do not have a bursa, but instead, cells either go to the fetal ***liver*** or remain in the bone marrow to be educated. So the 'B' in 'B cell' could also stand for 'bone marrow.'

Once educated, both the B and T lymphocytes are then employed and move throughout the body to where the jobs are. They tend to accumulate in the ***lymph nodes*** and ***spleen***. We will talk more about the education of lymphocytes below.

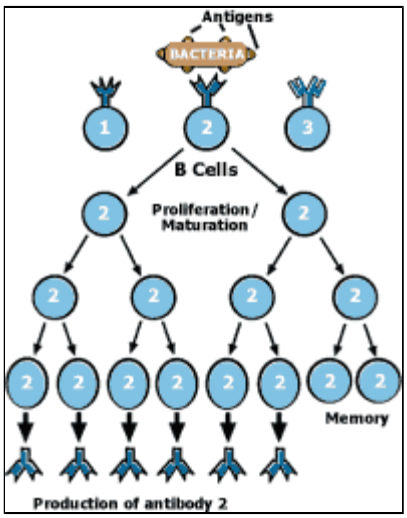
The immune response

What are antigens? Antigens are molecular structures on the surfaces of such particles as bacteria, viruses, and pollens. Antigens are recognized by the body as 'foreign' and stimulate the body to defend itself against them. Antigens have various sizes and shapes. They also have a specificity. That is, all of a certain type of bacteria, virus, or other foreign substance (e.g., pollen) will have the same, or almost identical antigens. A virus generally has several different kinds of antigens on its surface. The same is true for bacteria, parasites, pollens, etc.

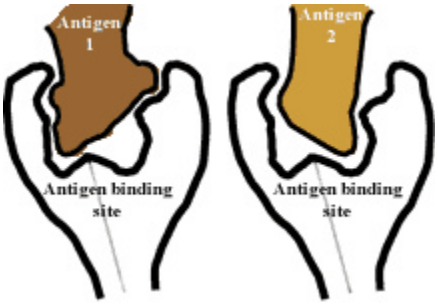
Education of lymphocytes and recognition of antigens: Each lymphocyte, whether a B cell or a T cell, is educated to identify one particular antigen, which has a certain shape and size. The educated B and T cells use antigen receptors on their surface to recognize antigens. The antigen and the receptor fit together like a lock and key. Some lymphocytes will only have receptors for a certain antigen (let us call it A1) on a parvovirus. Other lymphocytes will only have receptors for a hypothetical A2 antigen on the parvovirus. (The body may recognize many different antigens on one invader and respond to each of them.) Another population of lymphocytes has receptors for specific antigens on a *Salmonella* bacterium. Still, others only recognize a certain antigen on grass pollen. When you think about it, this is truly amazing. There are literally millions of antigens in the world, and mammalian bodies produce different lymphocytes which recognize each antigen.

The cells of the animal's body also contains antigens. The B and T cells are taught to ignore these and regard them as 'self.' The various blood types in people: A, B, AB, and O result from different antigens on the red blood cells. People with Type A blood have 'A' antigens on their red blood cells; people with Type B blood have 'B' antigens. The B and T cells of people with blood type A do not see the 'A antigen' as foreign, but the T and B cells of a person with blood type B would.

The B cell response, antibodies, and humoral immunity: When the receptor on a B cell recognizes and attaches to the antigen it was 'designed for' (again, we will use the hypothetical A1), it is a signal to the B cell to start mounting a defense. The B cell makes molecules called antibodies which are small disease-fighting proteins. B cells which produce antibodies are also called 'plasma cells.' Antibodies are sometimes referred to as 'immunoglobulins.' The antibodies have receptor areas on them, which will bind to the A1 antigens. These receptors are called 'antigen binding sites.' There are two antigen binding sites on each ***antibody***. The antigen and antibody bound together is called an 'immune complex.'



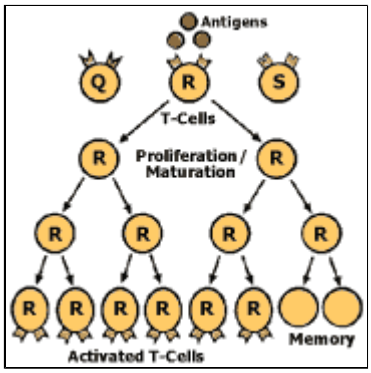
The antigen binding sites are not 100% specific. This means that although the antibody was produced in response to one antigen, in this case Antigen1, it may also be able to bind with other antigens, e.g., Antigen2. You can see how this may happen if you have ever put a puzzle together. You usually can find several pieces that are a close fit, but there is only one piece that really fits. Antigen receptors can sometimes bind with antigens that are close fits, instead of the one antigen they were designed for. When this occurs, it is called a 'cross-reaction.'



Cross reactions can be a problem when performing laboratory tests. Let us say you are testing the blood of an animal to see if it has antibodies to our hypothetical A1. Let us also say that antibodies to an antigen we will call B1 (which is from an entirely different organism) will also bind to antigen A1. If the blood of our animal has antibodies to A1, the test will be positive. But, if the blood does not contain antibodies to A1, but does contain antibodies to B1, the test will also look positive. But, in this case, it is falsely positive.

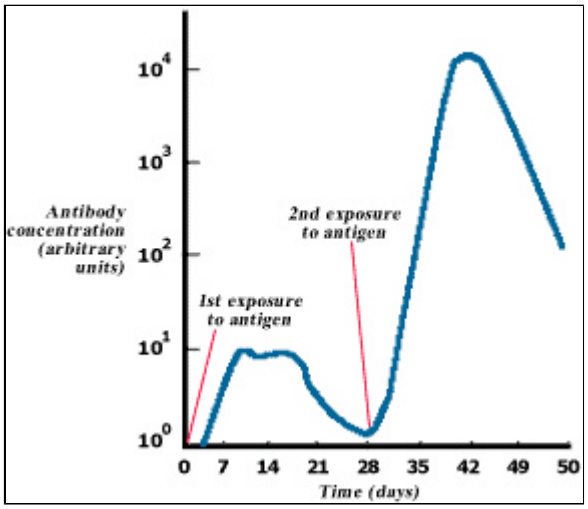
In the body, the binding of the antigen by the antibody can result in:

- Neutralizing a toxin if the antigen was on a toxin
- Deactivating a virus if the antigen was on a virus
- Activating a cell-killing series of proteins called 'complement'; antibody and complement together can lyse (break apart) bacteria and kill them
- Making the antigen (and what it is attached to) more appealing to phagocytes. This is called opsonization. Antibody bound to the antigen is like mustard on a hot dog - the phagocytes will eat it with more relish.



The T cell response and cell-mediated immunity: When the receptors on a T cell bind to an antigen it activates the T cell. Some T cells will bind to the foreign invader carrying the antigen and destroy it. Other T cells will become activated and make substances called lymphokines. These are chemical messengers to the macrophages and other phagocytes, calling them to 'come in and eat.'

Memory: Whether the body's response is primarily humoral (through antibodies) or cell-mediated, certain T and B cells become 'memory cells.' These cells remember their exposure to the specific antigens which were on the foreign substance. This is the mechanism by which vaccination helps protect the body from disease. If a dog, for instance, receives a combination vaccine containing distemper, hepatitis, and parvovirus, 3 different groups of memory cells will be produced: one group will remember the distemper antigens, another will remember hepatitis antigens, and the third group will remember the parvovirus antigens.



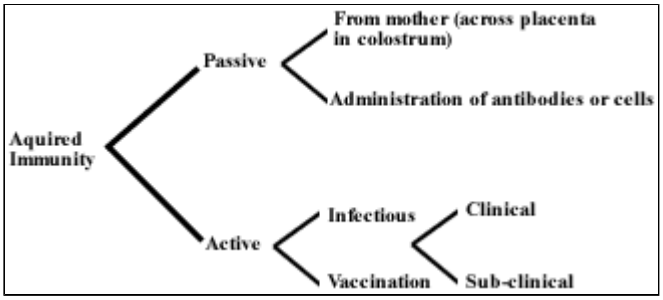
These memory cells help the body respond much faster and with a larger response, if they are ever again exposed to the antigen for which they have memory. For example, if the dog above was vaccinated against distemper, and then 3-4 weeks later vaccinated against distemper, the body's response to the second vaccination will be greater and much faster than after the first vaccination. This faster and higher response is scientifically termed a '***secondary response***' or an '***anamnestic response***.' This more efficient response is due to the memory cells. These memory cells are not produced instantly. The time period between exposure to the antigen (either through vaccination or an infection) and the creation of memory cells is generally 2-3 weeks.

The memory cells 'prime' the body in case of a subsequent exposure to the antigen. We have all heard of 'priming the pump.' An unprimed pump will take a lot of strokes of the pump handle before it produces any water. A primed pump, however, may produce a good deal of water on the first stroke. A 'primed' immune system will react more swiftly, just like a primed pump.

The memory cells created against some diseases live a long time, while those for other diseases may have a relatively shorter life span. Since memory cells do not live forever, in some cases, we need to revaccinate an animal to produce a new generation of memory cells. For some diseases, this is every year, for others 3 years or longer. When we talk about duration of immunity (length of time an animal is protected), we are really talking about how long a sufficient number of memory cells live, and how long the antibodies remain so that the animal is still protected.

Two ways to acquire immunity (active and passive)

There are two main ways in which an animal can acquire immunity.



Active immunity: When people or animals are exposed to a disease-causing organism by natural means or vaccination, the antigens on the organism interact with the cells of the animal's immune system. The B cells make antibodies to destroy the organism. T cells are activated and also help to eliminate the organism. When an individual has an immune system that will effectively protect it against a disease-producing organism, it is said to have immunity to that organism. When an animal's own immune system provides that protection, it is referred to as 'active immunity.'

Passive immunity: When an animal receives another animal's defense mechanisms (antibodies and/or lymphocytes), rather than developing its own defense system, we refer to it as 'passive immunity.' Examples of passive immunity include the antibodies received by a fetus through the placenta, antibodies the newborn receives from its mother through **colostrum**, antivenins to treat snakebite, and bone marrow transplants which help replace the lymphocytes. A disadvantage of passive immunity that the animal's body does not have the ability to replenish it (except in the case of a bone marrow transplant). As the antibodies which the animal received break down through natural aging, or are used up destroying disease-causing organisms, the animal's body cannot replace them. However, in the case of active immunity, more antibodies are produced whenever the immune system comes in contact with the sa organism again. Active immunity is self-perpetuating. Passive immunity is not.

Abnormalities of the Immune System

The immune system does not always function properly. Sometimes, it reacts to the wrong thing (autoimmunity), other times, it reacts too much (hypersensitivity), and sometimes, it simply does not react at all (immunosuppression and immunodeficiency).

Autoimmunity: In autoimmunity, the immune system mistakenly sees some part of body as foreign and starts to attack it. Both the T cells and B cells may be involved in autoimmunity. What causes autoimmunity?

- Genetics may play a role in the development of some types of autoimmunity. autoimmune disease called ***systemic*** lupus erythematosis (often just spoken of 'lupus'), is more common in German Shepherds than many other breeds.
- Certain drugs may alter the molecular appearance of cells. Some drugs attach themselves to red blood cells, making the cells appear 'foreign.' The body then attacks the red blood cells causing autoimmune hemolytic anemia.

- As with certain drugs mentioned above, in some cases, antigen-antibody complexes may adhere to cells and cause the same type of phenomenon - the body attacks the cells since they appear foreign. In some cases, a great deal of inflammation can accompany the killing of these cells. This type of autoimmune reaction is thought to contribute to rheumatoid arthritis.
- Errors in the 'education' of T and B cells may make them unable to distinguish 'foreign' from 'self.'

Many researchers are exploring the various aspects of autoimmunity and how it may differ between species of animals. In the future, we hope to have a better understanding of this condition and how we can prevent and treat it.

Autoimmune diseases are classified into two types: those in which the antibodies are directed at a certain organ, and those in which multiple areas of the body are affected.

Spectrum of Autoimmune Diseases in Dogs	
	Juvenile diabetes Pemphigus vulgaris (a skin condition) **Myasthenia gravis** (a nerve condition) **Autoimmune hemolytic anemia** **Rheumatoid arthritis** Polymyositis (a muscle condition) Systemic lupus erythematosis (SLE)

Hypersensitivity: A hypersensitive immune system is one which overreacts to a stimulus. In addition to T cells and B cells, various other cells can also be activated during an immune response. These cells produce chemicals such as histamines which can affect multiple parts of the body. In hypersensitivity, the body produces too much antibody, the wrong kind of antibody, a large number of antigen-antibody complexes, or antibody to proteins which are not really foreign. In addition, an excessive number of cells may be activated to produce histamine and other chemicals. There are four major **types of hypersensitivity**.

Immunosuppression and immunodeficiency: Certain drugs and disease-causing organisms can suppress the immune system. For organ transplantation, and in some cases of autoimmune disease, we want to suppress the immune system and use various drugs to achieve that goal. In some infections with parasites such as malaria, **trichinosis**, and **leishmaniasis**, the organism can suppress the immune system through various mechanisms, allowing the organism to grow and multiply within the person or animal. Immunodeficiency can occur as a result of a genetic defect in different breeds of cats and dogs. Some viral infections (e.g., feline immunodeficiency virus and canine parvovirus) can cause immunodeficiency, as well. Newborns, who did not receive adequate amounts of colostrum are immunodeficient and in great danger of becoming seriously infected with a number of diseases. Poor nutrition, such as Vitamin A, Vitamin E, and selenium deficiencies, and restricted protein or *calories* can result in suppression of the immune system.

Summary

The immune system is an incredible defense mechanism which protects the body from many kinds of disease-causing agents including bacteria, viruses, toxins, and parasites. The innate portion of the immune system, including the skin, is the first line of defense,

is nonspecific, and provides protection from many foreign invaders. The adaptive portion of the immune system is much more specific, reacts to unique molecules called antigens, and uses antibodies and cell-mediated immunity to rid the body of foreign substances. The adaptive portion of the immune system can 'remember' previous encounters with a foreign substance and react faster and to a higher degree with subsequent exposures. A body may acquire immunity through transfer from another animal (passive immunity), or through its own exposure and reaction to a foreign substance (active immunity). Sometimes, the immune system can malfunction and either attack its own body (autoimmunity), overreact (hypersensitivity), or react insufficiently (immunodeficiency or suppression).

References

Al-Sarraf, R. Update on feline vaccine-associated fibrosarcomas. Veterinary Medicine. 1998: 729-35.

American Association of Feline Practitioners/Academy of Feline Medicine. Recommendations for Feline Leukemia Virus Testing. The Compendium on Continuing Education for the Practicing Veterinarian. 1997:1105-7.

Bell, FW. Recommendations for FeLV- and FIV-positive cats with cancer. In August, JR (ed.) Consultations in Feline Internal Medicine. W.B. Saunders Co. Philadelphia, PA; 1997:572-8.

Bergman, PJ; Couto, CG; Hendrick, MJ; Macy, DW; Richards, JR; Starr, RM (contributors). Vaccine-associated feline sarcoma symposium. Sponsored by the Vaccine-Associated Feline Sarcoma Task Force and the Arm & Hammer Division of Church & Swight Co., Inc. July 25, 1998.

Brakeman, L (ed.) Researchers suspect genetic cause for vaccine site sarcomas. dvm 1998; July:1,41-45.

Cole, R. Rethinking canine vaccinations. Veterinary Forum; 1998; Jan: 52-7.

Greene, CE. Immunoprophylaxis and immunotherapy. In Greene, CE (ed.) Infectious Diseases of the Dog and Cat. W.B. Saunders Co. Philadelphia, PA; 1998;717-750.

Jarrett, O. Development of vaccines against feline leukemia virus. In Kirk, RW; Bonagura, JD (eds.) Current Veterinary Therapy XI. W.B. Saunders Co. Philadelphia, PA; 1992:457-60.

Pfizer Animal Health. Duration of immunity in companion animals after natural infection and vaccination. Pfizer Animal Health; June 30, 1998.

Roitt, I; Brostoff, J; Male, D. Immunology. CV Mosby Company. St. Louis, MO; 1985.

Rosen, DK. Feline infectious diseases and rational vaccine protocols for immunization. Presented at the Wisconsin Veterinary Medical Association Convention. October 10, 1998.

Schultz, RD. Current and future canine and feline vaccination programs. Veterinary Medicine. 1998; 233-253.

Tizard, I; Yawei, N. Use of serologic testing to assess immune status of companion animals. Journal of the American Veterinary Medical Association. 1998:213; 54-60.

Veterinary Learning Systems. Recombinant vaccine technology. Supplement to The Compendium on Continuing Education for the Practicing Veterinarian. 1997;19(2).

Veterinary Learning Systems. Vaccine technology in the 21st century. Supplement to The Compendium on Continuing Education for the Practicing Veterinarian. 1998;20 (8c).

Complete Blood Count (CBC)

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Whether it's a human, dog, cat, or even bird or ferret, when sick, their doctors typically draw a blood sample and perform some tests to help determine a diagnosis. These tests are generally one of two types. The first type is the complete blood count (CBC) which determines the number and types of blood cells present. The science concerned with this cellular portion of the blood is called hematology. The second type of test is a **blood chemistry panel** that measures the quantities of various ***electrolytes***, ***enzymes***, or chemical compounds in the liquid portion of the sample. Sometimes these tests yield little information about the case, but more typically, they are the fastest and best diagnostic tool available to the doctor.

Components of Blood

Blood is made up of a liquid portion plus all the various blood cells. It functions to transport ***nutrients*** and oxygen to the cells; wastes and carbon dioxide to the organs responsible for their removal or breakdown; and also to defend the body against bacteria, ***viruses***, and other organisms.

The liquid portion of blood is referred to as plasma if the blood was not allowed to clot, and ***serum***, if it was. This liquid portion, without the cells is generally a straw or light yellow color. The liquid portion of the blood is used in the chemistry tests.

Every drop of blood literally contains millions of blood cells. Although the sample drawn for a CBC may seem small, it contains such huge numbers of cells that it is an excellent and accurate portrayal of the total numbers of these cells found in the bloodstream. The CBC is concerned with the quantities and types of red blood cells, ***white blood cells***, and ***platelets***.

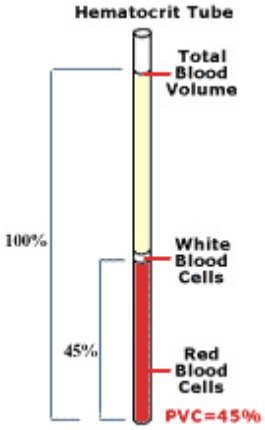
Red Blood Cells

First let us look at the red blood cells (RBC's). These are the tiny work horses that are responsible for carrying oxygen to the body's ***tissue***. RBC's contain the molecule hemoglobin. Oxygen that is taken into our bodies attaches to the hemoglobin as the RBC's pass through the lungs. The RBC's then deliver the oxygen to all the other cells in the body and take the carbon dioxide back to the lungs.

RBC's are formed in the bone marrow. The bone marrow constantly produces new RBC's since the life span of an RBC is only about 120 days. The body can respond quickly to maintain the number of RBC's present in the blood vessels. The body measures their numbers simply by evaluating the quantity of oxygen being supplied to its tissues. If not enough oxygen is available then the body sees that as a need for more working RBC's.

If more RBC's are needed quickly, then more immature cells (called reticulocytes) are released into the circulation from the bone marrow. However, if there are adequate cells present, it slows down the release of new ones.

Hematocrit: In the CBC, we determine the number of RBC's in several different ways. The quickest and easiest is called the hematocrit, also referred to as the ***packed cell volume*** (PCV). A blood sample is placed in a tiny glass tube and spun in a centrifuge. This device spins the tube round and round at several thousand revolutions per minute. The cells are heavier than the plasma and are compacted at one end of the tube. After the tube is spun, it is examined and the PCV is determined as the percentage of the cellular portion relative to the total amount of blood in the tube (i.e., remainder being the plasma). The normal for dogs is 40-59 and cats is 29-50.



If the PCV is low, there are fewer red cells in the body than we would expect. This condition is referred to as anemia. In severe cases of anemia, the animal would probably have pale membranes in its mouth and seem weak and tired since its body would be getting less oxygen than needed. Anemias are further classified as either regenerative or non-regenerative. In the former, even though the number of red blood cells is lower than normal, the body is responding by releasing new reticulocytes into the circulation. In the non-regenerative anemia, there are no or very few immature RBC's in the sample and the body continues to lose red blood cells but no new ones are produced. A nonregenerative anemia is very, very serious and will quickly become life-threatening.

When the PCV is greater than 55 it is said to be elevated. This is seen in dehydrated animals as their blood is becoming more concentrated. It is noted in other conditions such as some cases of shock, response to high altitudes (the air is 'thinner,' therefore there is less oxygen so more RBC's are put into circulation), diseases of the lungs, etc. Remember, anything that decreases the amount of oxygen reaching the tissues of the body will cause higher numbers of red blood cells to be found in the CBC.

Red Blood Cell Count: We can also measure the actual number of RBC's in a given quantity of blood. This is called the 'red count,' and is more difficult to perform than a hematocrit. The red blood cell count is not measured as a percentage of anything but rather the actual number of cells found in a microliter (µ l). To put things into perspective for those of us who do not relish the metric system, a liter is just a little larger than a quart and a microliter is one millionth of a liter. Each laboratory has their own set of 'normal' ranges for a RBC count, but the average is 5.6-8.7 x 10^6 RBC's per microliter for dogs and 6.1-11.9 x 10^6/µ l for cats.

Hemoglobin: A final way we can evaluate the RBC's is by quantifying the amount of hemoglobin present. In some anemias, the actual number of RBC's may not be real low, but if the cells contain less than the normal amount of hemoglobin, the signs of anemia could be quite severe. The normal hemoglobin level for a dog is 14-20 grams/deciliter and 9-15.6 g/dl for cats.

White Blood Cells

The other major type of blood cells are the white blood cells (WBC's) which are also referred to as leukocytes. There are many more RBC's than there are WBC's. For every leukocyte present in a sample there will normally be 600 to 700 RBC's. The major role of the white blood cells is to defend the body against invading organisms such as bacteria, viruses, and fungi. There are different types of leukocytes and a white blood count (WBC) is a total of all the various kinds. The normal range for a WBC count in the dog would be between 6,000 and 17,000 per microliter and in the cat 4,900-20,000/µ l. The number of WBC's is typically elevated when the body is fighting a severe infection or stressed by metabolic toxins (a patient that was in ***acute*** kidney failure with waste products building up in its body would normally have an elevated WBC). In addition, when extremely excited (if we overly excite or frighten the animal when drawing the blood sample) white blood cells will be released into the blood and the levels will rise. The WBC count will be lower than normal if an animal has been weakened from a prolonged, debilitating disease and in some viral infections.

WBC's are divided into two groups depending on how they react to the stains that are used to better observe them under a microscope. There are granulocytes (they are WBC's with granules that absorb the stain) and the agranulocytes (those that do not absorb the stain). The granulocytes include the neutrophils, eosinophils, and the basophils while the agranulocytes are the lymphocytes and monocytes.

Neutrophils: Neutrophils are also formed in the bone marrow. Mature cells have a multi-lobed nucleus and are referred to as 'segmented cells' (sometimes called 'segs'), while the immature ones have a single lobed nucleus and are referred to as 'bands.' The bands are younger than the segs - when first released from the marrow neutrophils are bands and after spending time in the circulating blood they mature into segs. These cells function by actually engulfing disease-causing bacteria and other small particles. In the presence of a bacterial infection, their number in the peripheral blood increases, the bone marrow releases more of the young cells into the circulation and the percentage of bands increases in relation to the segmented ones. The normal range for mature neutrophils is between 3,000 to 12,000/µ l. The normal for the bands is approximately 100 to 300 per microliter.

When total neutrophil numbers are increased it is usually a sign of a bacterial infection or some form of extreme stress. If the number of bands increases dramatically in relation to the number of segs it is thought to be a more severe reaction since the body is releasing more and more immature cells into the circulation to defend itself against the infection. In most viral infections, the total number of neutrophils decreases.

Eosinophils: Eosinophils are normally seen in fewer numbers than neutrophils. They are also produced in the bone marrow and their normal range is about 100 to 1200 per microliter. They also have the ability to eat up or engulf foreign particles into their bodies. Their quantities increase in the circulating blood when the animal is suffering from an infection with parasites, or has allergies. In conditions that cause extreme or prolonged stress to the dog or cat, eosinophil numbers decrease.

Basophils: The last of the granulocytes is the basophil. These are the least common of all the WBC's. In many samples, none are present. Their function is unknown but they are also produced with the bone marrow.

Lymphocytes: Of the agranulocytes, the most abundant is the lymphocyte. There are normally 500-4,800 of these in a microliter of dog's blood and 1,500-7,000/µ l in a cat's. They are formed and released from lymphoid tissue such as ***lymph nodes***, ***spleen***, etc. They are unable to eat or engulf organisms but fulfill their function of defending the body in other ways. The lymphocytes can be divided into two major types by their functions - B cells and ***T cells***, but these cannot be distinguished from each other through looking at them under a microscope. The B cells produce antibodies which are protein molecules that attach to and thereby destroy invading organisms or other foreign materials and particles. The T cells activate and help other cells destroy viruses and other foreign material. When lymphocytes numbers decrease it is referred to as a lymphopenia and is frequently noted in the initial stages of infections (a common example would be **parvovirus**) or following the use of ***corticosteroids*** like prednisone. There are other situations that bring about reduced lymphocyte numbers but they are fairly uncommon. An increase in the number of lymphocytes does not happen as consistently as might be expected but is noted in prolonged illnesses. Examples of this would be when bacterial or viral infections have gone on for a long time or in certain ***autoimmune*** diseases. A common cause of increased lymphocytes is leukemia, which is a cancer of blood cell production that is usually fatal.

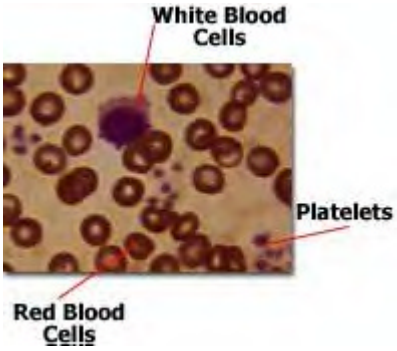
Monocytes: Monocytes develop and are stored in the spleen and bone marrow. Normally there are only 100 to 1800 of these per each microliter of dog's blood, and 0-850/µ l in a cat. They also have the ability to eat or engulf foreign material such as infectious organisms. Additionally, they secrete various protein molecules that help in the clean up of inflamed and irritated tissue. Their numbers do not very greatly unless there is a cancerous leukemia condition affecting their cell lines.

Platelets

The final component that we study when interpreting the CBC, are the platelets. They serve a vital function in the formation of clots. To recognize their importance, think of having a large cut and how it would be possible to bleed to death if normal clotting did not occur. In actuality, we are bleeding all the time. Microscopically small vessels often break within our bodies but we do not notice it since a clot forms within seconds and the amount of blood lost is insignificant. The platelets and a protein called fibrinogen are responsible for the repair of all damaged blood vessels. Even if there was never a cut on the outside of our bodies, without platelets and fibrinogen working together, we would bleed to death internally within a matter of days. If the platelet numbers are decreased, it may mean that the body has either used up a large quantity of the available cells in clot formation or that their number may be low and the animal is at great risk if bleeding should commence in the future.

Cell Morphology

A top quality laboratory that performs a CBC reports not only the quantities of the different cell types but also supplies a description of their size and shape. We refer to this as the cell morphology. Abnormalities are often seen that are very specific for certain diseases. An example would be in certain cancers that affected the blood cells themselves as is the case in many different forms of leukemia.



Many times the results of the CBC, when combined with a good physical exam and history, make diagnosis easy. A female dog was in heat 2 to 3 months previously, her water consumption is elevated and she seems weak in the rear quarters. The veterinarian is thinking she may have a severe uterine disorder called pyometra. The CBC comes back with a grossly elevated WBC count of 45,000 and the diagnosis is virtually confirmed.

When the results of the CBC are available to us, we are better equipped to determine the overall health of the animal. It will help us determine if an infection is present and to differentiate if it is viral, bacterial, or parasitic. A CBC can diagnose or help confirm other disorders such as allergies, autoimmune diseases, anemia, leukemia, and many others.

Normal Hematology Values for Dogs and Cats*

	Unit	Canine	Feline
Hematocrit (PCV)	%	40-59	29-50
Hemoglobin	g/dl	14-20	9-15.6
Red Blood Cell Count	$x10^6/\mu l$	5.6-8.7	6.1-11.9
White Blood Cell Count	/µl	6,000-17,000	4,900-20,000
Neutrophils	/µl	3,000-12,000	2,500-12,500
Lymphocytes	/µl	530-4,800	1,500-7,000
Monocytes	/µl	100-1800	0-850
Eosinophils	/µl	0-1,900	0-1,500
Basophils	/µl	<100	<100
Platelets	/µl	145-440	190-800

* normal values may differ from laboratory to laboratory.

Chemistry Panels & Tests

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A veterinary chemistry panel (also termed 'biochemical profile') includes tests for multiple chemical constituents within one sample. The quantities of these chemicals can reveal many things about the various organs of the body. Most veterinary chemistry panels check blood ***electrolyte*** and for diseases of the liver, kidneys and pancreas.

Whole blood is a combination of blood cells and liquid. The **Complete Blood Count (CBC)** deals with the cell portion and quantifies the different kinds of red and white blood cells, ***platelets***, and hemoglobin. The chemistry panel deals with the liquid portion of the sample after the cells have been removed. To obtain the liquid, the blood sample is allowed to clot within the tube and then the tube is spun in a centrifuge. This forces the clot to the bottom of the tube and the liquid remains at the top. The fluid left after the clot has been removed is referred to as '***serum***.' This is the portion used for a chemistry panel.

Many veterinarians can perform some small chemistry panels 'in house' which means within the veterinary facility. For larger panels, the tests are often performed by a local laboratory, frequently within a human hospital. There, a small quantity of the serum from the original collection is drawn into a single large machine. Tiny samples from that serum are tested for various chemical components. The results of each test are compiled and printed out on a single form. To make it easier for veterinarians and physicians, the form lists the patient's results along with the expected normal values for that species.

Types of panels

Since the laboratory equipment has the ability to run numerous different tests, there can be many different chemistry panels (e.g., liver panels, electrolyte panels, geriatric panels, pre-surgical panels) produced depending upon which individual tests are requested and included.

A typical veterinary chemistry panel will measure the following:

- Blood Glucose
- BUN
- Creatinine
- Calcium
- Total Protein
- Albumin
- Globulin
- Total Bilirubin
- Alkaline Phosphatase
- ALT (SGPT)
- Cholesterol
- Sodium
- Potassium

That is thirteen different tests that if run individually would cost hundreds of dollars. But when performed as a panel, the tests can be done at a more reasonable price. Not only is there a large saving in cost, but the panel often makes diagnosis of a wide range of disorders much, much easier.

It would be nice to state that all veterinarians are great diagnosticians. The truth is that numerous times every year veterinarians can be 'bailed out' or saved by a chemistry panel. In these instances, the panel leads us to a diagnosis that we had not even considered in our mental list of possible disorders. Sometimes a veterinarian can just listen to the history and examine the dogs and know immediately what is wrong. In other cases, the veterinarian can examine the pet closely every two hours for three days and not have a clue as to the underlying problem. In this latter situation, the chemistry panel is of unquestionable value. Sometimes the results are of little or no help in the process of making a diagnosis, but that is very, very rare.

Descriptions of specific tests

Blood Glucose: When the body takes in ***carbohydrates***, it converts them to glycogen, which is stored in the liver. As the individual needs energy, the glycogen is converted to glucose, which enters the bloodstream and is transported throughout the body. Blood glucose, is therefore, a measure of the animal's nutritional level, but it is more often used to monitor metabolism and physiology. The normal range for blood sugar is 60 to 120 mg/dl (that is milligrams of glucose for each deciliter of whole blood). If the results are lower than 60, the animal is said to have low blood sugar and is referred to as hypoglycemic. If the findings are much greater than 130, the dog is said to be suffering from hyperglycemia.

Hypoglycemia is a frequent problem in young puppies, especially the toy and smaller breeds. These animals may seem weak, uncoordinated, and even have seizures. Some adult dogs also have problems with hypoglycemia, especially during periods of increased or prolonged activity. This is very common in some of the hunting breeds. Low blood sugar is also seen in animals that have been sick and debilitated for a long time and in certain forms of cancer.

Slightly elevated blood sugar results are often found when the animal is stressed or very excited when the blood sample is taken. We have frequently seen results greater than 160 from excitement alone, especially in cats. However, when the level is over 180 mg/dl, it signals problems. At this point the threshold of the kidneys is exceeded. (While the blood is being filtered by the kidneys, the kidneys are supposed to prevent the loss of glucose in the urine. However, once this high level is reached, the ability of the kidneys to retain glucose is surpassed and 'sugar' spills over into the urine.) The most common cause of this is ***diabetes mellitus***. The full name of this disease is diabetes mellitus, which means 'sweet urine.' In this condition, the body does not produce enough ***insulin***, which is needed for glucose to enter the cells of the body. With inadequate insulin production, the glucose remains in the blood. We have seen blood sugar readings in diabetics as high as 900!

BUN: 'BUN' stands for Blood Urea Nitrogen. The proteins that animals consume in their diet are large molecules. As they are broken down and utilized by the body, the by-product of this metabolism is nitrogen-containing urea compounds. These are of no use to the body and are excreted by the kidneys. If the kidney is not working correctly and filtering these compounds from the blood, they build up to excessively high levels. When this happens to a human they are said to be 'uremic' and will probably be placed on a **dialysis** machine.

When the BUN result is high it is only an indication that the nitrogen wastes of protein are not being removed from the body. While kidney disease is the primary reason for studying the BUN level, there can be other causes for its elevation. We also see significant BUN elevations when the patient is dehydrated since there is just not enough fluid in the body for the kidneys to function correctly. Additionally, if anything causes decreased blood flow to the kidneys they cannot adequately filter the blood and the BUN will elevate. An example of this would be heart disease with decreased circulation. If there is an obstruction so that the urine cannot get out of the body, it will build up in the bladder preventing the kidneys from producing more. This would also elevate the BUN.

Lower than normal BUN levels are frequently noted in liver disease. This organ is one of the primary sites of protein breakdown. If this breakdown does not occur, the nitrogenous wastes will be found at lower than normal levels.

Creatinine: Creatinine is also used to measure the filtration rate of the kidneys. Only the kidneys excrete this substance and if it builds up to higher than normal levels, it is a sign of decreased or impaired function of these organs.

Calcium: Calcium is a mineral that is found in consistent levels within the bloodstream. While a dog is pregnant or nursing puppies, the calcium level can become seriously depressed in a disease called eclampsia. Additionally, certain medications, tumors, etc., can affect calcium levels. It is important to detect an abnormal blood level of calcium quickly before it leads to serious heart and muscle disorders.

Total Protein: The total protein level is a combined measurement of two blood protein molecules, albumin and globulin. Albumin is normally produced by the liver. We often see albumin levels depressed when the animal is receiving inadequate or poor quality nutrition or following ***chronic*** infectious diseases in which their stores have been used up and not yet replaced.

The term 'globulins' includes immunoglobulins which are produced by the body's ***immune system*** as part of the body's defense against bacteria and ***viruses***. In certain diseases, such as Feline Infectious Peritonitis, elevated globulins can occur.

An elevated protein level is usually a sign of dehydration.

Bilirubin: Bilirubin is by-product of the breakdown of hemoglobin. Hemoglobin is the molecule within red blood cells that is responsible for carrying oxygen to the ***tissues***. When the blood cells die or are destroyed, hemoglobin is released and quickly broken down and excreted by the liver as bilirubin. Therefore, bilirubin levels may be higher than normal when excessive numbers of red blood cells are breaking down or if the liver is diseased and unable to clear the bilirubin from the blood. If there is an obstruction within the liver or bile duct so that the bilirubin cannot be released into the intestine, blood levels will also elevate.

Alkaline Phosphatase: Serum alkaline phosphatase (often abbreviated 'SAP') belongs to a class of compounds called ***enzymes***. These are protein molecules that function to assist various chemical reactions. Although the normal level of alkaline phosphatase varies in different species of animals, alkaline phosphatase in a dog is seen at higher levels in certain forms of cancer and some muscle and liver diseases.

SGPT: Serum Glutamic Pyruvic Transaminase (SGPT) is also called 'alanine amino transferase (ALT).' It is an enzyme important in liver function. An elevation usually means that the liver cells are breaking down for some reason. The liver may be cancerous, have an infection within it, be congested or engorged with too much blood (as in heart failure), failing or worn out as in cirrhosis, obstructed so that the waste products and toxins it filters from the blood cannot be removed from the body via the bile duct, etc. Basically, anything that adversely affects the liver or its ability to function correctly will elevate the SGPT.

Cholesterol: Cholesterol does not have the same connotation as it does in human medicine. Hardening and obstruction of the vessels of the heart is not a common problem in canine and feline medicine. Rather, cholesterol deviations are generally secondary signs of other diseases. Animals with inadequately functioning thyroid glands often have elevated cholesterol. Starving animals or those with poor levels of nourishment may have lower than expected cholesterol.

Sodium and Potassium: Sodium and potassium levels are interpreted together. Their levels can be seriously affected in diseases of the ***adrenal glands***, heart, kidneys, or by various medications, etc. Conversely, changes in their levels can lead to very serious secondary problems such as preventing the heart, nerves, and kidneys from functioning correctly.

Conclusion

Compared to the **Complete Blood Count (CBC)** that looks at the cellular components in the blood, the chemistry panel frequently offers more information related to specific diagnoses. The tests listed above provide direct evaluations of the health of the liver, kidneys, adrenal glands, immune system, etc. Also, in addition to helping us make a diagnosis, the chemistry panel is just as helpful in determining a prognosis, (a forecast of the outcome of the disease). In some cases, however, a diagnosis only comes from watching the various parameters change over a period of time.

Still, as with the CBC, the chemistry panel is just a picture of the patient's body at one moment in time. The readings may be very different in 24 hours, or even one hour. The veterinarian must always take into consideration everything that is affecting the patient and in turn, how that may affect the test results.

Antioxidants

Jennifer Prince, DVM

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Antioxidants have been used by humans to slow the aging process by protecting the body from damage caused by ***free radicals***, to enhance immune system function, and to reduce the risk of ***chronic*** degenerative conditions such as cancer, arthritis, and cardiovascular disease. Free radicals are molecules which are missing an electron. Electrons in an atom or molecule are normally paired and spin in opposite directions to balance each other. They spin at nearly the speed of light. A free radical is created when one electron in a pair is dislodged. The molecule with an unpaired electron (the free radical) now grabs an electron away from another molecule in the cell such as protein or DNA to restore its stability. This process can ultimately cause damage to a cell.

A description in the *American Druggist* likens the process to a million mouse traps lined up side by side covering the entire surface of a football field. Each trap is cocked in its ready-to-spring position with a ping pong ball resting on each springing arm. Picture yourself standing on the sidelines with a single ping pong ball in your hand. This represents a free radical. When you throw this extra ping pong ball out onto the field, within seconds, you will have started a chain reaction resulting in hundreds of thousands of ping pong balls flying around. In fact, one unchecked free radical reaction can create hundreds of thousands of damaging incidents at the cellular level.

Free radicals can be caused by nuclear radiation, x-rays, ultra-violet rays from the sun, and exposure to pesticides, insecticides, and herbicides. Nature supplies antioxidants to protect us from the destructive effects of free radicals by providing us with antioxidant ***nutrients*** such as vitamin C, vitamin E, ***beta-carotene***, and the trace mineral selenium. Vitamin C is water soluble, and as such it can, if taken in sufficient quantities, saturate all of our cells and tissues to provide protection. Vitamin E is fat soluble and protects the fatty tissues of the body like the cell walls and cell membranes. Beta-carotene is one of the most effective and efficient scavengers of a free radical called 'singlet oxygen'. Selenium is needed by the body to synthesize sufficient amounts of glutathione peroxidase which is an important antioxidant ***enzyme*** that protects against free radical damage.

Using antioxidants helps slow down and prevent free radical damage that speeds up aging. The antioxidant gives one of its electrons to the free radical neutralizing the free radical. The antioxidant is no longer functional once it gives up the electron and more antioxidants are needed to replace it. The antioxidants work together to ***neutralize*** free radicals, and it is best to take several antioxidants rather than all one kind. The best food sources of antioxidant nutrients are fresh fruits, vegetables, and whole grains. Some of the antioxidants like selenium are toxic at high doses so contact your veterinarian before adding antioxidants to your pet's diet.

Antioxidants are found in foods of rich colors: dark red grapes, ruby red grapefruit, dark green leafy vegetables, broccoli, beets, green beans, peas, and dark orange vegetables like yams, carrots, and dark orange squashes. Choose the darker colors as opposed to the lighter in all varieties available. If foods rich in antioxidants are not available, they may also get them by taking supplements.

Overview on Nutrition in the Cancer Patient

By Monica Segal

There's much ado about raw vs. cooked diets for dogs. Everyone seems to have an opinion and I suppose that I'm no different so based on my experience of working with a multitude of ill dogs, here are a few thoughts to consider.

From the moment we bring home a puppy, we know that the time spent with this pet will be all too short. As the years go on, we pray that there will be many more left. Cancer is an ugly word that strikes fear and panic in to all of us and since we already know that an animals' lifespan is too short, we can become desperate to do the "right" thing.

Let me preface what I'm about to say with the fact that I feed my own dogs a diet that consists of both raw and cooked foods with the emphasis being on raw. One of my girls has an awful case of colitis that makes me walk a dietary tightrope daily. It is to her credit that I've been led down a path that shows me clearly that each dog is unique in needs and tolerances.

Opinions tend to be based on personal experience so it's easy to understand the emotion that lies behind a directive to feed one way or another. However, no two animals are exactly the same and what works for one may very well not be right for the next. Raw diets can be wonderful. They can also be problematic for the animal that has a compromised immune system. While a dog can *usually* deal with some bacteria that people can't, even a healthy animal may not always thrive on a raw diet. It depends on what else they're dealing with. For instance, gastro problems may or may not translate in to the gut being more permeable. If the mucosa has been compromised, the natural barrier against bacterium predisposes this animal to more problems. It affects the immune system in a big way and this shouldn't be overlooked. Adrenal gland function is also a consideration. The adrenal cortex comes into play when an animal has to adapt to stress. It releases hormones such as corticosteroids, which stimulate the body to extract energy from its reserves of fats and proteins. Consider the stress that chemotherapy may induce. The stress that a sick animal has to begin with!

Not to mention the trips back and forth to the vet which most animals find less than appealing even on a good day. And keep in mind that "stress" is not always what we think it is. A dog can feel stressed even during a walk when s/he meets other dogs. Excitement, whether it's the good kind or the negative kind is still stress on the body.

Something you might want to know is that an animal can be a subclinical carrier of an infectious disease. In other words, you might look at your dog and see nothing but great health. This would lead you to believe that things are going along merrily however, it's not always so. When the immune system is challenged, it can react in one of three ways. In the best case scenario, the body handles the bacteria or virus without much effort and in fact, we may never know that there was an invasion. The second possibility is that the disease takes hold because the immune system could not fight well enough. Eventually, the immune system will either win or lose to the infection. The third possibility lies somewhere in the middle. The immune system fights well enough so that clinical signs of disease are not apparent but the disease becomes "subclincial". This means that disease may resurface at any time when the body is ill disposed or sheds (sometimes for years) the bacteria in to the environment through bodily discharges etc.

Why am I discussing subclinical carriers? Because a dog that is battling cancer may also be carrying a sublcincial form of disease and now that the body is under stress, the disease may manifest. It's possibly why so many of my clients come to me

not only with cancer but with a range of other complaints at the same time. Yes, the ill dog may indeed have picked up something new in the way of disease but it's just as possible that a subclincial form of illness has resurfaced. Stress is one of the known factors in brining a subclincial disease to the forefront again. So when you decide on the diet for your dog, please consider that what you see may not always be what's actually happening. The body is able to do some some mysterious things!

Raw diets have healthful properties and I do not suggest that an animal suffering with cancer be fed only cooked foods. There are some misconceptions about raw foods and cooked foods at times and these may worth exploring.

Myth #1

The enzymes in raw foods mean that the body doesn't use it's own enzyme reserves

If the enzymes in a carrot were the digestive sort of enzymes, the carrot would digest itself before we could eat it- so I'm not buying in to this. Further, dogs are marvels at enzyme production and there really aren't a set number of enzymes in the bank that suddenly runs out. I'm not saying that the enzymes in raw foods are useless. Far from it! But comparing them to the digestive enzymes in the body doesn't make much sense.

Myth #2

Raw fat is better than cooked fat

Actually, this is true but it remains nothing short of a myth for the dog that has a gastro problem and can't handle raw fat. The key here is not to be blinded by sweeping statements that make sense on paper but have little value to your dog in a particular situation. Some dogs do exceptionally well on cooked meats while others do equally well on raw meats. A dog that has pancreatitis may do well on raw meats but the come back is much faster and easier when lean meat is cooked. I see this over and over and espeicailly so when cancer is a part of the picture.

Myth #3

Cooked foods lose all their nutrients

Not true! Some lose more than others but surprisingly, some actually gain nutritive value. One cup of carrots has far more vitamin A content than the same cup of raw carrots. Calcium content actually goes up if meat is cooked on the bone (the calcium leaches in to the meat) compared to a piece of raw meat being fed. Many values do indeed go *up*! Which is not to say that we necessarily *want* them to go up by the way. But the point is that cooking does *not* always diminish the value of a food.

The myths go on and on. Be careful as to what you believe and decide to incorporate in to your dogs' diet.

It might seem that I'm not in huge favor of raw diets for dogs that have cancer. Not so! I believe that dogs are scavengers and as such, can do very well on a variety of feeding methods. Cancer dogs need a careful approach in my opinion. Feeding a raw diet may be the perfect way to go but it depends on whether or not the animal is also trying to cope with another illness that may predispose it to more problems if bacteria laden foods are introduced too quickly. When starting a raw diet for these dogs, I prefer to go slowly and let the dog lead the way through reactions that become apparent. By cooking foods at first, we allow the body to adjust and the option of cooking less and less is something to consider at that point. If the pet shows us that s/he is tolerating things well, foods can be easily switched to a more raw state and finally to an all-raw diet. But the key in my opinion is to really let the animal be your guide and not have a game plan that's carved in stone.

Best Bets

There's been some success with diets that are full of cottage cheese and flaxseed oil. This may be fine for some dogs but not for all. If your dog has a heart problem that translates in to a need for less sodium, cottage cheese may not be your best choice. In this case, look at Ricotta cheese. It has

less sodium and is nicely balanced in the calcium to phosphorus ratio. A lactose intolerant dog may do nicely on white meats such as chicken but you'd probably need to increase the amount of Omega 3 in the diet. This is where the flaxseed oil comes in but if your dog can't handle this, consider Wild salmon oil instead. Just be sure that it's a pure source and not highly contaminated (some can be!) and keep in mind that the "wild" version is vastly different from regular salmon oil so go for the best! Other proteins that might be a consideration if your dog has food sensitivities: fish (from a clean/unpolluted source please!), eggs, rabbit…basically, white meats can work nicely.

Organic sources are also your best bet. They have better nutrient values than their regularly farmed counterparts and they offer a safer source of foods. If your pet has a thyroid problem, you may not want to use much in the way of kale, broccoli, brussel sprouts, cauliflower, cabbage or anything else that falls in to the cabbage family. Otherwise, the use of some of some of these vegetables is fine- not in large amounts though. My personal favorites include carrots, squash (winter and summer varieties), sweet potatoes as well as greens such as parsley, romaine lettuce, watercress and spinach (go easy on spinach because it can impede calcium uptake if overfed).

Supplements

I'll focus only on food supplements here but be aware that there are many sales pitches to be wary of. Not all supplements are created equally as I found out when I started testing my own supplements at a lab. Zoey was reacting horribly to everything I tried to give her until I found the real deal about some of these things. So be sure that what you buy is pure and not chock full of additives that may not be on the label!

Kelp and alfalfa powder for some mineral content (be aware that kelp can vary in its' iodine and arsenic content and the *freshness of alfalfa* as well as the time of year that it's harvested impacts the nutrient value as well as fiber content)

Multi B vitamin- the B groups is crucial to just about every body function you can think of

Vitamin E- the D Alpha Tocopherol is superior to the DL Alpha Tocopherol and if you have a dog that's allergic to soy, try using a soy freee/allergy free version because most vitamin E is derived from soy these days.

Vitamin C- ester c is easier on the stomach but you should know that large amounts of C can be a problem for other reasons. It works with gastrin in the stomach to increase the absorption of calcium which may sound good but… urine now includes calcium and excess C which is excreted as oxalic acid. Calcium + oxalate = potential crystal formation, especially in an acid urine which is something else that C promotes.

Flaxseed Oil or Wild Salmon Oil-good for Omega 3 but be sure of purity and especially so for any fish oils

Cod Liver Oil- high in vitamin A, which can be wonderful or a problem depending on the full diet. Also contains vitamin D and is useful for dogs that do not have access to direct sunlight daily. Gel caps are sometimes well tolerated when the liquid oil is not.

Calcium source- raw meaty bones, bone meal (from a pure/clean source!), egg shell powder or generic calcium such as calcium citrate can work well.

Oils to consider -primrose oil works quite well for inflammation, borage oil can be very helpful for skin problems

Hoping that this has given you food for thought!
www.doggiedietician.com
www.doggiediets.com

Suggested Follow-up Reading Material:
http://www.thensome.com/cancero.htm
http://www.hillsvet.com/clinic/monographs.asp.

Alternative Feeding Practices

By Susan Wynn

Over the past decades, the pet food industry has provided convenient and economical foods for domestic animals. Because the public has become comfortable with the idea that commercial pet foods can provide complete and balanced nutrition for the life of the animal, basic diet is no longer generally considered an important source of disease. Pet owners and veterinarians have literally been trained to look elsewhere for causes and treatment options.

By ignoring the basic diet when advising pet owners, doctors and retailers are forgetting basic physiological principles: the importance of fresh and varied foods in the diet and biochemical individuality. What food consumer in their right mind would believe that food in a bag or can would provide all the nutrition they (personally) would ever need? This is the basis for most "alternative feeding philosophies."

Individual Requirements

The Association of American Feed Control Officials (AAFCO) has published dietary recommendations for domestic species in the form of nutrient profiles. These nutrient profile recommendations are the result of expert evaluations of National Research Council (NRC) recommendations. The NRC recommendations were based on diets using purified nutrients, assuming 100 percent bioavailability. AAFCO, an organization composed of government, academic, and industry experts, evaluated these recommendations and initiated legislation requiring improved testing and labeling of pet foods (Dzanis, 1995). All pet foods must now conform either to AAFCO nutrient profiles or undergo AAFCO approved feeding trials before being marketed.

These improved procedures do not represent a perfect solution for nutrition of the individual animal, however. In the words of Quinton Rogers, DVM, PhD, one of the AAFCO panel experts, "although the AAFCO profiles are better than nothing, they provide false securities. I don't know of any studies showing their adequacies and inadequacies." Rogers also states that some of the foods which pass AAFCO feeding trials are actually inadequate for long term nutrition, but there is no way of knowing which foods these are under present regulations (Smith, 1993).

An additional consideration in domestic animals is breed and function. For instance, the diets of broiler chickens have had to be revised over time as birds with higher body weight gain rates were developed (Morris, 1994). A recent study showed that different breeds of dogs exhibit different abilities to digest the same diet (Zentek, 1994). Working animals may perform better (and therefore require) diets high in protein and fat, rather than carbohydrates (Kronfeld, 1977); diets like these are not commercially available. Breeds of dogs that may have developed over hundreds of years as lap-sitters (like the Chihuahua) may well have different requirements than a less popular working breed such as the Anatolian Shepherd, depending on how their diet was related to their locale of origin, their function, and how long they have been bred as pet animals eating commercial diets.

Even if our domestic animals were of a homogeneous "race" like their ancestors, such as the wolf, panther, buffalo, or wild horse, individual differences in physiology and metabolic processes exist. Biochemical individuality, pioneered by Roger Williams, applies in many ways to domestic animals. Williams determined that even in normal humans (who are of relatively consistent size and shape), the needs for most nutrients vary over a fourfold range, on average (Williams, 1977). These factors will vary further according to age, activity level, existing disease and concurrent drug

therapy. Recent advances in genetic research have led to a change in the way nutritional scientists view animal nutrition, a new paradigm, if you will.

More and more conditions are viewed as nutrition-responsive.

According to a recent review by Eckhardt (2001), gene based diversity in nutritional requirements will be an area of focus for human nutrition now that the human genome has been sequenced. In particular, researchers must determine what levels of diversity exist, and what the practical implications are for nutritional individuality. To illustrate the point, 30-40 nutrients are recognized as essential. If the metabolic pathway influencing nutritional requirements for EACH of them was affected independently by just two alternative alleles at a single genetic locus (which is probably an oversimplification), then the number of alternative genotypes for that nutrient would be over 200 trillion! Eckhardt said, ".... some nutritionists already are working at the cutting edge of genetic research, in a conceptual framework that sees our expanding knowledge of human diversity as broadening the concept of normality rather than as documenting an expanded array of infirmities." The new science of euphenics ("knowledge of individual nucleotide sequences can be used to optimize elements of each person's lifestyle") will impact veterinarians directly and force us to face every-day diet concerns in every animal as an individual, and adopt nutritional counseling as an everyday medical procedure.

It should be clear that, in addition to uncertainty about the more subtle animal requirements in general, individual animals vary so much in their metabolic function that a blanket recommendation for "any good commercial diet" may not address the individual pet's optimal health potential. In general, when we think about how to feed pets, we try to refer to the "Paleolithic" diet as a starting point. Carnivorous pet animals like the cat, (or facultative carnivores, like the dog) are presumed to need high quality meat, whole grain and high quality fiber sources, along with adequate fat levels, vitamins and minerals. Animals whose individual needs differ due to inbreeding or genetic abnormalities (perhaps common in purebreds) should receive individualized dietary consideration when problems of any sort occur. One extreme example is the Dalmatian. This breed has a tendency to form urate stones, and the prevention most commonly recommended is a vegetarian diet. Each breed, as well as each individual, represents a unique challenge.

HOME-PREPARED diets

The profession has historically recommended that owners NEVER feed real food (or table scraps) to pets. That position needs to be re-evaluated now. Some veterinarians now recommend supplementing the diet with meat and vegetables, for (facultative) carnivores such as dogs or obligate carnivores such as cats. This practice may provide the pet with phytochemicals and other vital nutrients that have yet to be recognized as essential by nutritional science. The National Cancer Institute has promoted their "five-a-day" program to encourage people to eat five to nine servings of fruits and vegetables a day-this is because studies examining individual nutrients, such as Vitamin A or E, simply haven't prevented cancer as well as real fruits and vegetables in the diet-and we don't know what is in real foods that works so well. Is it such a stretch to believe that we also don't know everything about carnivore nutrition?

Diets espoused by popular authors are in widespread use by many pet owners. These range from diets formulated on nutrition formulation programs which theoretically provide complete and balanced recipes (Strombeck, 1998), (Pitcairn, 1995) to more extreme diets such as raw, grainless and BARF (Bones and Raw Food) diets.
Biochemical and mathematical analysis of the BARF and other raw diets has shown that there are significant imbalances in some minerals. Calcium, phosphorus, zinc, magnesium and iron were either low or high in these analyses. The diets were also cultured for enteropathogens, and E. coli 0157 was found in one of the three diets examined.

Unfortunately, devotion to the BARF and other philosophies for feeding pets has reached near religious levels in some groups. Many owners will not divulge this practice to their veterinarians because of fear about the doctor's response. For this reason it is critical to ask owners about what diet they are using, and try not to be shocked or judgmental if they are feeding according to one of these plans. Note the animal's condition well, inform the owner that the diet does not fit classical "complete and balanced guidelines," and ask them to come in for check ups at six-month intervals to monitor the effects of this new diet. Many owners, proud of their discovery, may willingly follow these directions if they believe they are partners in diet research.

Special Considerations for Cats

Some alternative feeding philosophies teach that dry food is bad for cats, for a number of reasons. First, dry food encourages free choice feeding, which may lead to obesity and addiction in many cats. While cats are thought to naturally eat many small meals per day, these meals would not (in feral cats) consist primarily of grain, but of protein loaded bugs, lizards, rodents and birds. There is increasing suspicion that free choice dry feeding may complicate diabetes in cats, and some holistic practitioners wonder whether this practice may even predispose to diabetes. Finally, cats with chronic crystalluria or a history of stones should be managed by diluting the urine; this is naturally and more easily accomplished using canned or homemade food, rather than dry food.

Conclusion

Breed and individual genetic differences may be one reason why certain pet animals seem to require individualization of the basic diet. Formulas made by major manufacturers keep the majority of pet animals healthy and well, but for animals with problems, the nutritionally minded veterinarian will change diets and often discover very basic disease mechanism easily remedied with food therapy. Holistic practitioners use a variety of commercial diets especially Innova, California Natural, Pinnacle, Flint River, Wysong, NutroMax, Best in Show, Canidae/Felidae, Precise and Azmira; and sometimes those by the major manufacturers such as Hills, Iams, Purina and Waltham. If owners are interested in preparing homemade foods, there are a large number of choices available. A combination of commercial diet plus fresh meats and vegetables (50:50) may provide some assurance of safety AND the advantages of freshness and variety. As veterinarians, we are obliged to listen to these owners' concerns and help them find the best choice for their pet.

References

1. Buffington CA, LaFlamme DP. A survey of veterinarians' knowledge and attitudes about nutrition. JAVMA. 1996;208:674-675.
2. Dzanis D. The AAFCO Dog and Cat Nutrient Profiles. In: Bonagura J, ed. Current Veterinary Therapy XII. Philadelphia: W.B.Saunders; 1995:1418-1421.
3. Eckhardt RB, 2001. Genetic Research and Nutritional Individuality. J Nutr 131:336S-339S
4. Huber T, Wilson R, al e. Variations in digestibility of dry dog foods with identical label guaranteed analysis. JAAHA. 1986;22:571-575.
5. Kronfeld DS, Hammel EP, al e. Hematological and metabolic responses to training in racing sled dogs fed diets containing medium, low or zero carbohydrate. American Journal of Clinical Nutrition. 1977;30:419-430.
6. Morris JG, Rogers QR. Assessment of the Nutritional Adequacy of Pet Foods Through the Life Cycle. Journal of Nutrition. 1994;124:2520S-2534S
7. Pitcairn, Richard and Susan Pitcairn, 1995. Natural Health for Dogs and Cats, Rodale Press, Emmaus,PA.
8. Smith CA. Changes and challenges in feline nutrition. JAVMA. 1993;203:1395-1400.
9. Smith SA, Campbell DR. The University of Minnesota Cancer Prevention Research Unit Vegetable and Fruit Classification Scheme. Cancer Causes and Control. 1995;6:292-302.
10. Strombeck, D, 1998. Home Prepared Dog and Cat Diets. Iowa State University Press, Ames, IA
11. Williams RJ, Kalita DK. A Physician's Handbook on Orthomolecular Medicine. . New York: Pergaman Press; 1977.
12. Zentek J, Meyer H. Normal handling of diets-are all dogs created equal? Journal of Small Animal Practice. 1995;36:354-359.

Herbs in Small Animal Practices

Susan Wynn ■ United States

Why would a doctor choose to prescribe an herb, rather than a single active constituent such as those contained in a drug? It is true that a single active constituent may be more precisely characterized and that "extraneous" chemicals contained within the whole plant may complicate our understanding of its action? Doctors practicing botanical medicine believe, however, that prescriptions of whole plants provide these advantages: 1) synergistic action; and 2) safety.

Why herbs are different than drugs?

- Herbal formulas concentrate a therapeutic principle (different herbs with potentially different mechanisms of action for the same problem).
- Unique actions.
- Tonic actions and nutritional aspects of herbal vs. drug therapy.

Prescription systems

Traditional herbal medicine is based largely on ethnobotanical data, usually from ancient cultures such as China (giving us "Traditional Chinese Medicine" or TCM) or India (giving us "Ayurvedic medicine"). These practitioners, ancient or present-day, use an "energetic" system defined by characteristics such as yin, yang, heat, cold, cool, warm, moist, and dryness that herbs possess or impart to the patient. For instance, an older cat that is thin and dehydrated (and Yin deficient) would receive a "moistening" Yin tonic herb. These are forms of "energies," therefore; this kind of herbal medicine is sometimes called "energetic" herbalism.

Pharmacologic prescribing is more likely to be utilized by scientifically trained practitioners such as DVMs, MDs, and NDs. Since the science hasn't caught up with herbal practice at this time, even scientifically trained practitioners rely on empirical knowledge (like their clinical experience) and traditional knowledge when deciding on an herbal prescription.

Quality control

Quality control is a major concern. Check out www.consumerlab.com for some product analyses.

Herb Form	Preparation	Comments
Fresh plants	Picked from the herb garden and fed fresh	Not palatable in many cases
Dried bulk herbs	Available as whole, dried plant from health food stores and herb suppliers	Dried herb may be mixed with food, but often unpalatable
Dried powdered herb	Available as powder, or more commonly in capsules	May be mixed with food; may be unpalatable
Dried extracts	Available as powders, granules or capsules	May lose active constituents in processing
Tablets-	Dried herb is compressed with	Found in many health food

pressed	a binder to form firm tablets	stores
Pills	Dried herb is compressed with a binder to form firm pellets	Found mainly as Chinese patent herbal medicines
Teas, Water infusion	Hot water is poured over dried herb, steeped and allowed to cool	May be flavored with bouillon; herb constituents sometimes not water soluble so this form is not the most desirable
Oil infusion	Dried or fresh herb is steeped in olive oil for about one month; usually for topical application	Must be protected so that animal does not lick oil
Decoction	Herb is heated in water and simmered for 20–40 minutes	May be flavored with bouillon; herb constituents sometimes not water soluble so this form is not the most desirable
Tincture—alcohol extract	Dried or fresh herb is extracted by soaking in 30–70% grain alcohol	Unpalatable, however, preparation is likely to be more potent than water extracts (like infusions)
Tincture—glycerin extract	Dried or fresh herb is extracted by soaking in 40% glycerin	By far the most palatable liquid herb form due to sweet taste of glycerin; potency much less than alcohol tinctures
Poultice	Boiled and cooled herb is applied topically	Must be protected so that animal does not lick or destroy poultice
Compress	Cloth or gauze soaked with water extract (decoction or infusion) is applied topically	Must be protected so that animal does not lick or destroy compress
Standardized extracts	One (presumably most active) constituent is concentrated to a consistent percentage in each batch of herb	Consistency is a plus; preparation is semi-synthetic
Ointment	oil infusions of herbs are combined with beeswax and used for topical treatments	Must be protected so that animal does not lick ointment

Proportional recommendations for dogs and cats are as follows. Doses below are given q8–12h.

Species		Tincture	*Granules (tsp)	Tablets	*Patent pills	**Capsule (500mg)	Loose herb (tsp)
Canine	small	5-10 drops	1/8–¼	¼–1	1–3	1/3–½	½–1 ½
	medium	10-20	¼–½	1–2	3–5	½–1	1 ½–2
	large	20-40	½–¾	2–3	5–8	1–2	2–3
	giant	40-60	½–1	3–5	6–10	2–3	3–4
Feline		5-10	1/8	¼–½	2	1/8–½	½

* *concentrated extract*

***may be powdered or concentrated herb so dose is more variable*

Summary

Herbs are more than drugs and there are multiple systems to learn in prescribing them to their full potential. A more complete listing of single herbs, their characteristics and supporting science can be found in Wynn, 1999.

RESOURCES

Veterinary Herbal Therapy books

1. Wynn S, 2000. Emerging Therapies: Nutraceutical and Botanical Medicine for Small Animals, AAHA Press, Boulder, CO.
2. Schoen, A. and S. Wynn. 1998 . Complementary and Alternative Veterinary Medicine: Principles and Practice. Mosby-Yearbook, St.Louis, MO
3. Huiesheng, Xie , 1994.Traditional Chinese Veterinary Medicine. Beijing Agricultural University Press, Beijing, China
4. *Schwartz, C, 1996. Four Paws, Five Directions.Celestial Arts Publishing, Berkeley, CA.
5. Wulff-Tilford M, and G Tilford, 1999. AllYou Ever Wanted to Know About Herbs for Pets. Bowtie Press, Irvine, CA.
6. Fetrow CW, Avila JR, 2000. The Complete Guide to Herbal Medicines. Springhouse Corporation, Springhouse, PA.
7. Pizzorno J, Murray M, 1999. Textbook of Natural medicine. Churchill Livingstone, Baltimore.
8. Mills S and K Bone, 2000. Principles and Practice of Phytotherapy. Churchill Livingstone, New York NY.

Training for Veterinarians

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Chinese herbal medicine

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505-450-4325
FAX: 505-332-4775

Chinese herbal medicine

Healing Oasis Wellness Center

2555 Wisconsin St
Sturtevant, WI 53177
262-884-9549
FAX: 262-886-6460

Introductory courses in Western Herbal Medicine and Chinese medicine

Websites

Veterinary

Veterinary Botanical Medicine Association
http://members.fortunecity.com/swynn/VBMA

Websites on Traditional Chinese and Western Herbal Medicine in Humans and Animals

http://homepage.eircom.net/~progers/herblink.htm

Evidence based or scientifically oriented

HerbMed

http://www.herbmed.org
Excellent detailed monographs

Traditional

Southwest School of Botanical Medicine
http://chili.rt66.com/hrbmoore/HOMEPAGE/HomePage.html

When Traditional Veterinary Medicine Isn't Enough

-Written by: Lisa C. Beagan, DVM

So you have decided to pursue complementary medicine for your pet-welcome to the rapidly growing club! The majority of complementary veterinary practitioners are licensed veterinarians who have added training in complementary (sometimes called "alternative") medicine to their knowledge of Western medicine, but how do you find the right complementary vet for your pet?

As is often the case in matters such as these, word of mouth is the best method: your general practice veterinarian might have a suggestion for you, and if not, you can ask other pet owners that you know. Some veterinary schools have complementary practitioners on staff; at the very least, they should be able to offer a referral.

Unlike human complementary medicine, there is no licensing in veterinary alternative medicine disciplines-instead, veterinarians can become certified in acupuncture, Chinese herbs, chiropractic, homeopathy and other disciplines by taking examinations, and, in some cases, fulfilling externship and formal case study requirements. Several certifying organizations offer online directories of practicing complementary vets. You can check with the International Veterinary Acupuncture Society, the American Holistic Veterinary Medical Association, the Academy of Veterinary Homeopathy, and the American Academy of Veterinary Acupuncture, to see if there is a practitioner listed in your area.

Because there are so many disciplines that fall under the complementary medicine umbrella, the majority of practitioners will perform one or a few types but not all of them. However, if you are able to get a recommendation for an acupuncturist and you need an herbalist, you might be pleasantly surprised to discover that the doctor practices both types of medicine. If not, he or she most likely will be able to give you a good recommendation.

When evaluating whether a particular complementary medicine practitioner will be helpful in meeting your pet's needs, ask the doctor how long he or she has been practicing within this field. Also inquire whether he or she has had any cases similar to your pet's-and whether the outcome of these cases was successful.

Although experience is important, a less experienced practitioner might make more sense financially for some pet owners. Veterinarians are able to practice complementary disciplines prior and without certification; those who have not yet become certified will often charge lower prices or even practice free of charge for a period of time.

In some states, practitioners who have been schooled in human alternative medicine can practice on animals as well. This has been a very large controversy in the veterinary community for several years. Now that more veterinarians are taking courses in complementary medical disciplines, it should be easier for clients to find a veterinarian knowledgeable in these therapies for their pets, rather than relying upon a doctor whose training is primarily within the field of human medicine.

For more information please contact:

Chinese Medicine for American Pets
More Veterinarians Employ Alternative Therapies
Veterinarians Point to Acupuncture's Healing

Understanding Canine Cancer : An Herbalist's Perspective

By Robert McDowell
October 2001.

Cancer is a breakdown of the immune system, pure and simple. The main function of our immune systems (and those of our dogs) is to identify and destroy foreign, mutant and imperfect cells found in the body. It does so quietly and efficiently from day one and, it is only when this system is compromised, that cancers can develop.

There seems to be a cruel parallel between the rise in the incidence of Canine Cancers and the same trend in Human Cancers. Cancer in dogs was pretty rare not so long ago. Now Osteosarcoma and Lymphoma are becoming increasingly commonplace followed closely by others more recently including Fibrosarcoma, Melanoma, Thyroid and Anal Gland Carcinoma.

In the case of domesticated dogs, cancer is on the rise, developmental disorders are commonplace, life expectancy is shortening and domestic dogs are more fragile and more expensive to maintain nowadays, than ever before. There has also been a massive international industry built up around processed dog food, health treatments, and more recently 'snack foods' for our dogs which is in very spooky juxtaposition to the same trends in our own lives.

Horses still eat grass (most of them anyway) and Cats still catch birds (almost all of them).
Dogs nowadays don't get to eat much raw or ripening meat and don't get to eat many bones. They don't get to catch their own prey or scavenge for food. They don't eat the raw stomach contents of dead animals. Nowadays they only ever get to eat (gulp actually) cooked, commercial feeds, table scraps with a little raw meat, if they are lucky.

They are getting sicker and this is no surprise.

I came across the ultimate nonsense, 6 or 7 years ago when I was invited to comment on the new "natural" range of dog products being manufactured by an multi-national company with a factory in my home town in rural Australia. There was the display rack with rows and rows of brightly packaged snack foods for dogs and cats and 90% of them had no English writing on them at all, it was all in Japanese and Korean.

Then, these two bright young technicians tried to tell me that spraying a yoghurt derivative on the outside of a bone shaped object made out of what looked like treated plastic (not ground bone, because it was "too messy on the carpet") was somehow a healthy product innovation.

Neither Cancer nor good health is solely dependent on what we put in our mouths. In fact as humans, we are able to subvert our immune systems and our health in a vast number of different ways including what we eat, drink, inhale, inject, rub on, do, feel, sit in front of, work amongst, transmit as electromagnetic waves etc, the list goes on. We are subverting our dog's environment along with our own, by introducing stress, boredom, snack foods, overeating, poor exercise patterns, artificial lighting and over-medication to name a few.
Our dogs have somewhat less complicated lives than we do and, as scavengers, have an amazing range of feed substances which they can make use of. I do think plastic bones and woody weeks is pushing it though.

Our canine companions 'modern diet' and subverted exercise patterns are the two major factors in the increase of Canine Cancers.

Healthy Natural Diet

My friend, Veterinary Surgeon Dr Ian Billinghurst, has produced two simple and practical books, which have made his peers a little uncomfortable. These books are entitled respectively "Give Your Dog A Bone" and "Grow Your Pups with Bones". They are both based around what he calls the B.A.R.F. diet, which is an acronym for Bones and Raw Food.
I really have nothing much to add to his contentions that commercial dog food along with subverted exercise patterns in our modern dogs lives, is almost completely responsible for the decline in Canine health since the 1930's. This includes increasing incidence of Reproductive and Skeletal problems along with Cancers, Heart and Kidney problems, Arthritis, shortening life spans, poorer health and life quality generally. I can strongly recommend his books to you.

As a Herbalist, I endorse the simple and very practical approach to life that states we were designed within our environment and for the demands of surviving within it. Any time we subvert the support systems built into this environment, we run risks. Mankind, in the second half of the 20th Century, has embarked on a massive and unrestrained experiment in the subversion of almost all aspects of his environment, diet and support systems and is beginning to pay the price. In this experiment he has taken with him his faithful friend the Dog, who is now also now paying the price for all this foolishness.

Become familiar with, and practice the Bones and Raw Food principles of feeding. Re-establish biologically appropriate exercise patterns and see your puppies grow free of reproductive and skeletal problems and your ailing adult dogs, return to good health.

In his books, Ian suggests a combination of commercial and natural sources of supplements and nutrients along with bones, meat, offal, and a variety of vegetables and grains. I certainly agree with his recommendations regarding Eggs, Garlic and Honey for example and his raw lean meat and vegetable patty recipes. My suggestions below are to be seen as a herbalist's perspective on the same requirements, only really differing in the preference toward natural sources and in the more detailed understanding of the medicinal value of plants and grains as opposed to simply their nutritional value.

As a Herbalist, I don't see the need for a lot of commercial mineral and vitamin supplements. I suggest that natural sources of such things are preferable, usually cheaper, and more easily assimilated than the commercial variety.

Let us consider some of the Vitamins and Minerals one at a time.

Vitamin A: Is found in Eggs, Fish Oil, Carrots and Leafy Green Vegetables and is therefore much better fed as such, rather than as processed supplements.

Vitamin B: Is found in all grains, and the idea of giving Vitamin B supplements to animals which have grain in their diet is complete nonsense. Vitamin B12 is a specific cancer preventative and is best found in the herb Comfrey. This can be included occasionally and in small quantities in a green feed as a valuable supplement.

Bioflavinoids: Can be supplied with a little Buckwheat to provide Rutin especially for healthy blood vessels.

Calcium and Silica: Are found in Bones, Cereals and Leafy Greens. I contend that diets high in dairy food and calcium supplements are inappropriate and detrimental for pups and for adult dogs. This mostly because the balance between Calcium , other minerals and fat found in cows milk, while suitable to growing calves, is not suitable for dogs.

Carbohydrates: The specific cereals I strongly recommend be included in all dog diets are freshly

ground Millet and Linseed to which can be added some Buckwheat and fresh Wheat

Germ. All grains are high in carbohydrates and the Calcium:Silica balance found in Millet and Linseed is absolutely perfect for the growth, health and strength of bones and for the elasticity of ligaments. Buckwheat is high in Rutin and Wheat Germ in Vitamins E and B. In other words this simple cereal combination does it all.

Vitamin C: Is found in fresh greens in abundance. At times of illness, shock or unusual physical stress, a few Rosehips Tea Bags steeped in boiling water and allowed to cool will provide massive extra amounts of Vitamin C and Iron to aid in recovery from such an episode.

Choline: Is found in bitter vegetables and the leaves of Dandelions and is critical for effective liver function. A dandelion leaf can be included sometimes in the vegetable component of the raw food diet. Otherwise let a few dandelions and other weeds and grasses grow around the yard and watch your dog seek them out for liver support, occasionally.

Vitamin D: Is synthesised by the action of Sunlight on Skin and found in Fish Oils. Not needed so much for the working dog living outside, but could well be important for the house pet waiting inside all day for its owners return. Cod Liver Oil provides the entire
Vitamin A and D requirement.

Vitamin E: Is found in fresh wheat germ along with the whole range of Vitamin B's and is the commercial source of both E's and B's. A little fresh wheat germ included with the cereal components of the raw food diet is all that is required. Anything more expensive or more processed is a nonsense.

Iron: Is found in Meat, Wheat Germ and in Green Vegetables especially Parsley and Nettle. Dogs being fed raw meat will never need Iron supplements.

Trace Elements: Are all found in Kelp.

It all boils down to Meat, Offal and Bones, Eggs, Millet and Linseed, Green and Root Vegetables, Wheat Germ, Cod Liver Oil, Kelp and a small amount of table scraps. To this I would add Garlic as a protection against infection and a sulphur source, the odd weed like Dandelion and Comfrey and the odd exposure to Rosehips.

My Treatment Approach:

I base my treatments around the twin approach of providing the extraordinarily powerful antioxidant properties from the Maritime Pine Bark in extract form, along with a combination of other herbal ingredients in support of the immune systems' particular area of weakness.

The whole thrust of my treatment programs is to assist the body to reverse the process of cancer altogether and to act as both support and stand-alone treatment.

In addition to cancer specific formulations, I have developed mixtures supporting recovery from surgery and for recovery and damage minimisation from radio and chemotherapy protocols.

Many dog owners and their Vets, prefer to retain some aspects of their orthodox treatments whether it be surgery and/or radio or chemotherapy. There is no conflict in combining orthodox and herbal treatment programs although, after I have demonstrated a remission or a reversal, I strongly recommend ceasing ongoing or follow-up chemo or radiotherapy, as these treatments are so destructive to the immune system itself.

My experience with treating Canine Osteosarcoma and after following up on each individual case over the past 5 or 6 years is, that I expect to produce remission conditions often for many months with the absence of pain and a return of vitality. Dogs seem to respond quickly to these programs are remain able to sustain this improved life quality for 6 to 12 months or more in most cases. Quite often

then, they seem to deteriorate rapidly although I do have a significant number of cases, which appear to have been totally cured.

My success rate in treating Canine Lymphoma appears so far, to be better than for the Osteosarcoma program. This is probably due to two factors;

Firstly; the cell replacement rate in soft tissue and the lymphatic system within the body is much faster than it is in bone tissue, thereby allowing a more rapid response within the body.
·Secondly; unlike with my human patients, I am able to stimulate the lymphatic system and clear toxins more aggressively with my canine patients. The risk in humans is that being so aggressive could spread the cancer cells more widely in the early part of the treatment. This runs the risk of my being held legally responsible for a worsening of the prognosis in some instances. My canine patients seem to be able to cope with the more aggressive lymphatic tonics.

The Herbal Prescriptions:

Bone Growth, Bone Healing:

Along with the dietary recommendations made above, and especially the inclusion of Millet and Linseed in the daily diet, the herbal stimulants to healthy bone growth and healing are Comfrey, Equisetum, Nettle and Yarrow. With these I include the Bach Flower essence Oak.

Lymphoma Treatment Support:

Besides the Maritime Pine Bark extract the herbs I include in this treatment include Bladderack, Comfrey, Equisetum, Golden Seal, Parsley, Rosehips and Violet Leaves. With these I include the Bach Flower essences Oak, Olive, Pine, Water Violet, Walnut and Wild Oat.

Osteosarcoma Treatment Support:

Besides the Maritime Pine Bark extract the herbs I include in this treatment include Bladderack, Comfrey, Equisetum, Golden Seal, Parsley, Rosehips and Yarrow. With these I include the Bach Flower essences Oak, Olive, Pine, Water Violet, Walnut and Wild Oat.

Chemotherapy Support:

This combination seeks to minimise the damage done to the organs and systems in the body including the liver, pancreas, thyroid and the digestive and immune systems generally. Herbs I include are Chamomile, St Mary's Thistle, Alfalfa, Rosehips, Thuja, Parsley, Fennel, Blue Flag, Ginger and Liquorice. With these I include the Bach Flower essences Rescue Remedy, Walnut, Wild Oat, Scleranthus and Honeysuckle.

Radiotherapy Support:

This combination seeks to minimise the damage and impact of the radiation both during treatment and during the 3 months following treatment where damage continues to occur. Herbs I include are Comfrey, St Mary's Thistle, Kelp, Yarrow, Thuja, Fennel and Sage. With these I include the Bach Flower essences Olive, Scleranthus, Gorse, Holly and Wild Oat.

Too much of a Good Thing!

In my experience with Canine Cancer I have come across the most extraordinarily patient and accommodating dogs who are submitting themselves to the most complex and onerous treatment regimens by their owners.

These owners are the ones who are the most desperately attached to and concerned for their dogs. They implement programs, consisting of every single thing ever recommended for treating cancer which they read or are told about or which they found on the Internet. These elaborate treatment programs they sometimes list to me in exhaustive detail. More is not better. Your dog is only submitting to all this stuff only out of its love for you and its desire to ease your anxiety.

My advice is to institute immediately the B.A.R.F diet possibly modified as per my discussion on natural sources of vitamins above. Then settle on, and persist with, a simple program of immune system and antioxidant support along with other programs addressed to the specific type of cancer and to the health and treatment history overall.

Then enjoy, and let your pet enjoy, the health and improvement that flow from this. Don't give your dog any "treats" other than raw meaty bones and space to run freely in.

Keep the whole program going forever, even if recovery seems to be complete. Allowing bad habits to creep back, usually precedes dropping out of remission.

Courtesy of Robert McDowell

http://www.herbal-treatments.com.au

Glossary of Terms:

Adjuvant chemotherapy : Adjuvant chemotherapy describes the use of systemic chemotherapy following the control of the primary tumor using other modalities (i.e. surgery or radiation therapy)

Alopecia : Hair loss.

Alkylating Agents: An antineoplastic agent that forms highly reactive intermediate compounds that are able to transfer alkyl groups to DNA.

Analgesic: Any drug or technique that relieves pain.

Anaplasia : A description applied to cells or tissues from a cancer when they no longer resemble, in cell appearance or architecture, the tissue from which they originated.

Anaplastic: Used interchangeably with anaplasia.

Anemia: Decreased number of red blood cells. It can be a side effect of chemotherapy.

Angiogenesis: Formation of new blood vessels.

Anoxeria: The loss of appetite. Not eating.

Antagonists: Substance that completely or partially inhibits or reverses the effect of another substance.

Antiemetic: A drug that prevents or controls nausea and vomiting.

Antineoplastic agent: A drug that prevents, kills, or blocks the growth and spread of cancer cells.

Apoptosis: Programmed cell death.

Aspiration: Process of removing fluid or tissue from a specific area. Can also be known as a fine needle aspiration.

Benign : A term used to refer to tumors that are slow growing and do not spread throughout the body. Benign tumors are "well-differentiated," meaning that the tumor cells differ only slightly in appearance and behavior from their tissue of origin.

Biochemical panel : A battery of tests that are done on blood serum or plasma; these tests are used to evaluate function of such organs as liver and kidney, and to measure proteins and enzymes found in the blood.

B-Cells: Special B cells produce specific antibodies, proteins that help destroy foreign substances.

Biopsy: A diagnostic procedure involving the removal of a small piece of tissue for microscopic examination or testing. It is necessary to definitely identify the type of cell involved in a tumor. There are a variety of biopsy techniques: needle biopsy (for soft tissue tumors); skin punch biopsy ;(for skin and superficial soft tissue tumors); crocodile action "grav" biopsy forceps (for respiratory, GI and urogential tracts tumors); incisional; and excisional.

Biotherapy: Refers to a diverse group of therapeutic strategies for cancers. It is a treatment modality based on products of the cancer, products of the host response against the cancer, and products of the interaction between the cancer and the host.

Blast Cells: Immature white blood cells

Blood Count: The number of red blood cells, white blood cells, and platelets in a sample of blood. Also referred to as a CBC. (complete blood count)

Bone Marrow : A spongy tissue contained within the center of most of the bones of the skeleton. This is the site where neutrophils, platelets, and red blood cells are produced.

Bone Marrow Aspirate: The procedure by which a needle is inserted into a bone to withdraw a sample of the bone marrow.

Bone Marrow Suppression: A decrease in the production or number of blood cells. This decrease may affect any or all of the components of blood.

Bone Scan: A picture of the bones that shows bone damage from cancer, injury or other disease.

Cachexia of cancer : Is a syndrome where metabolic alterations in carbohydrate, lipid and protein metabolism (tumor induced), lead to loss of energy despite adequate energy intake This problem is significant as many times it is compounded by anorexia.

Carcinogen : Cancer-causing agents that affect the DNA and RNA of cells, leading to uncontrolled growth of these cells and tumor formation. For example, second-hand smoke is now known to be an environmental carcinogen. Back to Top

Chemotherapy Resistance : A tumor's lack of responsiveness to some or all chemotherapy drugs.

CBC : The complete blood count (CBC) determines the number of red blood cells (RBCs), white blood cells (WBCs), the total amount of hemoglobin in the blood, and the fraction of the blood composed of cells (hematocrit). Sometimes the platelet count is included in the CBC.

Clinical Trial: A clinical trial is a drug study to find out whether a medication is safe and effective to use against various disease.

Cycle: A series of chemotherapy drugs that are given at regular intervals to treat a particular cancer

Cytokines: Chemical messengers secreted by cells.

Cytological Analysis: Collection of cells from a tumor

Cytotoxicity : Describes the killing ability of cancer cells for a given drug

Dendritic Cells: Cells that hand-off antigen information to T-cells and stimulate their proliferation.

Differentiated :(or well Differentiated Cells): Cells that resemble the organ where they came from (liver from liver, stomach from stomach, etc.)

Drug Resistance: Refers to the condition where cancer cells have developed an ability to prevent being killed by anti-cancer drugs.

Effusion:

Epithelial cells: Cells that form the outer surface of the body, line the body cavities and form the glandular tissue of the body. Cancers that arise from epithelial cells are referred to as carcinomas.

Erythrocytes : Cells in the blood that bring oxygen to tissues and take carbon dioxide from them. Also known as red blood cells.

Extravasation: Refers to leaking of injectable antineoplastic agents into tissue surrounding the infusion site and it causing irritation to necrosis and often times tissue sloughing. If the drug It is necessary to immediately stop the infusion and apply moderate heat to disperse the drug (since it is rapidly absorbed to tissues). Sometimes an injection of hyaluronidase is administered to disperse the drug.

Excisional biopsy : A surgical procedure that is performed in an attempt to remove the entire tumor and, if possible, surrounding normal tissue.

Free Radical : Atom which carries an unpaired electron; free radicals can potentially injure cells and may be responsible for numerous age-related diseases.

G 0 phase: In the cell cycle, the Go is the dormant phase. This is the "time" in which dormant tumor cells can escape the effects of drug therapy.

G1 phase: (gap 1) In the cell cycle, the period of RNA and protein synthesis

Gastrointestinal Distress: The digestive system, which includes the mouth, esophagus, stomach, small intestine, colon, and rectum. Most of the cells lining the gastrointestinal tract divide more rapidly than most of the other types of tissue in the body. Because chemotherapy damages rapidly dividing cells, gastrointestinal side effects like nausea, vomiting, and diarrhea are common.
Hematocrit (Hct): Percentage of red blood cells in the blood. A low hematocrit indicates anemia.

Hematogenous metastasis : Hematogenous metastasis involves tumor cells entering blood vessels and being carried in the blood to distant sites.

Histology: A collection of tissue from the tumor.

Hypercalcemia: Excessive blood calcium levels. It is most commonly associated with lymphoma, adenocarcinoma, and other solid tumors.

Hypoglycemia: A condition that occurs when blood levels of glucose drop too low to fuel the body's activity. It is commonly associated with hepatic and large intra-abdominal tumors.

Immunotherapy : One of the categories under Biotherapy. Please refer to write-up on
Biotherapy for a detailed explanation of this novel form of treating cancer.

Incisional biopsy : A surgical procedure that removes a small piece of a tumor (this will be reviewed by a pathologist)

Induction chemotherapy: Refers to the use of drug therapy as the primary treatment of patients with advanced cancer or for which no other treatment options exist.

Infusion: Delivery of fluids and/or medications into the bloodstream over a period of time.

Intergumentary System: The skin and its appendages together.

Intramuscular (IM) : Administered into a muscle.

Intravenous (IV): Administered into a vein.

Killing Granules: Tiny packets of cancer cell killing materials made inside white blood cells.

Laparoscopy : A diagnostic procedure in which a fiber-optic tube is inserted into the abdominal cavity to visualize organs such as liver and spleen. If an abnormality is noted, it is often possible to collect biopsies from the tissue, using a biopsy instrument inserted into a chamber in the laparoscopic tube. Back to Top

Lesion: A lump or abscess.

Leukopenia: A low number of white blood cells.

Lumpectomy: Removal of a mass without resecting substantial amount of tissue.

Lymphatic system: A network that serves as a filtering system for the blood. The lymphatic system includes lymph nodes, lymph, and lymph vessels.

Lymph nodes: Tissue located in localized areas. Lymph nodes act as the first line of defense against infections and cancer.

Lymphocytes: White blood cells that kill viruses and defend against the invasion of foreign material

M phase: Cell cycle that begins with mitosis and ends with cytokinesis.

Macrophage: Macrophages are leukocytes (white blood cells) which are present in all tissues of the body. Macrophages develop from bone marrow

precursors which mature and enter the bloodstream as monocytes.

Magnetic Resonance Imaging: (MRI) A test providing in-depth 3-D images of organs and structures in the body using magnetic energy.

Malignant or malignancy : A term used to describe a cancer that generally grows rapidly and is capable of spreading throughout the body.

Mesenchymal Tissues: Tissues that are connective, blood and blood vessels. Lymphatic. Cancers that arise from mesenchymal tissues are referred to as sarcomas.

Metastasis : A site of tumor spread, it may be within a lymph node or also at a distant organ from the location of the original tumor. Two ways in which cancers can spread are either through the blood vessels of by the lymphatics. (lymph channels)

Metastatic: Term used to describe cells or a tumor that is capable of metastasizing (spreading). Up to 90 - 99% of tumor cells that gain access to the bloodstream die

Monocyte: White blood cell formed in the bone marrow.

Myelosuppression : Lack of production of white blood cells, red blood cells, and platelets in the bone marrow. (may be a side effect of chemotherapy)

Nadir : The lowest blood cell count caused by chemotherapy treatment.

Neoadjuvant Chemotherapy: Use of chemotherapy as initial treatment of a cancer that is localized and for which other definitive treatment options are available.

Neoplasia (plural) : Any new and abnormal growth; specifically a new growth of tissue in which the growth is uncontrolled and progressive . Malignant neoplasms are distinguished from benign in that the former show a greater degree of anaplasia and have the properties of invasion and metastasis.

Neutropenia : A low neutrophil count.

Neutrophil : White blood cells that are produced in the bone marrow and fight bacterial infection throughout the body.

Nitrogen Mustards: The most common subgroup of alkylating agents. Cyclophosphamide chlorambucil, melphalan are nitrogen mustards.

"-Oma" : A suffix used to identify a tumor, usually benign.

Oncologist : A medical specialist who practices in the study and treatment of cancer.

Palliative : A treatment/medication that is intended to decrease clinical signs.

Partial Remission: Partial remission refers to the situation in which a tumor decreases in size by 50% or more.

Platelets: Blood cells that are produced in the bone marrow.

Pathology Report: Conclusions drawn after the examination of tissue and body fluids under a microscope.

Pleural Tap: See Thoracentesis.

Polydipsia: Excessive thirst.

Polyuria: This is the formation and excretion of a large volume of urine.. It could be an indication of high blood calcium (sometimes associated with lymphoma)

Polyp: A growth of tissue protruding into a body cavity. It may be benign and rarely malignant.

Poorly Differentiated : Cells whose internal architecture no longer resemble the original

organ/structure from where they originated. (liver, stomach, lung, etc)

Primary Tumor : The neoplasm at the site at which the first tumor cells began to grow.

Prognosis: The projected outcome of a disease

Protocol : Refers to the specific regime of antineoplastic agents that are administered in various combinations, dosages and timing.

Radiotherapy. Radiation treatments.
Forms of Radiotherapy:
Brachytherapy: A form of radiotherapy in which the source of radiation is applied in or on the patient in one prolonged dose, using surface applicators, needles, seeds or suspensions for use in serous cavities.,

Electron: A negatively charged sub atomic particle arranged in orbits around the nucleus of an atom.

Gamma (g) Rays: High energy electromagnetic radiation emitted from the nucleus of a radioactive materiall. Gamma ray emission is one means by which an unstable atomic nuclei lowers its energy state.

Systemic radionuclide therapy: A form of radiotherapy in which the source of radiation is administered directly into the patient. Methods of delivery include oral administration and subcutaneous or intravenous routes.

Teletherapy: A form of radiotherapy in which the source of radiation is applied from a distance from the body.

Recurrence :The reappearance of cancer cells at the same site or in another location after a disease-free period.

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S phase: The phase in the cell cycle where DNA synthesis occurs.

Sigmoid curve: This curve can be defined between the dose administered and the effect, such as percentage of cells killed.

Staging : An assessment of the extent of the tumor.

Clinical staging systems are standard for each form of cancer and are proposed by the World Health Organization (WHO). For solid tumors there are usually three categories: "T" denoting tumor size; "N" denoting invasion of regional lymph nodes; and "M" for the presence or absence of distant metastases. Results from these categories then lead to a division of the disease into four clinical stages. Stage I, II, or III indicate local disease, local disease with some regional spread, or local disease with more extensive regional spread, respectively. Stage IV includes stage I-III with distant sites of metastases. Usually, prognosis becomes less favorable with advancing stage.

This procedure is necessary to assess the prognosis and to select a course of therapy that will provide the best outcome in terms of disease remission and quality-of-life.

Subcutaneous (SQ) : Administered under the skin.

Surface TNF : TNF which has migrated to the surface of white blood cells in preparation to kill cancer cells.

Systemic Disease: A disease that affects the whole body.

T-cells: White blood cells that attack invading cells or organisms. T-cells attack virus-infected cells, foreign tissue, and cancer cells. They also produce a number of substances that regulate the immune response.

Therapeutic index: Refers to the ratio of the toxic dose to the effective antitumor dose

Thrombocytopenia : A lack of functioning platelets. Platelets are necessary for normal blood clotting. In addition, platelets clump together to repair small holes in damaged vessels

TNF : Tumor Necrosis Factor, a protein made by immune system cells, to kill cancer cells.
TNF is made inside white blood cells and migrates to the surface of white blood cells.
White blood cells surround the cancer cell and TNF attacks the cancer cell (TNF actually pokes holes in the cancer cell) to kill it.

TNM: Denotes areas of involvement of a tumor while staging. T refers to the Tumor. A T1 tumor is small and not invasive. A T4 tumor is large and invasive. N refers to the Lymph nodes. N0 is a lymph node that is not involved with tumor, N1 is a freely moveable lymph node that is involved by the tumor and N3 is a non-moveable lymph node that is involved by the tumor. M refers to distant Metastasis. M0 means there is no metastasis and M1 means there is distant metastasis.

Tumor: An abnormal overgrowth of cells. Tumors can either be malignant or benign.

Tumor Markers: Cancer cells often produce molecules that are not produced by normal cells. Detection of these molecules within the body may be indicative of the presence of cancer. These molecules are referred to as tumor markers. The following are some tumor markers that have demonstrated an association with some canine cancers:

Skin Cancer : * Ki67; Mammary Cancer: c-kit proto-oncogene, MAb 1A10 (mammary cancer antibody); MAb SB2 (mammary cancer antibody); Type IX collagen

Lymphoma : * AgNOR, Plasma thymidine kinase, CCI-103F (nitroimidazole hypoxia marker); CD3 (T-cell lymphoma antibody); CD79a (B-cell lymphoma antibody)
Oropharyngeal Cancer (Mouth Cancer) ; BrdU labeling index; Pancreatic Cancer

Chromogranin A plasma concentration; Bladder Cancer : Basic fibroblast growth factor urine concentration; Other Solid Tumors: CCI-103F (nitromidazole hypoxia marker)
In addition to detection and diagnosis of malignant tumors, tumor markers may provide information on: prognosis (some markers indicate the degree of invasiveness of the cancer); staging (some markers provide an indication of how much the disease has spread); and monitoring (some markers indicate treatment efficacy or recurrence of disease following treatment).

Venipuncture: A procedure where a needle is inseted in a vain in order to either obtain a blood sample; to start an intravenous drip or to give administer medication.

Vesicant: An intravenous medication that, if leaked into tissues, could cause pain, swelling, tissue damage, and destruction. It can be a rare side effect on chemotherapy.

White blood cells (WBC): General term for a variety of cells responsible for fighting invading germs. Specific white blood cells include granulocytes and lymphocytes.

White blood count (WBC): The actual number of white blood cells seen in a blood sample.

The definitions used in this glossary either have been provided by the authors of the articles, or have been extracted wholly or in part, or paraphrased from the following sources: Dorland's Illustrated Medical Dictionary, 28th Edition, W. B. Saunders Company, Philadelphia, 1994; The Random House Dictionary of the English Language, Unabridged Edition, 1966; Webster's Ninth New Collegiate Dictionary, 1991; Yahoo.com medical search engine.

References:

Adams, W.M., S.J., Walshaw, R. et al. (1987) Radiotherapy of malignant nasal tumors in 67 dogs. Journal of the AmericanVeterinary Medical Association, (191), 311-15.

Christenson, Dawn E. Veterinary Medical Terminology, W. B. Saunders, 1997.

MacEwen, E.G., Withrow, S.J., & Patnaik, .K. (1977) Nasal Tumors of the dog: retrospective evaluation of diagnosis, prognosis and treaatment. Journal of the American Veterinary Association, (179), 45-8.

Merck Veterinary Manual, 8th Edition. Merck & Co., Inc. Whitehouse Station, NJ, USA in cooperation with Merial Limited, A Merck and Rhone-Poulenc Company.

Nelson Richard., Couto Guillermo C., Essentials of Small Animal Internal Medicine, Mosby Year Bookm 1992.

Ogilvie, G.K. Moore, A.S. (1995) Managing the Veterinary Cancer Patient (A Practice Manual).

Veterinary Learning Systems Co., Inc. Trenton, New Jersey.Hahn, K. & Owen, L.N. (1980) TNM Classification of Tumors in Domestic Animals. World Health Organization. Genera.

Richardson, R.C. (ed.) (1995) Cancer Chemotherapy: A Veterinary Handbook. Williams & Wilkins, Pennsylvania.

Sorenmo, Karin, Jeglum KA, Helfand S. Chemotherapy of Canine Hemangiosarcoma with Doxorubicin and Cyclophosphamide. J Vet Intern Med, 1993; 7 (6), 370-376.

Morris, Joanna & Dobson, Jane. Small Animal Oncology. Blackwell Sciences Ltd., Malden, MA, USA.

Saunders Manual of Small Animal Practice, Stephen J. Birchard, DVM, Robert G. Sherding, DVM, W. B. Saunders, 1st edition, 1994

Sorenmo, CMV, DACVIM; Frances Shofer, PhD. Goldschimdt,Michael, BVMS, DACVP; Survival in dogs with malignant mammary gland epithelial tumors, effect of spaying and timing of spaying. J Vet Intern Med, 2000;14:266-270

Sorenmo, Karin CMV, Lili Duda VMD, Lisa Barber DVM, Kim Cronin DVM, Carl Sammarco BVSc, Amy Usborne DVM, Michael Goldschmidt BVMS, Frances Shofer PhD, Canine hemangiosarcoma treated with standard chemotherapy and minocycline. J Vet Intern Med, 2000;14:395-398.

Withrow, S.J. & MacEwen, E.G. (1996) Small Animal Clinical Oncology, 2nd edn. J.B. Lippincott Company, Philadelphia.